HEALTH RISK ASSESSMENT IN THE WORKPLACE

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1 INTRODUCTION

1.1 Scope and Objectives

The practice of assessing risks of exposures to support decisions is a relatively recent development. Until the twentieth century, diseases had been observed to be associated with specific occupations, living conditions, and work-related hazards. However, these observations were qualitative. In addition, the focus on public health was predominantly associated with concerns about infectious disease until about the mid-twentieth century.

The quantification of risks took hold in the 1970s for the following reasons – shift from a high incidence of infectious disease to concerns about chronic disease; a new awareness of the risks resulting from exposures to work-related hazards; and scientific and technological advances such as chemical analysis, toxicity testing, epidemiology, and computers.

This chapter recounts the history and evolution of human health risk assessment, tracing the development of tools and models that made it possible, as well as the factors in society that made it indispensable. It defines the practice of risk assessment today, taking the reader through hazard and exposure analysis, risk characterization, the management of risk, and the public's reaction to risk.

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1.2 Basic Definitions

In the context of controlling environmental and occupational exposures to work-related hazards, *risk assessment* is the art and science of examining all relevant data about a hazard – its toxicity, environmental fate, routes of exposure, epidemiology, etc. – and characterizing its potential adverse effects on humans and/or the environment. The value of risk assessment is that it provides pertinent information to risk managers, business leaders, health practitioners, policymakers, and regulators in helping set priorities and make decisions.

Risk management is the process of evaluating various options and selecting among them. Risk management is discussed in detail in Section 6.

At its simplest, *hazard* may be defined as threat of harm to a resource of value. It is important to note that *hazard* and *toxicity* are not the same. *Toxicity* is an inherent property of a chemical, whereas the *hazard* presented by a chemical includes not just its toxicity but also the ease with which humans or animals can come into contact with the chemical.

When a substance is extremely toxic, it takes only a small amount to cause harm, whereas greater amounts are needed for less toxic substances.

Risk, refers to the probability (statistical chance) that harm, injury, or loss will occur.

Epidemiology is the study of patterns of disease in human populations and the investigation of the factors that affect these patterns. The discovery of an association between smoking and lung cancer is an example of a pattern discovered by epidemiology. Epidemiology is used to define the probability that certain effects are the result of specific causes.

2 HISTORY OF RISK

2.1 Risk Assessment – History and Evolution

2.1.1 3200 BC – Decision-Making Using Signs from the Gods

The first recorded instance of risk analysis was in about 3200 BC in the Tigris–Euphrates Valley. A priest-like group called the *Asipu* was consulted when risky, uncertain, or difficult decisions were to be made. The data were signs from the gods and, after weighing favorable vs. unfavorable signs, would issue an analysis, recommending the most favorable alternative for the client.

2.1.2 Fifth Century BC to the Middle Ages – Early Observations of the Environment and Its Effects

One of the earliest examples of anyone observing a connection between environmental conditions and human health was Hippocrates in about the fifth or fourth century BC when he made the association between malaria and swamps. Sometimes observations led to action – for example, in the first century BC, the Greeks and Romans observed the adverse effects of exposure to lead fume produced during casting and extrapolated this knowledge to recommending that water not be transported in lead pipes. In the Middle Ages, concern about coal smoke in London prompted King Edward I to commission a study of the issue. In 1306, he issued a royal proclamation prohibiting the use of soft coal in kilns.

2.1.3 Sixteenth to Nineteenth Centuries – Occupational Hazards – Qualitative Observations

Agricola, Evelyn, Ramazzini, Pott, and Snow made observations that linked adverse health effects to pollution, occupations, lifestyles, and living conditions. The major obstacles to finding the root causative agents and quantifying the strength of observed associations were several and included – lack of knowledge about biological, chemical, and physical processes; lack of instrumentation; and lack of rigorous observational and experimental techniques.

2.1.4 Early Twentieth Century to the 1970s – Setting Limits and "Safe" Levels – The Beginnings of Quantification

Assessment of risks associated with chemicals developed along with the industrial revolution. The chemical industry and the industrial revolution were intimately related. Two of the main branches of modern chemistry were industrial (dye and explosives) and agricultural. Dye manufacturing began in England in the mid-1800s and quickly led to industrial competition between Great Britain and Germany. Although the American industry was developing during the nineteenth century and before the Great War, the initial emphasis of EI DuPont was on the manufacture of gunpowder. In the agricultural area, President Lincoln appointed the first chemist, Charles Wetherill, to the Bureau of Chemistry at the Department of Agriculture in 1862. Twenty years later, in 1883, Dr. Harvey Wiley was appointed chief chemist in the Bureau of Chemistry and began campaigning for legislation that would protect consumers from tainted or adulterated food and drugs. In 1906, the Food and Drug Act prohibited interstate commerce in misbranded and adulterated foods and drugs (1).

In 1937, between 73 and 107 people, most of them children, died from taking Elixir of Sulfanilamide (1, 2). The elixir was touted as an antimicrobial but contained diethylene glycol. As a result of this disaster, the Food and Drug Act of 1938 was passed. This act required drugs to be safe before marketing, initiated the use of safe tolerance for unavoidable poisonous substances, and authorized factory inspections (1). This Act was the first US regulation to require toxicity testing in animals (2).

The Federal Insecticides, Fungicide, and Rodenticide Act (FIFRA) was passed in 1947 and gave the Department of Agriculture authority to regulate pesticides. This authority was transferred to the USEPA in 1972.

In 1954, safety limits for pesticide residues were developed based on safety factors (3). In 1958, the Food Additive Amendment (1958) prohibited the use of any food additive that was associated with cancer development in either humans or animals, referred to as the Delaney Amendment. The Food Additive Amendment of 1958 exempted about 200 chemicals already in use at the time of the legislation and classified them as generally recognized as safe (GRAS). As a result of the phthalidomide scandal, Congress passed the Kefauver–Harris Amendment in 1962 that required pharmaceutical companies to demonstrate the effectiveness of a product before marketing it and to obtain informed consent from patients taking unapproved drugs. In 1983, Dourson and Stara, referenced a 1954 article by Lehman and Fitzhugh, who suggested that the amount of additives or contaminants allowed should be derived from a chronic animal no observed effect level (NOEL) or no observed adverse effect

level (NOAEL) (measured in mg kg^{-1} of diet) by dividing by a 100-fold uncertainty factor (UF) (4).

These 100 years of food safety regulations set the stage for many of the occupational and environmental health regulations. For example, Toxic Substances Control Act (TSCA) exempted thousands of industrial chemicals already in use in 1976; Occupational Safety and Health Administration (OSHA) obtained the right of entry into American workplaces in exchange for forfeiting the right of employees to sue their employers; under the FIFRA of 1972, Environmental Protection Agency (EPA) could approve and register a pesticide even if it had been shown to significantly increase the incidence of cancer if the economic benefits outweigh the risk (5).

Increasing concern about the effects of chemicals on the health of workers, a strengthening labor movement, and advances in scientific method and analytical technology led to the impetus behind the setting of *workplace exposure limits*. In 1946, the American Conference of Governmental Industrial Hygienists (ACGIH) adopted its first list of exposure limits, then referred to as Maximum Allowable Concentrations (MACs) (6).

After World War II, more attention was directed to hazards posed by chemicals found in air, water, soil, and food. By the middle of the century (1950s), medical and societal achievements, such as antibiotics, vaccinations, and improved sanitation had significantly decreased the infectious disease threats such as cholera and tuberculosis. The 1950s also saw dramatic increases in the use of industrial chemicals and pesticides.

The focus on hazards posed by contaminants in the environment and in food led to an era of environmental reform in the 1960s and 1970s, spurred on by works such as Rachel Carson's book *Silent Spring*.

The Clean Water Act, Clean Air Act, the Occupational Safety and Health Act, Safe Drinking Water Act, and the Resource Conservation and Recovery Act (RCRA) are all products of the 1970s along with the creation of the EPA, the OSHA, and the Mine Safety and Health Administration (MSHA).

2.1.5 *Latter Twentieth Century to the Present – A Focus on Carcinogens and the Beginning of Modern Risk Assessment*

Cancer has historically been treated differently from noncancerous diseases such as pneumoconiosis, chronic obstructive pulmonary disease (COPD), asthma, and diabetes. The association of chemicals with cancer was recognized early by Potts and began to be examined scientifically in the twentieth century. By mid-century, the concept of some chemicals that promoted cancer and other chemicals which induced cancer had taken hold, giving rise to the multistep theory of cancer development. By the end of the century, it was recognized that cancer is not one disease but a collection of a variety of diseases and that certain chemicals are associated with particular tumors.

As more became known about carcinogenicity through animal testing, the Food and Drug Administration (FDA) increased the safety factor for carcinogens from 100 : 1 to 5000 : 1. By 1950, however, the FDA had concluded that no safety factor could be justified for a carcinogen because there was no scientific proof of a threshold level. Congress actually imposed the zero-tolerance level in something known as the "Delaney Amendment." The Delaney Amendment A provision in the US Food, Drug, and Cosmetic Act (1958) states that no food additive shall be deemed safe after it is found to induce cancer when ingested by human beings or animals, at any dose level.

In 1973, the FDA, using the mathematical models that scientists had first theorized about in the 1950s and 1960s, proposed the first regulation that required extrapolating from animal models to quantified human risk. *The FDA proposed using risk assessment.*

The EPA also used quantitative risk assessment in the early-to-mid-1970s, even though risk assessment per se was not yet a formally recognized process. The first EPA risk assessment document was completed in 1975: *Quantitative Risk Assessment for Community Exposure to Vinyl Chloride*. The preamble to a 1976 document outlined procedures and guidelines for health risk assessment, the EPA signaled its intent that "rigorous assessments of health risk and economic impact will be undertaken as part of the regulatory process." At this stage, EPA used a two-step approach to risk assessment: (i) Is the agent a likely human carcinogen? and (ii) If the agent is a likely human carcinogen, what is the expected public health impact?

While the FDA and the EPA voluntarily turned to risk assessment, other agencies were compelled to use it. In 1978, the OSHA tried to lower the Benzene Permissible Exposure Limit (PEL) from 10 parts per million (ppm) to 1 ppm. Since OSHA's cancer policy held that there was no safe level for carcinogens, OSHA based the new Benzene standard on a "lowest feasible level" policy. This was challenged in Court and was vacated because OSHA did not show significant risk.

In 1981, Executive Order 12291 was issued, requiring regulatory agencies to verify that "significant actions" involved benefits to society that outweighed their costs. This encouraged the use of risk assessment. *The Benzene Decision was an important impetus to the development of risk-assessment techniques.*

In 1983, the National Academy of Sciences (NAS) published a groundbreaking report titled *Risk Assessment in the Federal Government: Managing the Process* (National Research Council (NRC), commonly referred to as the "Red Book"). This publication was the first place that the risk assessment process was codified in a formal way. Agencies integrated risk assessment principles outlined in this report

into their practices. *By the mid-1980s, risk assessments were a consideration in virtually all decision-making involving the regulation of chemicals.*

2.1.5.1 Evolution of Models and Tools Leading up to the growth and establishment of risk assessment were several necessary advances:

- *Animal test species*: until the early 1900s, no uniform animal colonies were available, so animal testing was regarded as unreliable for human safety determinations. During the 1910s, scientists began to develop colonies of pure strains of rodents on which to conduct tests. As these strains became available, large-scale animal toxicity testing became feasible.
- *Quantification*: Reproducible animal testing and the use of statistics and untreated controls allowed for quantifiable studies rather than qualitative observations of human experience.
- *Inhalation chambers*: Developed and improved throughout the twentieth century, inhalation chambers permitted investigators to expose test subjects to consistent atmospheres of dusts, vapors, and gases. Consistent dosing regimens helped establish more reliable dose–response relationships.
- *Analytical techniques*: Detection methodology improved from a sensitivity in the range of 20–50 ppm in the 1950s to a measurement of parts per trillion and parts per quadrillion possibly today.

With the establishment of the National Toxicology Program (NTP) in 1978, the two-year chronic toxicology study became the gold standard for cancer experiments. These studies consist of four groups of 50 male and female mice and rats each: the control group and three treatment groups are exposed to three different dose levels. The doses given to the animals in this type of study are intentionally high, with the highest dose often resulting in systemic toxicity, because the researchers wanted to ensure that they would be able to observe measurable effects without using thousands of mice and rats.

There are six mathematical models that can each estimate effects at low doses by extrapolating from the experimentally recorded high doses: probit, multihit, multistage, Weibull, one-hit, and Moolgavkar-Knudson-Venzon (MKV) (7, 8). Crump (9) formulated a multistage model in which the upper 95% confidence interval on the dose is used for each of the steps in carcinogenesis to calculate the likely incidence of cancer. This model provides the most conservative estimate because the final probability is a multiple of the 95% upper confidence interval for each of the steps in carcinogenesis. These steps in carcinogenesis are four: tumor initiation, tumor promotion, malignant conversion, and tumor progression.

During the 1980s, several useful tools became available that helped standardize risk assessment practices and make them more accessible:

- The *personal computer* placed sophisticated modeling within the reach of virtually all scientists.
- A number of *handbooks and guidance documents* were published. The 1983 NAS "Red Book" outlined the risk assessment process.

With the requirement to use well-conducted quantitative risk assessments in defining regulatory standards, the scientific community continued to refine the models and science employed.

Improvements in the tools, models, analytical methods, and understanding of toxicology will continue to advance and refine the ability to characterize the risk from environmental and occupational exposures.

2.2 Road to Modern Risk Assessment

Table 1 summarizes the key characteristics and scientific outcomes during each era.

References not specifically cited thus far, but used to develop this section's history are listed as (10–22).

3 RISK ASSESSMENT

3.1 Hazard Identification

Hazard identification is a scientific, qualitative evaluation of all available toxicological, epidemiological, biological, and structural analogy data. In the context of human health, it has been explicitly defined elsewhere as:

"The process of determining whether *exposure* to an agent can cause an increase in the *incidence* of an adverse health condition." (23).

Its principal function is to identify the predominant type(s) of adverse health effects that a particular toxicant might produce as a result of human exposure. It is inclusive of all health endpoints from irritation to cancer and uses all toxicological information including sophisticated mechanistic work like physiologically based, pharmacokinetic (PB-PK) study. Governmental *hazard identification* often results in complex documents generated by contractors, refined by agency scientists, and ultimately reviewed by external scientific review committees, such as the USEPA Science Advisory Board (SAB).

Hazard identification sometimes results in a single summary classification of effect for a substance such as a cancer classification or reproductive toxicant classification; often such classifications are based upon a detailed review document that is comprehensive in scope.

TABLE 1 The road to modern risk assessment.

Era	Characteristics	Scientific result
Ancient times to Industrial Revolution (1900s)	• Human observation studies: – Observations of associations between jobs, lifestyle, and diseases. Early basis for current approach to human health risk assessment. – No uniform animal colonies available for testing – No statistics – No reproducibility – Not quantified • Increased industrialization and urbanization • 1850, London Epidemiological Society formed • 1882, Henle-Koch's postulates for infectious disease developed	• Judgmental safety evaluations • Focus on infectious disease
Early to mid-twentieth century	• Increased attention paid to workplace hazards and food safety • Use of qualitative risk assessment • Improvements in scientific methods: – Animal testing – colonies of rodents developed 1910–1919, allowing large scale animal toxicity testing – Epidemiology – emergence of chronic disease concept after WWII. Intensified debates on chronic disease causality using epidemiological data – Statistics – Reproducibility – Advancement of analytical methods • Dramatic increase in chemical production and use	• "Safety Factors" used to determine safe levels • First large scale animal toxicity testing • Workplace exposure limits first recommended • Early efforts in quantification of dose–response, exposure, risk • Shift from infectious disease focus to one on chronic disease
Mid-twentieth century to 1972	• Increased attention to environmental hazards • Findings that carcinogens have no threshold • Increasing analytical sensitivity • Continued improvements in epidemiology • 1964, US Surgeon General sponsored standards to address use of observational human data (HEW, 1964). Framework for epidemiological debates • 1965, Bradford Hill Criteria, expansion of earlier 1964 standards	• Period of environmental reform, new Agencies, and regulations • FDA: Safety factors abandoned for carcinogens in food: chemical bans based on limit of detection • Lowest feasible limits used by OSHA • First standards to address use of observational human data
1970s, early 1980s	• Mathematical modeling for low-dose extrapolation refined. EPA cancer principles and early use of quantitative risk assessment for low dose extrapolation • 1973, FDA proposed use of risk assessment. Actual use in 1976 to regulate carcinogenic animal drugs • Analytical sensitivity showed banning carcinogens in food infeasible • 1975, use of quantitative risk assessment in the United States and Canada • 1978, early CPSC use of quantitative risk assessment • Industry demanded proof of significance of risk • 1980, Benzene Decision, other court decisions required risk assessment to regulate "significant" risk • 1980, Society of Risk Analysis formed • 1981, Executive Order 12291, required Agencies to verify "insignificant actions" involving benefits to society that outweighed their costs • Continued improvements in epidemiology	Modern risk assessment: • Agencies began to quantitatively show that specified levels decrease risk • Use of quantitative risk assessment in the United States and Canada

(*continued overleaf*)

TABLE 1 *(continued)*

Era	Characteristics	Scientific result
1980s to present	• Continued refinement of modeling and scientific understanding • Emergence of computers, risk assessment guidance documents, and standardized risk assessment • 1983, risk assessment codified, National Academy of Science (NAS) report "Risk Assessment in the Federal Government: Managing the Process" • 1990, use of quantitative risk assessment in Europe, Australia, and Asia	• Increasingly sophisticated risk assessments • Risk assessment methods used to set standards for pesticide residues, food additives, drinking water guidelines, and ambient air standards, as well as exposure limits for contaminants found in the workplace, indoor air, consumer products, and other media • Use of quantitative risk assessment in Europe, Australia, and Asia

Source: Paustenbach (10); Alice Ottoboni (11); Paustenbach (12); Risk Assessment and Federal Policy, 1970–1990., Hutt, PB. Use of Quantitative Risk Assessment in Regulatory Decisionmaking under Federal Health and Safety Statutes; Hiatt, GFS. Risk Assessment lecture given April 26, 1988. Cassarett and Doull's Toxicology, 2nd Edition, edited by John Doull, Curtis D Klaassen, Mary O. Amdur, Macmillan Publishing Co, Inc., New York, 1980; Mausner and Kramer (17); National Research Council (NRC) (18); National Research Council (NRC) (19); Environmental Protection Agency (EPA) (20); Anderson (21).

3.2 Dose–Response Assessment

Once a health hazard has been identified, the next task is to estimate the *dose–response* relationship for that substance.

The traditional toxicological paradigm for noncarcinogens is to test animals (or in some cases humans) with continuously lower doses until a dose with no toxicological effect (or no effect that is statistically different from untreated controls) is found. This is the NOEL. The NOEL is then lowered (i.e. divided by "safety factors" or "UFs") to determine a "safe" level of exposure with presumably no risk. These "safe" levels are then forwarded as exposure limits or quantitative levels of allowable exposures for humans. The ACGIH threshold limit values (TLVs) for noncarcinogens are examples of this approach.

In the case of carcinogens, using low *dose–response* modeling presents a significantly different paradigm. If it is determined that the substance is genotoxic (i.e. capable of causing cancer by interacting with or altering the genome) then it is assumed that no threshold of effect exists. The available *dose–response* data are extrapolated to zero dose (with an assumed zero risk) and the dose at an estimated allowable level of risk is set as the exposure limit. For nonoccupational exposure, the allowable risk is often set at 1 in 1 000 000 lifetime risk of cancer using this methodology. For occupational carcinogens, the resulting exposure limit often occurs around a lifetime cancer risk of 1 in 10 000 to 1 in 1000 (24).

Especially in the case of carcinogens, the actual animal *dose–response* data occur at doses that are typically several orders of magnitude above the actual exposure that humans would be subjected to at their respective exposure limits. The model of choice for carcinogens by the regulatory community has been a linear extrapolation; however, like all models without data, it remains an untested hypothesis (25).

3.3 Exposure Assessment

Exposure assessment is simply the determination of the actual amount of a substance that comes in human contact. In the case of inhaling a toxicant, the following relationship has been used as a general operational definition: that is, as the product of (concentration) × (time) in the air that the person breathes over the period in which he or she breathes it (26):

$$\text{Exposure} = \int (\text{Concentration})\,(\text{time})\,dt$$

$$\text{dimensional units} = \text{mg}\ \text{m}^{-3} \cdot \text{h}]$$

The above equation indicates and allows that the airborne concentration of a toxicant in contact with the breathing zone of the human can vary over the time of exposure under consideration. For toxicants where acute exposures are critical, the length of this time integral is typically quite short, on the order of minutes or hours. For toxicants in which chronic exposure is more important, the time-integrated exposure can be an average daily exposure averaged over many days.

Seen in a more general sense, this equation reinforces the precept that it is the time-integrated average of toxicant contact over the time frame of interest that is the critical element of any exposure assessment. That is, all activity involved in the elucidation of this time-integrated exposure is exposure assessment.

Exposure assessment for any individual or population should include all the sources of a substance and all the routes of exposure (inhalation, dermal, and ingestion). Often, one source and route clearly dominates the exposure of a person or population.

Exposure is typically either measured or modeled (27). Ideally, these two critical tools (i.e. modeling and monitoring) should be employed to evaluate exposure (28).

3.4 Risk Characterization

Risk characterization is the combination of the inherent toxicity of the material with the estimate of the actual exposure. The following equations have been used to portray this process:

$$\text{Risk} = \left(\frac{\text{Probability of health effect}}{\text{Unit exposure}}\right) \times (\text{Level of exposure})$$

The first part of this relationship (probability of health effect/unit exposure) is the inherent toxicity or potency of the material. Exposure limits are purposely designed to integrate this relationship in a single number that is the reciprocal of this entity. Thus, if one assumes that an exposure limit embodies the reciprocal of the first half of this equation then it can be rewritten:

$$\text{Risk} = \text{HI} = \frac{\text{Level of exposure}}{\text{Exposure limit}}$$

This ratio is the classic hazard index (HI). Both numerator and dominator must be in the same units. Typical units are $mg\,kg^{-1}$, $mg\,m^{-3}$, and ppm. When the HI is less than 1.0, it indicates a risk characterized as "low" or of "no significance." An HI greater than 1.0 characterizes a risk that may be "unacceptable."

The careful reader will note that in this portrayal, the exposure limit and the level of exposure are assumed to be single deterministic numbers or values. This is indeed the case in many characterizations of risk; however, this is obviously not reflective of reality in which uncertainty in these values exist within each from either natural variability or a relative lack of information or knowledge. Uncertainty analysis, especially for the level of exposure output from the exposure assessment, dramatically increases the legitimacy and value of the risk characterizations by showing and gauging the range of the characterization. This analysis also points the way to areas of refinement that will reduce the uncertainty and increase the confidence in the risk characterization (29, 30).

3.5 Quantitative Health Risk Assessment – Strengths and Shortcomings

3.5.1 Strengths

Quantitative health risk assessment (QHRA) is a process which quantifies hazards and exposures so that measures of risk can be expressed and evaluated numerically. The strength of QHRA is that it provides an identified exposure level deemed to separate "safe" from "unsafe" conditions for people both occupationally and environmentally.

3.5.2 Weaknesses

Weaknesses of the QHRA can be characterized by (i) *scope* and (ii) the *separation of risk assessment from risk management*. The weaknesses grouped under scope encompass at least three aspects: the number of different chemicals introduced every year into the environment; the interaction of more than one toxicant within the recipient; and the effect of physiological states on the metabolism and toxicology of toxicants. This complexity highlights the weaknesses of QHRA.

3.5.2.1 SCOPE As regards *scope*, tens of thousands of new chemicals are manufactured every year. More than three thousand are manufactured or imported in amounts greater than 1 million pounds per year in the United States alone. At best, only a fraction of these have occupational and/or environmental exposure limits.

Use of *in vitro* techniques to analyze hundreds of toxicants at a time is emerging as a possible screening tool for the myriad chemicals that are introduced every year. This technique addresses the need to analyze a large number of toxicants but exacerbates the problem of relating the results to meaningful guidance in the establishment use of new and existing toxicants. The uncertainty introduced with *in vitro* methods may be greater than the uncertainty that already exists because *in vitro* methods totally exclude normal physiological processes that significantly affect, the health effects associated with exposure to toxicants.

QHRA has traditionally focused on one toxicant at a time. Most exposures, and certainly most environmental exposures, are not typically one or two individual toxicants, but a whole variety of chemicals and exposures.

3.5.2.2 SEPARATION OF RISK ASSESSMENT AND RISK MANAGEMENT The *separation of risk assessment from risk management* was initially proposed to remove politics from the development of exposure limits and provide a venue in which science could evaluate the dose–response curve without pressure from special interest groups.

Valid scientific data are open to interpretation. Ways to manipulate the statistical outcome of experimental data include meta-analyses and re-analyses. Meta-analysis is "a technique to obtain either a quantitative or qualitative synthesis of research literature on a specific topic or question (31)." Several studies are combined to provide a larger number of subjects. The increase in the number of subjects increases the sensitivity of the statistical methods employed, but it may also change the outcome depending on the results of the studies included in the meta-analysis. Re-analysis simply re-interprets the data. William Ruckelshaus, who served as the first and fifth Administrator of the EPA (32), suggested that "risk assessment data can be like a captured spy: if you torture it long enough it will tell you anything you want to know." The separation, however, has remained.

Another problem with the separation of risk assessment from risk management is that the question of why the chemical is being used in the first place is not routinely asked. Risk assessment evaluates only the toxicological data. Most chemical toxicants are produced to achieve a specific goal.

3.6 Unitary Risk vs. Integrated Risk

3.6.1 Types of Risk

Risk is ever present in our daily lives, as well as in public and private sector organizations (33). There are many types of risk including, among others, technological, financial, human resources (capacity, intellectual property), health, and safety. There are many sources of risk both external and internal. External risks include political, economic, and natural disasters, while internal risks include reputation, security, knowledge management, and information for decision-making. And finally, there are variations in our ability to control risk: *operational* – greatest control; *reputation* – moderate control; and *natural disasters* – least control (34, 35).

Furthermore, there are many definitions of risk. Each definition equates to some perception as to what constitutes "safe." The common theme in all risk definitions is "uncertainty" of outcomes. The difference between risk definitions resides in the type of outcomes. For the same set of circumstances, people and organizations often vary in their risk tolerance. When accurately assessed and managed, risk can lead to innovation and opportunity. Safe does not mean zero risk.[1]

In conventional industrial hygiene terminology, risk is often defined as the probability of an undesirable effect (related to some potential hazard) times the extent of its impact or consequence, Risk = Consequence × Likelihood (36).

Getting back to a technical understanding that risk as the calculation of the "probability of an undesirable effect" implies a quantitative or qualitative analysis. Risks can be thought of in two ways – *unitary risk or integrated (cumulative) risk.*

3.6.1.1 UNITARY RISK *Unitary risk* focuses on one aspect or impact of risk, such as workplace exposure to a single chemical.

3.6.1.2 INTEGRATED RISK *Integrated risk*, is sometimes thought of as cumulative risk or total exposure, and combines the processes of risk estimation for humans, biota, and natural resources in one assessment (37, 38). The objective of an *integrated risk assessment* is to support broad decision-making by creating a means to discuss, compare, and evaluate substantially different risks.

[1] See Patty's chapter entitled **Decision Making in Managing Risk**

3.6.1.3 FRAMEWORK FOR RISK ASSESSMENT Frameworks for human and environmental risk assessment and management are primarily based on the 1983 *"Red Book: Risk Assessment in the Federal Government: Managing the Process,"* which was published by the US NAS (39). Designed originally for human health assessment alone, the framework was later adopted for ecological risk assessment (40–42).

In 2008, the NAS published a report entitled *Science and Decisions – Advancing Risk Assessment* (NRC, commonly referred to as the "Silver Book"). Several important findings put forward by the NAS have direct application to the discussion of unitary vs. integrated assessments of risk.

The integration of both health and ecological risk assessments offers advantages over unitary risk assessments.

3.6.1.4 EXPRESSING ASSESSMENT RESULTS An expression of integrated health and ecological risk assessments provides a strong basis for action to support decision-making. However, when the results of independent health and ecological risk assessments are inconsistent and the bases for the inconsistency are unclear, decision-making is complicated (43).

3.6.1.5 INTERDEPENDENCE Ecological and human health risks are interdependent (44, 45). To focus the improvement of occupational health only on evaluating and reducing exposures in the place of work has the potential to miss nonoccupational sources of significance or to implement expensive controls which have no impact on improving health outcomes. Programs on *Total Worker Health®* recognize the health and safety of workers require consideration of both on and off the job exposures, activities, and behaviors. See **Advancing the Well-being of Workers: An Introduction to *Total Worker Health®* Approaches** for additional information about *Total Worker Health®*.

3.6.1.6 SENTINEL ORGANISMS Because nonhuman organisms are often heavily exposed to environmental contaminants and may be more sensitive, they can serve as sentinels, suggesting potential sources of human hazards (46–48). However, there are significant technical difficulties in extrapolating from nonhuman species to humans (49). For example, if fish have tumors or birds have deformities, the public that shares the environment with these organisms will be concerned, and assessors who have not integrated the health assessments with ecological assessments may have difficulty explaining to the public why they should not be concerned.

3.6.1.7 QUALITY The scientific quality of assessments is improved through sharing of information and techniques between assessment scientists in different fields. The data sets available for the safety evaluation of chemicals in human food and drinking water are relatively large and are used

to support intensive assessments. In contrast, ecological risk assessments for chemicals have relatively small data sets and few resources to perform assessments even though the receptors include thousands of species including plants, invertebrates, and vertebrates.

3.6.1.8 EFFICIENCY Integration of human health and ecological risk assessments offers significant increases in efficiency. Isolated assessments are inherently incomplete when both humans and ecological systems are potentially at risk. For example, the processes of contaminant release, transport, and transformation are common to all receptors.

3.6.2 Integrated Risk Assessment Design

An integrated approach offers the opportunity to develop and focus on assessment questions common to both health and environmental perspectives. An integrated approach also helps to ensure adequate consideration of risks to humans through evaluation of risks to other organisms which influence human health and welfare.

3.6.3 Risk Management

Risk management is viewed as an organization-wide issue that, as one of several co-coordinated initiatives, improves decision-making, and enables results-based management. Integrated risk management requires looking across all aspects of an organization to manage risk better.

3.6.4 Conclusion

Integrated risk assessment and integrated risk management advance a more systematic and integrated program by protecting human health, welfare, and the environment in an increasingly complex world. The cumulative risk analysis process provides an approach for improving our understanding of risks and impacts in a full, real-world context.

3.7 Regulatory and Legal Drivers

Protection of workers, the public at large, and the environment remain a technical and political challenge in a modern industrial society.

Safety, occupational health, and public health regulations are dynamic and changing throughout the world. Organizations such as International Organization for Standardization (ISO) develop and publish International Standards which can be adopted and utilized to provide uniformity. "Regulators and governments count on ISO standards to help develop better regulation, knowing they have a sound basis thanks to the involvement of globally-established experts" (50).

The safety, industrial hygiene, and public health communities, both domestic and international, have been establishing safe levels for occupational exposures and providing tools to mitigate risk for nearly a century. The National Safety Council (NSC), founded in 1913 and given a congressional charter in 1953, has a mission to "educate and influence people to prevent accidental injury and death." The American Cancer Society (ACS) also founded in 1913 has sought to educate the public on risk factors the individual cannot change and lifestyle-related factors that have been linked to cancers. The National Conference of Governmental Industrial Hygienists (NCGIH) convened its first meeting in 1938 and changed its name to the ACGIH in 1946. The ACGIH has developed over 600 TLVs and Biological Exposure Indices (BEIs) over the years. Some of the TLVs® have been *incorporated by reference* into occupational safety and health laws and standards of various nations, including many of the OSHA PELs in the United States. Insurance companies, public health agencies, state and local governments, industries, and unions have all developed methods, procedures, and measurement tools to promote safe working conditions and to encourage attitude and behavior changes.

3.7.1 Occupational Safety and Health Administration (OSHA)

In 1972 and 1975, OSHA promulgated regulations related to asbestos and coke oven emissions. OSHA relied on epidemiologic studies to estimate risks for both the new asbestos standard as well as the new coke oven emissions standard. At the time, OSHA denied that any risk estimate was required for setting health standards.

OSHA has also continued to develop important new guidelines that are not regulations. For example, OSHA has issued guidelines such as Healthcare Workplaces Classified as Very High or High Exposure Risk for Pandemic Influenza. These guidelines differentiate between occupations considered to be "very high exposure risk" and "high exposure risk." This obviously required a risk determination.

3.7.2 Environmental Protection Administration (EPA) Agency and Other Acts of Congress

The EPA operates under several different environmental statutes and Executive Orders that relate to risk and risk assessment. Following is a short list of these statutes and Executive Orders: Clean Air Act 42 U.S.C. § 7409(b)(1); Clean Water Act 33 U.S.C. § 313(c)(2)(A); Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) 42 U.S.C. § 9621(b); Endangered Species Act 7 U.S.C. 136; 16 U.S.C. 460 et seq. (1973); Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) 7

U.S.C. § 36a(c)(5)(D); Federal Food, Drug, and Cosmetic Act (FFDCA) 21 U.S.C. § 346a; Food Quality Protection Act (FQPA) 7 U.S.C. § 136; Resource Conservation and Recovery Act (RCRA) 42 U.S.C. § 6924(m); Safe Drinking Water Act 42 U.S.C. § 300(g)-1(b) and 300(h); Toxic Substances Control Act (TSCA) 15 U.S.C. § 2605(a); EO: 12898 Federal Actions to Address Environmental Justice in Minority Population and Low-Income Populations; EO: 13045 Protection of Children from Environmental Health Risks and Safety Risks; EO: 13101 Greening the Government Through Waste Prevention, Recycling, and Federal Acquisition; EO: 13158 Marine Protected Areas; and EO: 13175 Consultation and Coordination With Indian Tribal Governments

In 1976, Congress passed the Resource Conservation and Recovery Act (RCRA). One aspect of RCRA is to manage the present and future disposal of hazardous waste with respect to human health and welfare. RCRA established a Corrective Action Process (CAP) which included a Resource Conservation and Recovery Act Facility Assessment (RFA), a Resource Conservation and Recovery Act Facility Investigation (RFI), a Corrective Measures Study (CMS), and a Corrective Measures Implementation (CMI). This CAP process is a sequential risk assessment which moves from simple screening techniques to a detailed risk assessment.

For more detailed information about hazardous wastes and the risks associated with them, the reader is referred to **Hazardous Wastes**.

3.7.3 European Union Initiatives

On 1 June 2007, REACH entered into force with a phased-in set of requirements which spanned eleven years. The *Registration, Evaluation, Authorisation, and Restriction of Chemicals* (REACH) is a European Community Regulation addressing chemicals and their safe use (51).

REACH gives greater responsibility to industry to manage the risks from chemicals and to provide safety information on the substances they sell. Manufacturers and importers are now required to register the health and safety information of their products in a central database run by the European Chemicals Agency (ECHA) in Helsinki (52). The ECHA will act as the central point in the REACH system, managing the databases necessary to operate the system, coordinating the in-depth evaluation of suspicious chemicals and running a public database in which consumers and professionals can find hazard information.

REACH also calls for the progressive substitution of the most dangerous chemicals when suitable alternatives have been identified. Risk assessment resides at the heart of the REACH requirements.

3.8 Differences in Methodologies

3.8.1 Background

The professional disciplines of industrial hygiene, environmental affairs, safety, and process safety all address human health risks that could be associated with the operation of businesses which produce products or services.

In defining potential risk scenarios, each risk scenario associated with an operation has some probability of occurring and some adverse consequence if a failure should occur. The probability and consequence in a risk ranking and profiling are often rated numerically using standard definitions that reflect the significance of each component's contribution to the risk. The probability rating is then plotted against consequence rating to form a risk ranking matrix (Section 5.2, Figure 10). Each risk ranking, subsequently, has a companion set of risk management and risk communication actions that address the specific risks identified.

3.8.2 Episodic and Cumulative Risk Scenarios

Potential risk scenarios can lead to events that are *episodic* or *cumulative* in nature. A chemical release is an example of an *episodic event*, while ongoing exposure of a worker to a chemical agent over years of employment is *cumulative* in nature. Typically, with an *episodic* exposure, prior exposure may not contribute to a future risk. By contrast, with a *cumulative* risk, past significant exposures are additive or even multiplicative in their contribution to the individual risk.

3.8.2.1 CONSEQUENCES *Safety*: Traditional or "hard hat safety" classifies an adverse health outcome as an "injury." These injuries may be classified by the type of care required to treat the injury: (i) first aid case, doctor's visit, hospitalization, (ii) recordable, lost time or fatality, (iii) injury such as foreign object in the eye requiring a first aid visit, a cut that takes several days to heal, a broken bone that will temporarily incapacitate the worker, or (iv) an injury irreversibly disabling the worker, a fatality.

Industrial Hygiene: Industrial Hygiene typically addresses adverse human health risk associated with exposures (chemical, physical, biological, or biomechanical hazards). The target of these risks may be employees, contractors who work on the premises, individuals who reside near the production site, and consumers of products produced by an operation.

If the risk scenario is associated with an *episodic* release or event, the appropriate exposure limits used to judge the significance of the adverse health impact may be the national AIHA's emergency response planning guidelines (ERPG) or the US EPA's acute exposure guidelines levels (AEGLs). Both types of guidelines classify health outcomes by three levels of increasing severity associated with relatively short durations of exposure (minutes or hours).

If the risk scenario is associated with longer-term exposure (cumulative) and normal operating conditions, an occupational exposure limit (OEL) such as an ACGIH TLV or an OSHA PEL might be used. The consequence rating assigned from Table 8 is adjusted to reflect the degree of overexposure (such as >10 times the OEL) and the number of individuals potentially affected.

Environmental: If the target of the potential exposure is the community, community exposure guidelines should be used that consider the sensitivity of the receptor population. Community in this case means those individuals who could come into contact with the agent and is not restricted to individuals who live near the facility. These guidelines may be more restrictive than the OEL because communities often include individuals who are very young or old, may not be as healthy as the typical worker, and may encounter the agent for longer periods of time (24 hours per day) rather than the typical eight-hour workday. This adjustment is included because, at least with the eight-hour Time Weighted Average OELs, the OELs are set at an exposure level which can occur over weeks, months, and years without an adverse health effect in nearly all workers.

3.8.3 Summary

Risk ranking and risk profiling methodology do not typically include absolute limits of acceptable or unacceptable risk, but rather, assure that risks are ranked consistently and that the outcome of the assessment can be categorized in a manner that can be used to link risk assessment outcomes to risk management and risk communication strategies. The acceptable risk level may differ depending on the objective of the risk assessment and the originator's (e.g. company, agency, organization) tolerance for risk.

3.9 Application of Occupational Exposure Limits (OELs) and Guidance

3.9.1 Background

OELs have been used for approximately 100 years. A discussion of the history of OELs, their challenges, and possible future directions can be found in a 2009 green paper titled "Occupational Exposure Limits – Do They Have a Future?" (53).

3.9.2 Discussion of the Application of an OEL

The use of OELs as a component of human health risk assessment is based on a fundamental concept of how humans interact with their environment.

The challenge is to establish OELs that are protective for most individuals, while at the same time not imposing undue restrictions on their ability to complete the duties associated with their jobs, or aggravate or increase other risks that could impose other forms of physical, social, or financial harm. For additional information about OELs; see **The History and Biological Basis of Occupational Exposure Limits for Chemical Agents** which discusses the history and basis of OELs.

TABLE 2 Exposure ratings associated with OEL exposure bands (54).

Exposure rating	OEL exposure bands; statistical interpretation (OEL)[a]
0	$X_{0.95} \leq 0.01 \times$ Occupational exposure limit (OEL)
1	$0.01 \times \text{OEL} < X_{0.95} \leq 0.1 \times \text{OEL}$
2	$0.1 \times \text{OEL} < X_{0.95} \leq 0.5 \times \text{OEL}$
3	$0.5 \times \text{OEL} < X_{0.95} \leq 1.0 \times \text{OEL}$
4[b]	$X_{0.95} > \text{OEL}$

[a] $X_{0.95}$ is defined to be the 95th percentile of the data distribution.
[b] Exposure rating 4 is further divided into additional categories based on respirator applied protection factors (APFs).
Source: Modified from Hewitt et al. (55).

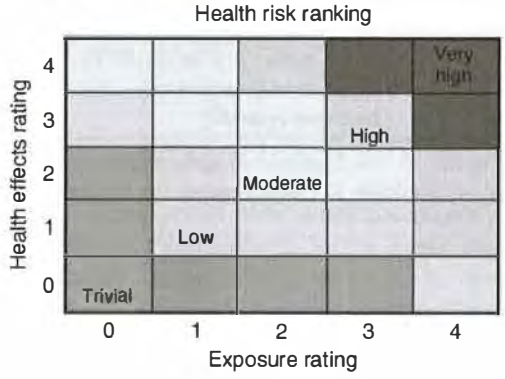

FIGURE 1 Health risk ranking.

3.9.2.1 Basic Components of Industrial Hygiene Risk Assessment Table 2, presents the exposure strata or categories presented in the AIHA Strategy document titled "The Assessing and Managing of Occupational Exposures" (2015) (54).

The risk ranking levels presented in Figure 1 are used to prioritize actions along with establishing the urgency of those actions. These, in turn, are incorporated into risk management and risk communication efforts.

Table 3 presents descriptions of health effects associated with various health ratings. The specific criteria used in both Tables 2 and 3 are left to the discretion of the risk assessor. But whatever criteria are selected, they should be applied uniformly and consistently across all exposure and risk assessments to ensure that risk management and communication efforts are comparable and consistent.

TABLE 3 Health effect rating (54).

Health effect rating	Description of the health effect
0	At most, nuisance effects (e.g. watery eyes or obnoxious odor)
1	Reversible irritation or discomfort (whiff of ammonia)
2	Dermal or inhalation sensitization or reversible toxicity that can impair ability to function or the individual's judgment
3	Dysfunction effects (e.g. lung, kidney, liver, blood), risk of cancer due to suspected human carcinogens, or severe adverse short-term health effects
4	Significant reproductive effects, irreversible neurotoxicity, irreversible toxicity to a significant body system, known human carcinogenicity or mortality from a single exposure (e.g. carbon monoxide, phosgene, hydrogen cyanide)

Source: Stenzel, M: "An Overview of Exposure Assessment Techniques." Presented at GeoHealth I: Building across the Geological and Health Sciences, Reston, VA (2008).

TABLE 4 Exposure control strategy (55).

Exposure ranking[a]	Recommended control or action
0 (<1% of OEL)	No action
1 (<10% of the OEL)	General HazCom
2 (10–50% of OEL)	+ chemical Specific HazCom
3 (50–100% of OEL)	+ exposure surveillance, medical surveillance, and work practices
4 (>100% of OEL)	+ respirators & engineering controls, work practice controls
5 (Multiples of OEL, e.g. based on respiratory APFs)	+ immediate engineering controls or process shutdown, validate respirator selection

[a]Decision statistics = 95th percentile.
Source: Modified from Hewitt et al. (55).

The exposure rating from Table 2 (x-axis) is plotted against the health rating Table 3 (y-axis) to form a risk matrix. The overall risk ranking process is illustrated in Figure 1.

Risk ranking allows the Industrial Hygienist to incorporate both the intensity of the exposure and severity of the hazard. In general, the more severe the health rating, the lower the OEL; however, this is not true in all cases and both the health effects rating and the exposure rating must be considered in determining risk which, in turn, dictates risk management and risk communication efforts.

The exposure ranking levels are associated with various action strategies such as those outlined in Table 4.

Table 4 identifies recommended controls and actions, but a determination must be made regarding the feasibility of these actions and controls. Feasibility generally encompasses technical feasibility and economic feasibility.

Technical feasibility involves questions such as: does the required technology to produce the desired result exist; how difficult will it be to build; and does the employer have adequate experience to use the technology?

Economic feasibility is the analysis used to evaluate the effectiveness of a new system or process from a financial perspective. If benefits outweigh costs by a sufficient margin, then the decision is made to design and implement the system.

Economic feasibility should consider the health hazard rating; number of workers potentially affected; frequency and duration of the exposure scenario (unique work assignment); whether the degree of exposure is in excess of the OEL; and the number of layers of protection required to eliminate or reduce risk to an acceptable level. Note that, in determining economic feasibility, personal protection equipment is not considered a layer of protection.

For example, if one had an exposure scenario with a very high-risk ranking (Figure 1), in which multiple workers are exposed daily to an irreversible neurotoxin (health rating 4) at exposures greater than ten times the OEL, the economic feasibility criteria might suggest that the financial assets to implement engineering and administrative controls be expended or, if they are not expended, conclude that the process cannot be operated safely.

3.9.3 Discussion – Characterization and Development of OELs

Considering the role of the OEL in the overall exposure assessment, risk assessment, risk management, and risk communication processes, it is apparent that the development and application of OELs are rather complex. Standard metrics must be identified to uniformly determine conformance or compliance with the OELs. In most cases, these metrics are some form of an upper bound of the exposure. While a more detailed discussion of appropriate metrics can be found in subsequent sections of this chapter, examples of metrics associated with the above mentioned OELs can be found in Table 5.

- OELs are developed with various intents and these intents must be considered in their application. Not all the OELs are equivalent and the confidence in decisions related to exposure assessment, risk assessment, risk management, and risk communication should decrease with the order of the bullets presented.
- *Health-based or authoritative exposure limits* identify the level at which it is thought that most workers can be repeatedly exposed over minutes, days, months,

TABLE 5 Exposure metrics.

Type of OEL	Working statistical definition
Ceiling	99th percentile instantaneous exposure or short-term (i.e. less than 15 minutes) exposure within each shift
STEL	95th percentile 15-minute exposure within each shift
TWA	95th percentile full-shift
LTA[a]	Depending of the reference: 10–25% of the TEA OEL or 33% of the TWA OEL

[a]The averaging time should not be more than one year for most environments and no more than two years for stable work environments.
The exposure distribution associated with an exposure scenario is usually not normally distributed but rather log-normally distributed (skewed to the right). Because of this phenomenon, even highly trained exposure assessors sometimes fail to properly judge exposure as acceptable or unacceptable (56).
Source: From Hewett, P. (2007): Technical Report 07-02 – Industrial Hygiene Exposure Assessment – Data Collection and Management. Exposure Assessment Solutions, Inc. (www.oesh.com). © 2007 Exposure assessment solutions.

or years without experiencing effects adverse to their health. Examples of health-based exposure limits include the ACGIHs TLVs, AIHAs workplace environmental exposure levels (WEELs) or the National Institute of Occupational Safety and Health (NIOSH) recommended exposure limits (RELs).
The failure to address feasibility in the development of the OEL does not mean that feasibility is to be ignored, but rather that the feasibility assessment is to be conducted for each unique work setting and may vary between processes, facilities, or employers.
There is also an issue with analytical feasibility. Analytical feasibility relates to the availability of suitable methods to measure exposure. Typically, suitable quantitative analytical methods must be able to reliably measure exposure down to levels of approximately 1/10th of the exposure limit.

- *Regulatory OELs* are limits that are promulgated by a regulatory agency. Failure to comply with these limits can result in monetary fines or other penalties. These limits are developed under specific procedures identified in the law.

Corporate exposure limits are developed in the private sector and may be limited to a single company or to an industry through an industry group. The limits are usually established by company experts for use within the affected companies and may also be communicated to customers. These limits are usually considered guidelines and are meant to provide internal direction for the company's occupational health programs.

- *Provisional or working OELs* are sometimes used when other OELs are not available. They may be developed from risk phrases such as those used in Control Banding (57), calculated from no effect levels or lowest adverse effective levels in animals such as the derived no-effect levels (DNELs) associated with the European Union REACH program (51), or derived from analogous chemicals in the same family.
- The OEL setting process usually involves experts in the fields of toxicology, industrial hygiene/exposure assessment, epidemiology, and occupational medicine. The process of setting an OEL is very complicated and requires considerable knowledge and expertise (58).

Typical OEL methodologies include analogy, correlation, low dose extrapolation, and safety/UFs. Safety and UF methodology uses the following formula to establish an OEL:

$$\text{OEL} = \frac{(\text{Reference level})}{(\text{UF}_{1,2,3} \times \text{SF} \times \text{MF} \times A \times V)}$$

where $\text{UF}_{1,2,3}$ is composite uncertainty factors; SF is safety factor (severity and confidence); MF is modifying factor (bioaccumulation, sensitization, etc.); A is absorption (bioavailability) correction factor; V is volume of air inhaled in eight-hour shift (10 m^3).

Sources of uncertainty include human-to-human variability in response; animal-to-human extrapolation; lowest observed adverse effect level (LOAEL) to NOAEL extrapolation; study duration; and exposure route. The assignment of the UFs is based on the experience and knowledge of the expert.

The pertinent data used to establish the OEL (critical health endpoints, methodology, and rationale) should be documented so that the user of the OEL can properly apply the limit as it relates to exposure assessment, risk assessment, risk management, and risk communication efforts.

3.9.4 Conclusion

On the surface, the use of an OEL appears to be as simple as deciding if the observed exposure is less than the OEL. The previous section attempted to: provide the rationale that supports the use of OELs; describe the role of the OEL in the exposure assessment, risk assessment, risk communication, and risk communication processes; identify the issues and concerns in applying OELs; and discuss the characterization and development of OELs.

3.10 AIHA Exposure Risk Model

Risk assessments are impacted by the accuracy and quality of exposure assessments.

Assessment (exposure, eating, drugs, or recreation) is but one component in a five-step model related to risk. These five-steps are Assessment, Characterization, Communication, Benefit–Cost Analysis, Management (59).

First, risk assessments depend on human health studies that attempt to correlate the excess risk of an adverse health outcome with the exposure levels (intensity and duration). Second, if a risk assessment is performed on individuals, uncertainty in the exposure assessment contributes to the uncertainty in the risk assessment. Unfortunately in both cases, the exposure assessment must rely on the existing record and there is no opportunity to go back in time and collect additional data.

It is important to note that an individual's complete exposure experience must be known rather than simply the times that a person was thought to encounter high or overexposures. If the exposure record is not available for the periods during which exposures are thought to be low and the exposure is assumed to be zero, the individual's risk may be underestimated. In addition, in epidemiological studies, the occurrence of an adverse health outcome is usually evaluated over a range of exposures. If only the high exposures are known, the lack of data can contribute to exposure misclassification that reduces the study's ability to identify the actual relationship between exposure and an adverse health outcome.

A risk assessor needs a comprehensive exposure assessment (intensity and duration) on all agents that an individual encounters in his/her working experience. This section will discuss the AIHA Strategy documented in "The Assessing and Managing of Occupational Exposures" in 2015 (54).

3.10.1 Required Characterizations

Ideally, a risk assessment requires a complete record of the agents an individual encounters during their work assignments. An exposure scenario is defined to be the exposure to a particular agent encountered while working a specified assignment. The intensity and duration of exposure should be established and documented for each exposure scenario encountered by the individual, including those agents with low or minimal exposure.

The AIHA exposure assessment strategy and the AIHA risk assessment strategy are provided to increase the reader's understanding of how the AIHA proposes that Industrial Hygienists address exposure and risk assessments.

3.10.1.1 Exposure Distributions This discussion is included because the actual distribution often runs counter to normal intuition that suggests that an individual's exposure performing his/her job does is roughly "constant." "Constant" means that there is minimal day-to-day variability in individuals' exposure over periods such as months or years. This is not the case. Typically, day-to-day exposures for workers performing the same job assignments are log-normally distributed (illustrated in Figure 2). The blue dashed vertical lines correspond to the peak of each curve and represent the distribution's geometric mean (GM). The GM corresponds to the median (divides the set of exposure values into two equal parts) of the lognormal distribution. The term geometric standard deviation (GSD) is a measure of the variability of the distribution. A GSD of 2.5 is the most typical observed value associated with a large number of occupational jobs (60).

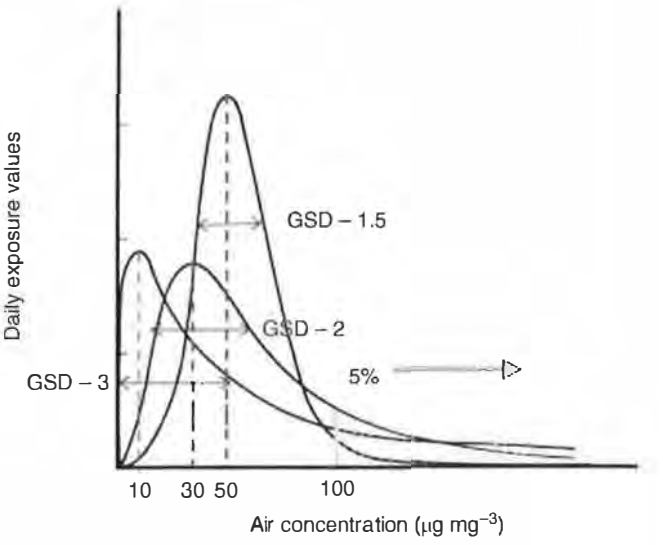

FIGURE 2 Log-normal distribution. Source: From Control Banding: Issues and Opportunities, ACGIH (2008) © 2008 American Conference of Governmental Industrial Hygienists.

The large observed variation in daily exposure values is due to natural variation in the workplace and process, variation in an individual's responsibilities, and variations in work practices; it is not due to uncertainty in analytical measurements. Examples of workplace variations include temperature, wind direction, and velocity, the opening or closing of windows or doors, or the condition of ventilation equipment. Variation in process may include the composition of raw materials, quantity of agent being used, and type of application. Variation in responsibilities may include the number of times per day specific tasks are performed and the variation in the duration of each task. Work practice may include how close the worker is positioned to a source or variability in the performance of defined procedures.

The risk assessor needs to be aware of how the Industrial Hygienist uses the data to meet industrial hygiene related exposure needs. This means that risk assessors may have to convert reported industrial hygiene exposure data into metrics useful for their risk assessments. Another difference resides in the fact that the Industrial Hygienist is

primarily interested in where the exposure distribution falls with respect to an OEL, whereas the risk assessor attempts to identify the likelihood of an adverse health outcome due to exposure. The metric typically used by Industrial Hygienists is an upper bound metric such as the 95th, 98th, or 99th percentile (Table 5). The risk assessor, on the other hand, is usually interested in a dose metric such as the arithmetic average or cumulative average. And finally, in animal studies, the exposure is a near-constant level for the duration of the study, whereas in human exposure scenarios, most of the cumulative exposure occurs during a relatively small number of the days worked. The risk assessor needs to judge the biological relevance of this highly variable exposure.

The percentiles used by the Industrial Hygienist can be calculated in the following manner (note: the Industrial Hygienist does not generally report an average).

$$95\text{th Percentile} = (\text{GM}) * (\text{GSD})^{1.645} \qquad (1)$$

where GM is geometric mean; GSD is geometric standard deviation; 98th Percentile: Exponent is 2.055; 99th Percentile: Exponent is 2.325.

If exposure data are log-normally distributed and only the GM and GSD are provided, the average (which a risk assessor utilizes) can be calculated using the following equation:

$$\text{Average} = \exp(\text{LN GM} + 0.5 * [\text{LN GSD}]^2) \qquad (2)$$

where Exp means to raise the term in brackets to the expediential of the base of the natural logarithm (e); LN GM is the natural logarithm of the geometric mean; LN GSD is the natural logarithm of the geometric standard deviation.

Although Eq. (2) looks somewhat complicated, a typical calculator has all the required functions to perform the calculation.

Small datasets: The skewness of the log-normal distribution makes it very difficult to properly characterize the distribution when only a few measurements are available. The following simple example is presented to illustrate this problem.

Assume an exposure distribution that is definitely considered "unacceptable" such as a case where 50% of all the exposures exceed the OEL (based on two full-shift measurements collected to assess the exposure). Figure 3 illustrates the four combinations of sample results or cases that are possible.

The arrow in each case indicates if the measurement is above or below the OEL. Each case has an equal probability of occurring. In Case 1, the first measurement was below the OEL and the second was above the OEL. In Case 2, both measurements were above the OEL. In Case 3, both measurements were below the OEL, and in Case 4, the first measurement was above the OEL and the second below. The

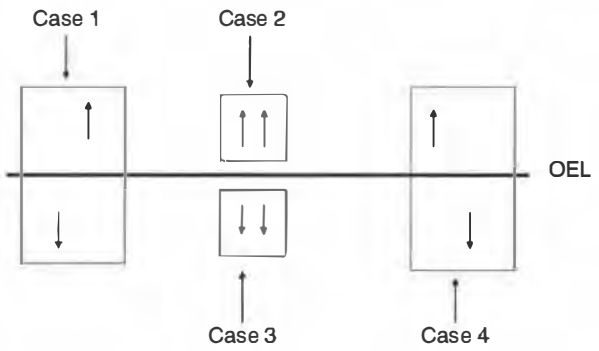

FIGURE 3 Combinations collecting two samples. Source: From Bullock, W.H. and Ignacio, J.S.: (editors): A Strategy for Assessing and Managing Occupational Exposures, Third Edition. Fairfax, VA: American Industrial Hygiene Association (2006).

Industrial Hygienist most likely will judge the exposure to be "unacceptable" if any single measurement is above the OEL. The correct judgment is that the overall exposure is "unacceptable."

In Case 1, Case 2, and Case 4, the Industrial Hygienist will correctly judge the exposure to be "unacceptable." But in Case 3, the Industrial Hygienist will typically judge the exposure to be "acceptable." Considering each of the four cases has an equal probability of occurring, Case 3 will occur 25% of the time. The scenario of a worker being overexposed 50% of the time is a very extreme case and likely be considered "unacceptable."

Performance of sampling strategies: The challenge that a log-normal distribution presents to the Industrial Hygienist is that a high portion of the observations are very low, making it more difficult to observe high exposures even when exposures are "unacceptable." As stated above, the Industrial Hygienist usually uses the 95th percentile as the metric to judge the "acceptability" or "unacceptability" of exposure.

Assume the case in which the 95th percentile is equal to an OEL of 1.0 ppm. That is the 95th percentile $= 1 = (\text{GM})*(\text{GSD})^{1.645}$. Any OEL could be used, but an OEL of Eq. (1) simplifies the illustration. Table 6 below illustrates the effect of the skewness of the log-normal distribution at various GSD's when the 95th percentile is on the border between "acceptability" and "unacceptability."

Table 6 illustrates the distribution of exposures in the simple case in which the OEL is equal to Eq. (1). Again, if the 95th percentile is equal to the OEL, the exposure is considered to be borderline and still judged to be "acceptable"; if the exposure were higher than the OEL, it would be considered "unacceptable." Note that the GM is the point at which 50% of the exposures are above the GM's numeric value and 50% below. This means that at a GSD of 2.5, 50% of the actual exposures would be no higher than 0.22 ppm, while 81% would be below 0.5 ppm or one half the OEL. It is

TABLE 6 Skewness of a log-normal distribution (61).

GSD	GM	Percent of exposures below 50% of the OEL	Percent of time that 2 measurements will be below 50% of the OEL
2.0	0.32	74%	55%
2.5	0.22	81%	66%
3.0	0.16	84%	71%

Source: Stenzel, M: "An Overview of Exposure Assessment Techniques." Presented at GeoHealth I: Building across the Geological and Health Sciences, Reston, VA (2008).

common practice to use an action level of 50% of the OEL as a conservative decision point. A common sampling strategy used by Industrial Hygienist is to collect two measurements and, if they are both below the action level, the exposure is judged to be "acceptable." Table 6 illustrates that if two measurements were collected, there would be a 66% chance that both observed measurements would be no higher than 0.5 ppm (or one half the OEL). Table 6 supports the common practice.

Another way to think about the example is as follows: if in a year an individual works 250 days, and the exposure level (95th percentile) associated with his/her job was equal to the OEL of 1.0 ppm, then on 125 of those days (or 50% of the total), the worker would experience exposure levels no higher than 0.22 ppm, and on 202 of those days (or 81% of the total), the workers' exposure levels would be below 0.5 ppm. In this example, the correct judgment was that the exposure was "acceptable" but only "borderline acceptable." The purpose of this example was to illustrate that even in this borderline case, if the exposure was any higher, it would be "unacceptable," even with a very large portion of the actual exposures falling below the chemical's action level (or 50% or the OEL). This means that, if only 1 or 2 measurements are collected to determine an individual's exposure, the Industrial Hygienist may fail to observe exposures at the high end of the actual exposure distribution. In a study which evaluated Industrial Hygienists' ability to correctly judge exposure ratings using small datasets (56), it was found that there was a bias towards underestimating the correct rating.

There are ways around this problem. In the above-mentioned publication (56), the authors provided statistically based rules that were shown to improve the Industrial Hygienist's judgment. In addition, a very simple rule can be used if one has a very small dataset. It can be shown mathematically that the 95th percentile is about 3 times the dataset's arithmetic average. Therefore, if only a few samples have been collected, the exposure assessor can average the limited dataset and multiply by 3 to obtain a reasonable estimate of the 95th percentile. In addition, if the risk assessor has data reported as a 95th percentile, the risk assessor can divide by three to obtain the dataset's average if this is the metric of choice in the risk assessment.

In summary, the log-normal distribution can lead to results counter to our intuition. There may be a need to convert the metrics used by Industrial Hygienists to those appropriate for use by risk assessors. Also, interpreting small datasets results in a bias toward judging "unacceptable" exposures as "acceptable," with the high portion of low values in a log-normal distribution requiring that more data be collected to properly characterize exposures.

3.10.1.2 AIHA Exposure Assessment Strategy The AIHA exposure assessment strategy is illustrated in Figure 4.

Major Steps: The major steps in the risk assessment strategy are as follows:

1. *Strategy:* Establish the exposure assessment strategy.
2. *Basic characterization:* Gather information to characterize the workplace, workforce, and environmental agents.
3. *Exposure assessment:* Assess exposures in the workplace in view of the information available about the workplace, workforce, and environmental agents. The assessment outcomes include
   (a) Groupings of workers having similar exposures.
   (b) Definition of an exposure profile for each group of similarly exposed workers.
   (c) Judgment about the acceptability of each exposure profile.
4. *Further information gathering:* Implement prioritized exposure monitoring or the collection of more information on health effects so that uncertain exposure judgments can be resolved with higher confidence.
5. *Health hazard control:* Implement prioritized control strategies for unacceptable exposures.
6. *Re-assessment:* Periodically perform a comprehensive re-evaluation of exposures. Determine whether routine monitoring is required to verify that acceptable exposures remain so.

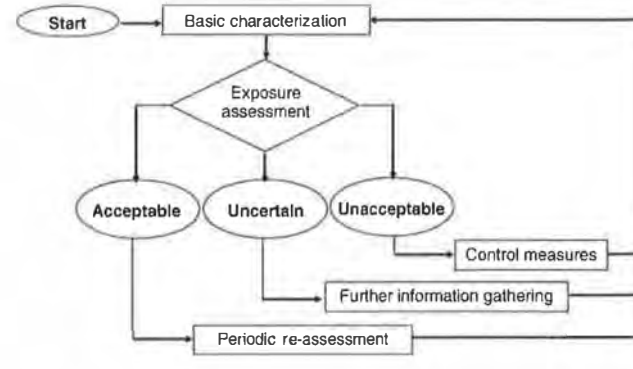

FIGURE 4 AIHA's: a strategy for assessing and managing occupational exposures (54).

7. *Communications and documentation:* Although there is no element in Figure 4 for "communication and documentation," the communication of exposure assessment findings and the maintenance of exposure assessment data are essential features of an effective process.

Assessment Process:

1. Identification of Exposure Groups: The AIHA exposure assessment strategy is organized around exposure groups referred to as similar exposure groups (SEGs) that are defined as follows:

Similar Exposure Group (SEG): "Group of workers having the same general exposure profile for the agent(s) being studied because of the similarity and frequency of the tasks performed, the materials and processes with which they work, and the similarity of the way they perform tasks."

The overall objective of the exposure assessment process is to establish the exposure rating (Section 3.9.2.1, Table 2) for each agent in the SEG.

As described above, there is a need to understand the full spectrum of exposures that could be encountered by the individual rather than just high exposures alone. An individual's complete exposure history can be obtained by linking his/her work history to various SEGs worked. Note that the work assignment corresponding to an SEG may be a single task or a series of task that could cover the entire shift or even a series of shifts. The controlling factor is that the work assignment must be consistent with the definition of the SEG. The advantage of this approach is that all of the data associated with a unique exposure scenario need only be collected once and the documented information, including the intensity and duration of all exposures of all workers, would be available for future risk assessments.

The SEG is based on information obtained through a workplace, workforce, and work practice characterization.

The optimum number of SEGs at a site is not determined by the Industrial Hygienist, but rather is dependent on how many distinct SEGs are needed to satisfy the above SEG definition.

All chemical agents, physical hazards (e.g. noise, heat stress), biological hazards (e.g. mold), and biomechanical hazards (e.g. ergonomic) are compiled for each SEG. Information compiled for each hazard agent includes the composition of chemical agents; OEL; health hazard information, target organs; and hazard rating. In addition, other information such as hazard communication training requirements; medical surveillance requirements; personal protective equipment (PPE), and respiratory protection requirements may also be tied to the SEG and based on the outcome of the exposure assessment.

2. Qualitative Screening Process to Determine Exposure Ratings: To address the problem that there are likely a very large number of exposure scenarios that need to be assessed and that quantitative measurement data will be lacking or at least very limited, the IH must use other approaches to assess exposures. One of these approaches uses information collected in the characterization step to identify various determinants of exposure that are used to predict exposure ratings (Section 3.9.2.1, Table 2). Examples of these determinants include type of controls; efficiency of controls; distance from a source; size of container openings; surface area; composition of mixtures, vapor hazard ratio, quantity of agent; and application method, to name a few. These determinants are inputs into various qualitative, semi-quantitative, and quantitative assessment methods used to establish the appropriate exposure rating.

3. Modeling Quantitative Assessment Methods: More robust assessment methods include various type of modeling techniques include

- Mathematical models using the agent's chemical and physical properties and the principles of fluid dynamics (27, 28).
- Deterministic models that rate the contribution of various parameters such as level of control, frequency, and duration that the activity is performed and the agent's exposure index which is a measure of the agent's potential to exceed its OEL (61).

Again, modeling may lead to the conclusion that the exposures are acceptable, uncertain, or unacceptable. Corrective action is required for the unacceptable exposures. If the exposure is determined to be uncertain, more data may be collected or actions may be taken to move the exposure from being uncertain to being acceptable. The time required to model is usually on the order of minutes or hours. However, the development of advanced quantitative exposure models will require years of research which should ultimately be cost-effective to the overall process. However, the development of advanced quantitative exposure models will require years of research which should ultimately be cost-effective to the overall process (62).

The exposure rating may be based on quantitative measurements alone. In this particular case, a 95th percentile is calculated from the specific quantitative measurements, with the resulting 95th percentile being used to establish the exposure rating. This is as opposed to determining an exposure rating based on the specific measurements alone. An individual measurement collected on a specific day may be compared to an OEL, but as discussed in Section 3.10.1.1, exposure data varies significantly from day to day. Although the measurement does identify the exposure for the day measured, it does not provide much useful information about the overall exposure distribution encountered over an extended period of time such as months or years unless the data point is included in a much larger dataset of representative measurements.

4. Professional Judgement vs. Opinions: The term "professional judgment" is often used. There is a difference between professional judgment and professional opinion. The AIHA defines professional judgment as follows:

"The application and appropriate use of knowledge gained from formal education, experience, experimentation, inference, and analogy. The capacity of an experienced professional to draw correct inferences from incomplete quantitative data, frequently on the basis of observations, analogy, and intuition."

3.10.2 AIHA Risk Assessment Strategy

The AIHA risk assessment strategy can best be described as follows. The agent's health rating is presented in Table 2 (Section 3.9.2.1) and the exposure rating presented in Table 2 (Section 3.9.2.1). The health rating is plotted against the exposure ranking to form a risk ranking matrix as illustrated in Figure 1 (Section 3.9.2.1). The risk assessment is completed for each agent within a SEG. Finally, specific risk management and risk communication activities are linked to each risk ranking illustrated in Table 4 (Section 3.9.2.1).

3.10.3 Summary

The AIHA exposure assessment strategy is a comprehensive approach that can address many needs, including the needs of the risk assessor. It addresses all exposures rather than just the highest exposures. A complete exposure history is critical in risk assessment. In addition, data collected on other individuals can be utilized in completing an individual exposure assessment. The AIHA exposure assessment strategy provides a method which effectively and efficiently leverages available human and financial resources.

3.11 Measuring for Effectiveness

Metrics and their measurement are important in any scientific and management process. One cannot manage what one cannot measure. Whenever mankind has been able to measure things, it has made great progress both in understanding and controlling them (63). Measurement forms the basis of input and continuous improvement. If appropriate metrics are not selected, the effectiveness of the health, safety, and environmental management systems can be undermined as reliable information may be lacking to inform managers how well risks are controlled.

3.11.1 Measuring Performance

The primary purpose of measuring health, safety, and environmental performance is to provide information on the progress and current status of the strategies, processes, and activities used by an organization to control risks to health, safety, and the environment. Measurement provides information on how the system operates in practice, identifies areas where remedial action is required, provides a basis for continuous improvement, and provides feedback and motivation. Measurement can help all levels of an organization or community to determine if a system is in place across all parts of the organization and if there is a supportive culture in the face of competing demands for resources.

3.11.2 Different Information Needs

An effective risk management system is built on a set of linked metrics which reflect the structure of an organization. Performance measures are necessarily derived to meet *intra*-organizational needs, to efficiently measure and provide feedback to a specific risk-related issue. There will be a more limited number of metrics which can be used *inter*-organizationally.

While the primary focus for performance measurement is to meet the internal needs of an organization, there is a need to demonstrate to external stakeholders (i.e. regulators, insurance companies, shareholders, suppliers, contractors, neighbors, the public) that effective controls are in place for health, safety, and environmental risks. Local community and society pressure for accountability reaches broadly through routes such as corporate social responsibility. The challenge for organizations is to communicate their performance in ways that are meaningful to their various stakeholders.

3.11.3 Traditional Metrics

Traditional business management performance metrics include earnings before interest, taxes, depreciation, and amortization (EBITDA), return on investment, and market share. A common feature of these measures is they are generally positive (i.e. achievement) rather than negative (i.e. failure).

On the other hand, risk-related performance metrics have often been presented as trailing indicators. Some examples of trailing indicators are injuries, the recordable incident rate, workers' compensation costs or violations, and penalties. Such metrics look "after the fact" and are measures of failure as opposed to looking forward (or predictively).

Trailing indicators do not always reveal everything about the health of a business or risk management plan. Trailing indicators can prove useful in a number of ways:

- Safety improvement opportunities
- Trends analysis
- Prioritized safety initiatives
- Verified intervention effectiveness
- Regulatory statistics

3.11.4 Hazard Metrics

All activities have inherent hazards and potential risks. The range of activities undertaken by an organization will necessarily create hazards, risks, and benefits, all of which will vary in nature and significance. The range, nature, distribution, and significance of the hazards will determine the risks which need to be controlled. Ideally, the hazards should be completely understood and the risks should be eliminated altogether, but this is not always reasonable or practical. Information regarding hazards provides important inputs into the planning and review processes to ensure that proportionate effort, prioritization, and emphasis are allocated to the control of risks.

3.11.5 Prospective Metrics

Health, safety, and environmental risk management success is the *absence* of an outcome (injuries or ill health) rather than a *presence*. This differs from other processes that get measured. Organizations need to recognize that there is no single reliable measure of health and safety performance. What is required is a 'dashboard' of measures, providing information on a range of health, safety, and environmental activities. All metrics in the toolbox should meet the five criteria: (i) specific, (ii) measurable, (iii) attainable, (iv) realistic and relevant, and (v) time constrained. It is usually best to have employees and stakeholders develop their own metrics.

Leading predictive metrics should be intent on preventing incidents or illnesses from occurring. Metric performance reports can be developed and distributed to provide a timely indication of daily performance. Some leading metric examples include

- *Recordable events ratio* – measures the number of recordable injuries in relation to the number of first aid events.
- *Investigation timeliness* – measures the success rate for line supervisors to promptly perform an initial investigation when safety incidents occur.
- *Assigned corrective action completion* – measures the timeliness of completion for assigned corrective actions and preventive actions after an incident has occurred.
- *Training completion* – measures the completion status of assigned EHS training.

3.11.6 Reactive Metrics

Failures in risk control need to be measured (reactive metrics), to provide opportunities to check performance, learn from failures, and improve the risk management system.

Reactive metrics identify and report:

- injuries and work-related ill health,
- other losses such as damage to property,
- incidents such as those with the potential to cause injury, ill health, or loss,
- hazards and faults, and
- weaknesses or omissions in performance standards and systems.

Root Cause Analysis and Preventive Actions should:

- investigate incidents ranked as high risk.

Reactive monitoring should address questions such as:

- Are injuries/ill health/loss/incidents occurring?
- Where are they occurring?
- How serious are they?
- What are the costs?
- What improvements in the risk management system may be needed?
- Is the trend getting better or worse?

3.11.7 Measuring Culture

The risk management system is an important influence on the culture, which in turn, impacts the effectiveness of the risk management system. Cultural metrics, therefore, form part of the overall process of performance measuring. Many of the activities which support the development of a positive risk control culture need to be measured. These activities are control, communication, cooperation, and competence.

3.11.8 Management Engagement

It is critical to engage all levels of management to drive results in any organization. Line, middle, and upper management assume different roles within companies, each having a unique contribution as to how decisions are made. Developing an organizational engagement plan for risk reduction may be one of the most critical parts of any risk reduction process.

Executive management must help define, understand, communicate, and support the risk management metrics so that proper expectations and behaviors are developed throughout every level of management. It is critical to work through line and middle-level management to gain understanding and support so communication efforts with executive management are successful.

3.11.9 Performance Metrics

The use of performance indicators and other process feedback tools has become widely popular because of recent advancements in computers and internet technology. It is critical that the performance metrics and indicators measure the elements that are most critical to the risk management process.

The SMART process is a popular and effective method for assessing the quality of a specific performance metric. In short:

S = *Specific*: clear and focused to avoid misinterpretation; includes measurement assumptions and definitions which are easily interpreted.

M = *Measurable*: can be quantified and compared to other data. Avoid "yes/no" measures except in limited cases, such as start-up or systems-in-place situations.

A = *Attainable*: achievable, reasonable, and credible under expected conditions.

R = *Realistic*: fits into the organization's constraints and is cost-effective.

T = *Timely*: doable within the time frame given.

3.12 Integrating Risk Assessments into Cost–Benefit Analysis

When Federal government agencies issue regulations with the purpose of saving lives or preventing illnesses or injuries, these regulations often include a Regulatory Impact Analysis (RIA). "RIA's provide objective information and analysis that is essential for evidence-based decision making and include a cost–benefit analysis (CBA) as well as other analyses mandated by various statutes and executive orders." (64).

Even though it may be appropriate to keep risk assessment separate from risk management, CBA has been wrongly categorized as being a part of risk management alone (56). Nevertheless, CBA is a powerful tool in helping to advance valuable health and safety policies. When it is combined with risk assessment, it allows analyzing lifesaving policy actions using a science-based approach which draws heavily on physical and life sciences, engineering, probability and statistics, psychology, and economics. One major advantage of this combined analysis is that it addresses how unforeseen market or consumer behaviors may lead to offsetting risks. This science-based approach to health and safety policies can help establish regulatory priorities based on relative risk, promote wise policy investments while minimizing unintended risks and unforeseen burdens of regulation, and deploy market-oriented policy instruments that may stimulate innovation while minimizing costs (65). Risk assessment is a process, like CBA, that can help risk managers decide whether a potential hazard is of enough significance that it needs to be managed or regulated.

3.12.1 Types of Risk Assessment

Risk assessment is, according to the NRC definition, the use of a factual base to define the health effects of exposure of individuals or populations to hazardous materials and situations. Examples of different types of risk assessments include baseline risk estimates, pathway analyses, comparative risk assessment, and multi-criteria decision analysis.

- *Baseline risk assessment* – provides estimates of existing risks that are attributed to a particular agent or hazard in the absence of any control or mitigation effort. Baseline estimates are useful in CBA because they provide a basis from which reductions in risk can be estimated and translated into benefits (66).
- *Pathway analysis (PA)* – helps determine where in the production system certain risks of exposure are more likely to occur or where controls have a greater effect.
- *Comparative Risk Assessment (CRA) and Multi-Criteria Decision Analysis MCDA* – CRA compares interrelated risk associated with a specific problem or policy choice. CRA makes trade-offs explicit when evaluating competing risk management objectives and comparing different alternatives in their potential impacts or outcomes.

3.12.2 Safety Assessments

Safety assessments are a technique for deriving reference doses (RfD) or exposure limits from human and animal data by selecting a "point of departure" or POD, based on some critical health endpoint, such as the NOAEL and then dividing that by a safety factor composed of multiple "UFs" and "modifying factors (MFs)" selected by the risk assessor. Safety assessments are different from quantitative risk assessments in that instead of estimating the probability that something will happen, they are used to estimate the amount of a hazardous agent that is either safe or acceptable. Safety assessments are not compatible with CBA, but they are with cost-effectiveness analysis (CEA).

Safety assessments for chemicals usually rely on animal toxicology with the assumption that humans are more sensitive than the most sensitive animal species tested. For example, the EPA's noncancer RfDs and Reference Concentrations (RfCs) are considered safety assessments and not risk assessments. Because the RfD and RfC provide a bright line between possible harm and safety instead of a quantified risk their use in CBA and other analytical tools such as risk–risk and risk–benefit comparisons is limited. Similarly, cancer potency values which use animal data are derived from estimating a point of departure using a lower bound estimate – usually 10% – of the dose associated with tumor incidence and then drawing a line from the origin to

the POD. The assumption of a low dose linear relationship is not a central estimate and overestimates overall risk (67).

A similar problem can arise when judging the effects of radioactivity or the toxicity of some substance assuming a linear response model without a dose rate below which there is no ill effect, or in other words, a threshold. This model is referred to as the linear no threshold (LNT) model. To analyze data using a model that does not allow even the possibility of a threshold effect can lead to false conclusions regardless of how good the data are. This can make imaginary risks appear as real risks (68).

Nevertheless, RfCs or upper bound estimates are used as policy objectives. For example, when a decision is made to follow a predetermined objective, such as reducing the exposure of a certain chemical to a level determined by a safety assessment, cost-effectiveness analysis (CEA) is used to find the least costly way to achieve this objective. A more detailed explanation of CEA can be found in Section 3.12.5.

3.12.3 How Market Failure Relates to Risk

Risk is equal to cost. Economic activities including the production of a good or service are carried at a cost and therefore imply risk. However, like risks, not all costs are the same. A producer's private costs include costs that are reflected in a firm's production statements and include costs of capital equipment, depreciation, costs of labor, and materials among other costs of running a business. External costs are costs that are not reflected in the firm's production statement and are paid by someone else and are usually a consequence of economic activity affecting others.

By considering social costs, policymakers may look for ways for firms to internalize the external costs incurred from their production decisions and thus reduce social costs and social risks. As illustrated below, the difference between private and social costs of an economic activity is the external cost (69).

Social costs = Private costs + External costs

If external costs >0, then private costs < social costs.[15]

3.12.4 How Risk Assessment (RA) Components Relate to Cost Benefit Analysis (CBA)

Thus, CBA is very similar to risk assessment (except safety assessment). Quantitative risk assessment (QRA) methods use probability distributions instead of deterministic calculations when deciding among options. It also calculates the combined effect of a model's various uncertainties in order to calculate an outcome distribution (70). Advances in Bayesian approaches used in QRA have led to the creation of models that can be integrated into an economic analysis because a QRA model helps to account for every possible value or unit risk that each variable can take and weighs each scenario by the probability of its occurrence.

QRA uses Bayesian methods; CBA uses economic theory. Net benefits are maximized when marginal benefits equal marginal costs.

The classic economic approach to finding the optimal level of expenditure to reduce risk is when the total costs of risk is minimized (R^*). In Figure 5, the total costs are equal to the sum of the costs of reducing risk and the expected costs (i.e. health losses) due to risk (71).

3.12.5 Approaches to Life and Health Valuation

In the last few decades, the federal government has launched many regulations with the purpose of saving lives or preventing illnesses or injuries. These regulations work by addressing the value of reducing risks of premature death, illness, or injury to populations or subsets of populations such as workers and consumers. The change in risks related to death is known as "statistical lives."

CBA carries considerable controversy, especially because it provides ways to measure health, safety, and statistical lives in monetized terms. This is referred to as the "value of a statistical life" (VSL). According to estimates by Leigh et al. (72), the total cost of occupational-related injuries and illness in 2005 was about $171 billion. This estimate was derived using the Cost of Illness (COI) approach. COI typically includes direct costs (medical spending) and indirect costs (productivity losses, lost wages, including the costs of finding and training replacements (73).

For example, using the COI approach considers direct medical costs, lost time (74), and lost wages. For certain diseases, such as cancer, the medical costs can be derived from available data. Techniques that address the direct cost of medical treatment do not incorporate costs related to pain and suffering as does the Willingness to Pay (WTP) approach, nor do they fully account for costs borne by the worker and the worker's family.

3.12.5.1 Direct Cost of Illness Approaches Other valuation approaches can include direct COI approaches to estimates that include society's WTP or the VSL. WTP refers to what consumers, voters/taxpayers show they will spend in their own risk decisions. WTP for one's own risk reduction depends on factors such as aversion to risk, income, and voluntary nature of the risk. Despite its limitations, WTP estimates are widely used in the Federal Government. WTP results of these estimates come from wage premium studies which measure the tradeoff between wages and risk for computing the VSL (75). Most agencies use a single value and apply it to all persons and all risks of death. For example, the US Department of Transportation (DOT) uses $9.6 million, the United States Department of Agriculture (USDA) uses $8.9 million and the US FDA uses $9.5 million, while the US EPA uses $10 million (76). The economists at FDA also use COI and WTP but also include Quality

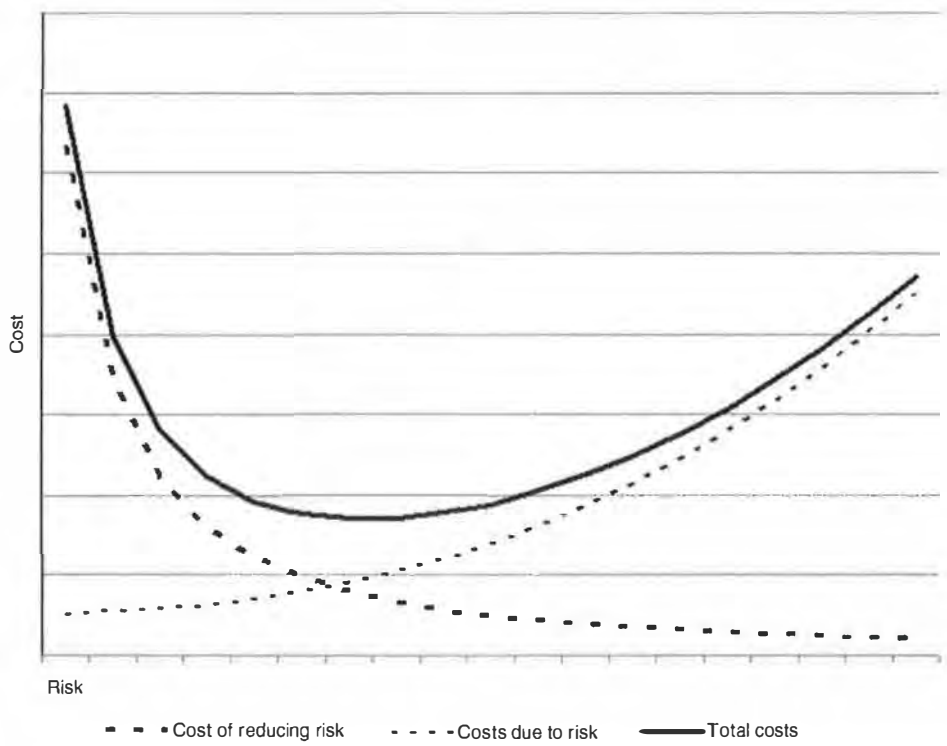

FIGURE 5 Cost of risk. Source: Modified from Morgan (71).

Adjusted Life Years (QALYs) as inputs into a CB analysis. Traditionally, QALYs are used as a nonmonetary scale in CEA where "1" represents perfect health and "0" represents a state no better than death. FDA, the health and longevity impacts of a policy choice are measured on a QALY scale and bounded by the WTP/VSL estimate of $9.5 million (77).

Monetizing health and the value of life or death, although controversial, is a necessary component of CBA especially when deciding how to allocate taxpayer dollars for safety. CBA forces complex issues into open tradeoffs that would otherwise not be apparent. The controversies related to this topic are addressed in Section 6.2.

3.12.5.2 Discounting Benefits and costs do not always take place at the same time. When they do not, it is incorrect to add all of the expected net benefits or costs without taking account of when they actually occur. If benefits or costs are delayed or otherwise separated in time from each other, the difference in timing should be reflected in an analysis. Discounting is the primary process used in estimating the time value of money. For example, discounting future values to produce present values allows comparing different values across time (78).

3.12.5.3 Cost-Effectiveness Analysis CEA is different from CBA because it analyzes the costs of different options for reaching a pre-determined policy objective. CEA does not consider that there might not actually be a way to achieve the objective in a way in which the benefits exceed the costs. In a CEA, health and longevity are measured on a nonmonetary scale such as QALYs and cost-effectiveness ratios.

A firm deciding between various control options may well consider doing a CEA to arrive at the best feasible control scenario that minimizes cost. A complete evaluation of the options would need to include all of the appropriate costs, both fixed and variable, and would need to consider discounting future costs to a common basis as a present value.

4 HAZARD AND EXPOSURE ANALYSIS

4.1 Role of Epidemiology – From Association to Causation

The epidemiological notion of "cause" is one in which a causal factor is any event, condition, or characteristic that increases the likelihood of disease. Moreover, a "statistical association" is thought to be "causal" if an alteration in the frequency of exposure E is followed by a measurable change in the frequency or severity of disease D.

4.1.1 Infectious Diseases

The discipline of epidemiology initially focused on *infectious diseases* which provided the original models for the study of epidemiology. It arose out of interest in learning the cause of the epidemics of diseases, such as bubonic plague, typhus, and cholera which swept through Europe and Asia prior to the end of the nineteenth century, leaving huge death tolls in their wake.

The classic microbiologic definition of cause was initially proposed by Jacob Henle in 1840 and later modified by his student Robert Koch in 1882. The *Henle-Koch's postulates* explained disease etiology in terms of a near one-to-one ("deterministic") relationship between an agent and disease. Limitations in explaining both infectious and noninfectious diseases are now widely recognized (79). For additional information about infectious diseases, see **Airborne and Emerging Infectious Diseases.**

4.1.2 Chronic Disease

With the emergence of *chronic disease* as the primary causes of morbidity and mortality, the epidemiologic approach that met with the most success was based on a biostatistical understanding of causes and contributors to the disease process. Many of the advanced biostatistical methods of studying chronic disease were motivated by the lack of success met by other approaches in identifying the causes and predictors of increasingly prevalent chronic diseases. In addition to the problem of uncertain etiology, many *chronic diseases* were (and are) characterized by insidious onset, occurring only after prolonged exposure to the etiologic factor.

Chronic diseases are diseases of long duration that seldom result in complete cures. Because they often result in a loss of function, impairment, and long-term disability, chronic diseases are also called degenerative diseases.

4.2 Common Analytical Methods and Tools

4.2.1 Introduction

The tools and methods we use to calculate risk are models intended to replicate, simulate, or mimic our natural environment and the fauna and flora which occupy it. The fundamental model for this analysis is the Source-Pathway-Receptor model (Fate and Transport model) conceived visually as shown in Figure 6.

The results of a risk assessment will never exceed the quality of the data used as input to the process. There are, however, software products that provide a methodology and structure to the entire risk analysis process. There are two primary types of risk analysis methods:

Qualitative risk analysis is a simplified process of identifying hazards and judging the significance of the risks. A

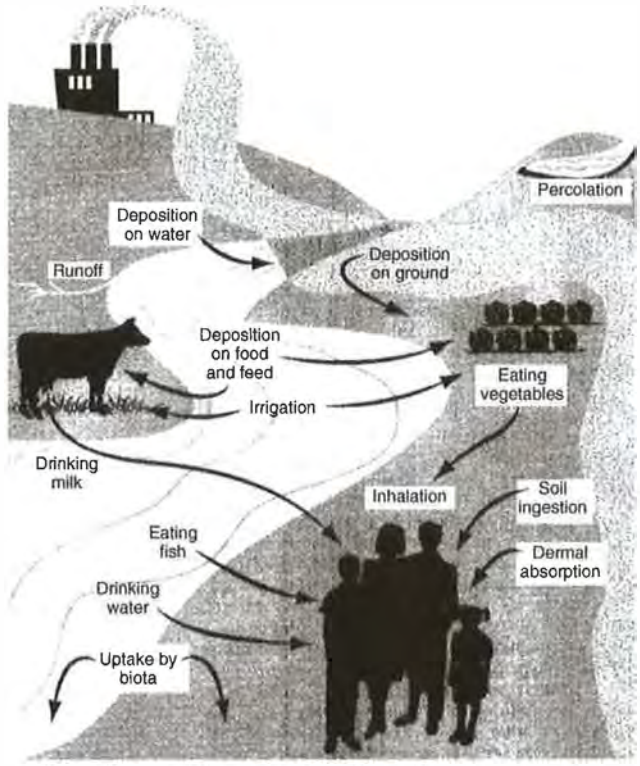

FIGURE 6 Source-pathway-receptor model.

qualitative assessment, however, may not by itself be used to determine the cause but may be sufficient to rule out the significance of particular risks or contributions. More complex questions, forensic investigations, and root cause analyses will require a more advanced risk analysis.

Quantitative risk analysis requires data, equations, references, and judgments. Even with a quantitative process, there are relatively simple screening-level models based on "look up" tables and more sophisticated models using physiologically based pharmacokinetic (PBPK) modeling. The appropriateness of a particular quantitative process will depend on the complexity of the questions, availability of resources, and the implications of the analysis to risk management or risk mitigation.

This "tiered approach," moving from qualitative to quantitative, from screening levels to site specific, and based on the type and quality of the available information, is common in industrial hygiene as well as in environmental analyses and assessment of risk.

4.2.2 Occupational Health

In terms of sequence, an *exposure assessment* must precede a *risk assessment*. Qualitative tools can often be used when conducting an exposure assessment. An empirical exposure assessment taking into consideration data quality has greater

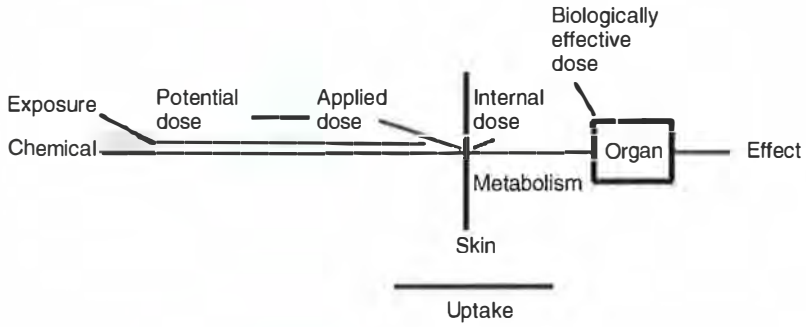

FIGURE 7 Dermal route of entry.

scientific confidence, and probably validity, than a screening-level assessment based on unsubstantiated facts and anecdotal recollections.

4.2.2.1 CONCENTRATION Industrial hygienists can perform "worst-case" calculations using a steady state model:

$$C = G \div Q$$

where C is concentration at steady state; G is contaminant generation rate; Q is volumetric flow rate.

$$P_A = \gamma \cdot X_A \cdot P_A^0$$

where P_A is the partial pressure of the solvent in the mixture; γ is the activity coefficient; X_A is the mole fraction of solvent in the mixture; $P_A{}^0$ is vapor pressure of pure solvent.

4.2.2.2 DOSE Dose is defined as the mass of the agent uptake in the body per unit time. Using a dose analysis as a risk assessment tool depends of the quality and quantity of data and whether there is dose comparison information. The general dose equation is expressed as the Average Daily Dose (ADD):

$$\text{ADD}_{\text{int}} = [C \times \text{IR} \times \text{ED} \times \text{EF} \times \text{AF}] \div [\text{BW} \times \text{AT}]$$

where ADD_{int} is average daily dose internal; C is average concentration at the body boundary; IR is average intake rate; ED is exposure duration; EF isexposure frequency; AF is absorption factor; BW is body weight; AT is averaging time.

Exposure can be a concentration or quantity of an agent that contacts external body parts. The ADD can be calculated for each route of entry (dermal, inhalation, oral) from the following exposure and uptake diagrams and principles:

a) Dermal – The *dose model for the dermal route of entry* can be portrayed as follows (Figure 7):

The dose model for dermal absorption shows that Exposure, Potential Dose, and Applied Dose are equivalent at the outside boundary of the skin. The Internal Dose is based on characteristics of absorption through intact or broken skin.

Partial Immersion in a Liquid (area of the skin in contact is known) – Mathematically, the dose for dermal route of entry liquid where at least partial immersion occurs would be calculated:

$$\text{ADD}_{\text{int}} = [C \times \text{KP} \times \text{SA} \times \text{ED}] \div [\text{BW} \times \text{AT}]$$

where ADD_{int} is average daily dose internal; C is concentration at the skin surface; KP is permeability coefficient; SA is surface area; ED is exposure duration; BW is body weight; AT is averaging time.

Applied Dose (Area of the skin in contact is not known) – Mathematically, the dose for dermal route of entry liquid where a dose is administered or applied would be calculated:

$\text{ADD}_{\text{int}} = [C \times M_{\text{medium}} \times \text{AF}] \div [\text{BW} \times \text{AT}]$ where ADD_{int} is average daily dose internal; C is concentration at the skin surface; M_{medium} is amount (mass) of carrier medium material applied to the skin; AF is absorption factor; BW is body weight; AT is averaging time.

b) Inhalation – The *dose model for the inhalation route of entry* can be portrayed as follows (Figure 8):

The dose model for inhalation shows that Exposure is related to the concentration in the breathing zone outside the nose or mouth. Potential Dose is the amount which passes through the upper respiratory system while Applied Dose is the amount at the point of transfer or activity typically in the lower respiratory system. The Internal Dose is related to characteristics of transfer in the alveolar region, the Applied Dose per unit time, and the duration of the dose.

Single-Step Intake – Assuming potential dose and applied dose are approximately equal, the internal dose after intake can be estimated by:

$$D_{\text{int}} = D_{\text{app}} \times \text{AF} \approx D_{\text{pot}} \times \text{AF} = C \times \text{IR} \times \text{ED} \times \text{AF}$$

where D_{int} is dose internal; D_{app} is dose applied; D_{pot} is dose potential; AF is absorption factor; C is concentration in the breathing zone; IR is intake rate; ED is exposure duration.

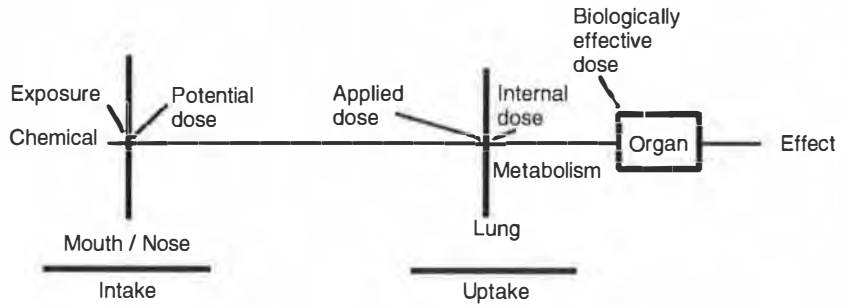

FIGURE 8 Inhalation route of entry.

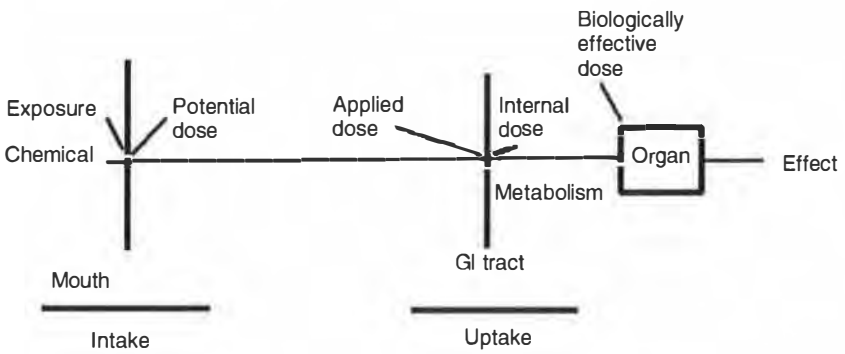

FIGURE 9 Oral route of entry.

Two-Step Intake/Uptake – The ADD_{int} for the two-step intake/uptake process can be estimated by:

$$ADD_{int} \approx ADD_{pot} \times AF = [C \times IR \times ED \times EF \times AF] \div [BW \times AT]$$

where ADD_{int} is average daily dose internal; ADD_{pot} is average daily dose potential; AF is absorption factor; C is average concentration in the breathing zone; IR is average intake rate; ED is exposure duration; EF is exposure frequency; BW is body weight; AT is averaging time.

c) Oral – The *dose model for the oral (ingestion) route of entry* can be portrayed as follows (Figure 9):

The dose model for ingestion shows that Exposure is related to the concentration outside the mouth. Potential Dose is the amount which passes into the mouth and is typically swallowed while Applied Dose is the amount at the point of transfer or activity typically in the gastrointestinal system. The Internal Dose is based on characteristics of transfer in the gastrointestinal (GI) tract region. The equations for Ingestion would be identical to those for Inhalation however the values for AF, IR would be different.

d) Exposure Reconstruction of Total Exposure – Often, *total exposure (proportional to potential dose) is a concentration over an interval of time.* The general equation for intake processes (e.g. inhalation and ingestion) is the integration of the chemical intake rate (concentration of the chemical in the medium times the intake rate of the medium, e.g. C times IR) over time. It is given as the formula:

$$D_{pot} = \int_{t_1}^{t_2} C(t)\ \ IR(t)\ dt$$

The above formula can thus be transformed to the following general formula:

$$D_{pot} = \overline{C} \cdot \overline{IR} \cdot ED$$

where D_{pot} is dose potential outside the body; C is average concentration (eight-hour TWA every day over the course of a year); IR is average intake rate (breathing rate, ingestion rate, transfer rate); ED is exposure duration (years).

Dose potential is an amount (mass, number, etc.) as opposed to a concentration. For the inhalation route of entry, the individual's intake rate (e.g. breathing rate) is typically not known, and intake rate is typically not used when assessing the significance of inhalation exposures of individuals. For the inhalation route of entry, epidemiological and industrial hygiene literature expresses total exposure (often interchangeably referred to as dose) in the units of

concentration times time as opposed to an amount (e.g. mass or number). Thus for the inhalation route of entry, the above equation reduces to:

$$E_{\text{Total}} = C \times \text{ED} \propto D_{\text{pot}}$$

where E_{Total} is total exposure outside the body; C is average concentration (eight-hour TWA every day over the course of a year); ED is exposure duration (years); D_{pot} is dose potential; α is proportional to.

This formula serves as the basic model for conducting an exposure reconstruction assessment for the inhalation route of entry.

4.2.3 *Other Health, Environmental, and Ecological Tools*

The US EPA has a range of tools available for considering *exposure assessment* and *risk assessment*, mitigation and control, and background levels. A few of these tools have application to assessing occupational questions as well.

These tools provide risk calculations to assist risk assessors, remedial project managers, and others involved with risk assessment and decision-making.

4.3 Health Hazard Analysis

4.3.1 *Biomonitoring*

Biomarkers are defined by the NAS as "xenobiotically induced alteration in cellular or biochemical components or processes, structures or functions that is measurable in a biological system or sample (80)." Biomonitoring is the science of measuring those alterations in body fluids, tissue, or exhaled air over a period of time.

One of the important advantages of biomonitoring is that it allows the internal dose to be quantified. Air monitoring quantifies the concentration of the contaminant in ambient air, or the external dose, but the internal dose depends on absorption factors during inhalation, ingestion, and dermal contact. In addition, biomonitoring can provide human internal dose data and eliminate the need to extrapolate from one species to another.

4.3.2 *Ecological Risk Assessment*

The US EPA (81) developed a three-pronged ecological risk assessment with each aspect directly linked to risk management. The three aspects of ecological risk assessment are *problem formulation, analysis*, and *risk characterization.* This model emphasizes the importance of problem formulation and requires stakeholder input and discussion between risk assessors and risk managers during this initial stage. The analysis stage requires that the expected concentration of a toxicant be divided by the concentration at which the effects of the toxicant are deemed acceptable (82). Typically, these concentrations are framed as lethal dose or concentration for 50% of the population under study. The third stage of ecological risk assessment requires characterization of the risk. The specific risk has to be evaluated both in terms of the uncertainty associated with the calculation of the risk and the importance of the risk compared to all the other possible agents of adverse effects in the ecosystem.

The idea of ecological risk assessment emerged in the nineties and is based on two essential premises: (i) human health depends directly on a healthy environment, and (ii) the environment is a well buffered, delayed response system that absorbs a multitude of insults without apparent negative consequences until it catastrophically collapses.

4.3.3 *Network Theory*

Biomonitoring and ecological risk assessment both evaluate complex, self-correcting, multi-nodal systems or networks that can absorb a multitude of insults without apparent decrease in function. When collapse occurs, however, it typically does so catastrophically and without prior warning. The use of single thresholds to monitor the health and predict outcomes in either of these systems is primitive at best.

In 1999, Barabasi and Albert (83) reported that networks follow a power law distribution rather than a Poisson distribution associated with randomly organized systems. The concepts of growth and preferential attachments account for the nonrandomness of scale-free networks (84). Cell biologists and neuroscientists use network theory to model how cells and the human brain work and react to complex environments. Network theory can be used to investigate how over-fishing can cause trophic cascades or predict responses to perturbations of the food web (85). Network theory also provides a model to integrate social and ecological activity (86).

4.4 Beyond Occupational Exposure Limits and Guidance – The Nonoccupational Arena

OELs are, by definition, standards to be applied to a working population, that is, folks who are encountering their exposure as a result of and during the practice of their occupation. The ACGIH TLV exposure limits (87) are a prime example of OELs.

Despite these admonitions, this has not prevented the use of TLVs by some as the basis for constructing rational schemes that set exposure limits for nonoccupationally exposed persons. An example of this is a detailed method forward by Drs. Calabrese and Kenyon in their 1991 book,

Air Toxics and Risk Assessment, Lewis Publishers (88). In this book, they develop and forward a method in which the TLVs are divided by various factors such that the resulting nonoccupational exposure limit is invariably lower than the OEL.

In the United States, the regulation of occupational exposure is performed by OSHA, whereas nonoccupational exposures are dealt with by EPA. The EPA sets nonoccupational exposure limits using a scheme known as the Integrated Risk Information System (IRIS).

The IRIS nonoccupational exposure limits are significantly lower than the ACGIH TLVs, typically by many orders of magnitude. For example, the RfC (for noncancer risk) for epichlorohydrin is 0.001 mg m^{-3} https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?&substance_nmbr=50.

The current TLV for this compound is 1.895 mg m^{-3} – or about 2000-fold higher.

EPA typically uses the Linearized Multistage Model of carcinogenesis to calculate the low dose risk of a chemical using dose–response data from animals https://www.epa.gov/risk/guidelines-carcinogen-risk-assessment. If one uses this method to calculate the risk at the exposure obtained at TLV values for carcinogens, the estimated risk often falls around a lifetime probability 1 in 1000 of incurring cancer. Acceptable exposure/risk to carcinogens in many nonoccupational settings as determined by the EPA and some state authorities occurs at a dose (and exposure limit) that is about 100- to 1000-fold lower than this level. That is about 1 in 100 000 to 1 in 1 000 000 estimated lifetime risk.

Exposure limits for nonoccupationally exposed persons are invariably lower than for those that are occupationally exposed, and this has a direct impact on how precise and accurate the determination of exposure needs to be. These much lower exposure limits in the realm of nonoccupational exposure also require much more refined models in order to be able to predict conformance with these limits.

5 RISK PROFILING

5.1 Background

The risk ranking and risk profiling methodology do not typically include absolute limits of acceptable or unacceptable risk but rather assure that risks are ranked consistently and that the outcome of the assessment can be categorized in a manner that can be used to link risk assessment outcomes to risk management and risk communication strategies. The acceptable risk level may differ dependent on the objective of the risk assessment and the originator's (e.g. company, agency, organization) tolerance for risk.

5.2 Discussion

Health risk profiling requires the identification of possible risk scenarios, the ranking of the risk using standard criteria, and prioritizing the ranked risks in support of risk management and risk communication efforts. The prioritization is based on estimated probabilities and ensuing consequences.

The steps involved in the risk profiling process include the following:

- Data collection
- Identification of risk scenarios
- Risk ranking each risk scenario
- Risk profiling all risks
- Communicate results of the risk ranking and risk profiling effort
- Conduct feasibility studies
- Develop conformance plan
- Track to completion

Examples of sources of risk scenarios include exposure assessments; incident investigations, inspections, interviews with workers, management and health professionals, and audits. The risk scenario must be expressed as a risk.

Risk matrices can take several forms with an example presented in Figure 10, Risk Ranking Matrix.

The letter ranking "E" represents the highest priority and letter ranking "A" the lowest priority.

Risk management and risk communication responses must be defined for each rating level (E–A). The following issues should be considered in developing the criteria associated with each risk ranking category.

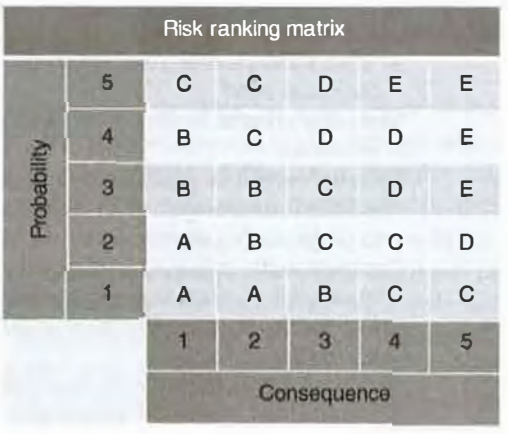

FIGURE 10 Risk ranking matrix. Source: Stenzel, M: "An Overview of Exposure Assessment Techniques." Presented at GeoHealth I: Building across the Geological and Health Sciences, Reston, VA (2008)

- Who should be informed of the risk ranking results?
- What actions are associated with each risk level? For example, the company could decide that all category D and E risk must be lowered to at least category C risk within a specified time frame.
- What are the feasibility criteria (technical and economic) to be used in deciding if a risk level must be lowered? Obviously, the higher the risk, the greater sum of money would be considered financially feasible.
- Who will prepare the mitigation plan and how will conformance with the plan be tracked?
- What are the criteria (e.g. timing of mitigation efforts) that need to be established related to conformance plans?
- Will the mitigation of risk be incorporated into management's performance evaluation?
- What is the risk communication plan as it relates to workers, supervisors, site managers, corporate executive management, and other entities such as government agencies, community leaders, individuals potentially affected by the risk and the press?

Following is an example of the type of criteria that could be used to establish consequence level for the risk matrix.

The consequence levels may be adjusted based on the type of exposure (episodic, chronic, or short-term), the degree of overexposure, or the number of individuals involved (Table 7).

TABLE 7 Consequence levels.

Consequence level	Description of the health effect
1	At most, nuisance effects (e.g. watery eyes or obnoxious odor)
2	Reversible irritation or discomfort (whiff of ammonia)
3	Dermal or inhalation sensitization or reversible toxicity that can impair ability to function or the individual's judgment
4	Dysfunction effects (e.g. lung, kidney, liver, blood), risk of cancer due to suspected human carcinogens, or severe adverse short-term health effects
5	Significant reproductive effects, irreversible neurotoxicity, irreversible toxicity to a significant body system, known human carcinogenicity or mortality from a single exposure (e.g. carbon monoxide, phosgene, hydrogen cyanide)

The probability rating can use several approaches depending on the type of exposure scenario including information from known comparable risk scenarios (episodic exposures); layers of protection (episodic exposures); routine or full-shift chronic exposures; or task or short-term exposures. Table 8 presents examples of probability criteria.

TABLE 8 Probability levels (1–5).

5	*Scenario*: Event is likely to occur at this location sometime during the life of this facility, or; Event has occurred in this specific type of process at another facility using this technology, or; Number of people with excess risk[a] of adverse health effects is more than 100 people, or; *Layers of Protection*: Single failure can cause the event, or; human error(s) alone can cause the event, or; *Routine Chronic Exposures (full-shift)*: all, or; *Task or Short-Term Exposures*[b]: Frequency-Duration Level 4
4	*Scenario*: Event is almost certain to occur in this specific type of process somewhere within the industry during the life of the process, but not necessarily at this location, or; Number of people with excess risk[a] of adverse health effects is 25–99 people, or; *Layers of Protection*: Single level of safeguard *plus* operator interface, or; Failure of safeguard or operator allows the event, or; *Task or Short-Term Exposures*[b]: Frequency-duration level 3
3	*Scenario*: Event is likely to occur somewhere within the industry during the life of this general type process, or; Number of people with excess risk[a] of adverse health effects is 5–24 people, or; *Layers of Protection*: At least two reliable independent levels of safeguards exist, failure of one NOT allowing the event, or; *Task or Short-Term Exposures*[b]: Frequency-duration level 2
2	*Scenario*: Similar events are unlikely to occur, but have occurred infrequently somewhere in the world in a similar process, or; Number of people with excess risk[a] of adverse health effects is 2–5 people, or; *Layers of Protection*: At least three levels of reliable independent systems are in place, failure of two NOT allowing the event, or; *Task or Short-Term Exposures*[b]: Frequency-Duration Level 1
1	*Scenario*: Event should not occur during the life of the process, or; No historical industry experience to suggest that it will occur, or; Number of people with excess risk[a] of adverse health is less than 2 people, or; *Layers of Protection*: At least four levels of reliable independent systems are in place, failure of three NOT allowing the event, or

[a]Number of people with excess risk = (Probability of effect) × (Population at risk).

[b]See frequency and duration adjustment table.

TABLE 9 Chronic exposures – task or short-term exposures. Adjustment for frequency and duration – apply to probability table.

Frequency rating	Task frequency
6	>2 times/day
5	1–2 times/day
4	>2 times/week
3	1–2 times/week
2	>2 times/month
1	<1–2 times/month
Duration rating	*Task duration*
6	>4 hours/day
5	2–4 hours/day
4	1–2 hours/day
3	30–60 minutes/day
2	10–30 minutes/day
1	<10 minutes/day
Frequency-duration level (probability rating)	*Frequency × duration*
4	28–36
3	19–27
2	10–18
1	1–9

The calculation of the frequency and duration level, mentioned under Task or Short-Term Exposures can be found in Table 9.

Examples of various types of layers of protection include the following:

- Preventative measures
  - check valves, control systems, alarms
- Administrative measures
  - training, operating procedures, preventive maintenance schedules
- Mitigation measures
  - relief valves, secondary containment, fire suppression systems

Note that PPE is not a layer of protection.

5.3 Summary

The risk profiling process allows management to proactively identify risk scenarios and their severity rather than risk identification through incidences. The risk profiles can be used to efficiently allocate resources (personnel and financial) to assure that the operation is run consistent with the company's tolerance for risk.

6 MANAGING RISK

6.1 Insurance and Legal Implications

Legal and insurance issues arise for risk assessment when they are done poorly, incorrectly, or even in circumstances when they are appropriately done, but claims are asserted nonetheless. For all subsequent claims of injury related to an alleged causative exposure, the assessment will be viewed with hindsight and criticized for the slightest real or perceived fault.

It is not possible to provide in the abstract every issue that should be considered and addressed or all situations in which legal issues may arise. There are, however, several considerations that can be addressed generally for any risk assessment.

Timing of the risk assessment. For new product releases, risk assessment should be done in advance of sales. For exposures in the workplace, a risk assessment might be performed before, during, or after exposures. Repeat assessments may be warranted depending upon the circumstances. Timing can be a significant issue if there are later claims related to an exposure (claimants allege that there was early notice of an issue and assessment should have been done earlier). Risk assessment in the courtroom will usually be postexposure and disease.

Risk assessments are not performed in the abstract and should be viewed in light of the purpose of the assessment, as well as future claims or issues that might arise. Consultation with legal counsel may be appropriate where the assessment is for new products, environment, or worker health. Risk assessment can also be approached from a multidisciplinary approach. Risk managers should seek guidance from experts in the fields impacted by their work environment and production.

6.2 Economic Implications

Economic analysis includes an assessment of the costs, benefits, and cost-effectiveness of risk management actions, as well as assessments of the costs, benefits, and cost-effectiveness of the most promising alternative actions. To compare the effects of proposed regulations with the effects of promising alternatives, economists estimate both the incremental benefits and costs associated with increasing the stringency of regulation and the incremental foregone benefits and cost savings associated with decreasing the stringency of regulation (89). The information on incremental costs and benefits helps risk managers choose which controls to include and which to exclude when presented with a variety of options for dealing with a public health problem. Economic analysis may also point out ways to increase the cost-effectiveness of regulation.

The standard paradigm states that risk analysis is made up of three components: *risk assessment, risk management*, and *risk communication*. It has been argued that these components should be kept separate in the interest of scientific integrity and to make sure results are not affected by political pressure.

Many tools in economic analysis are often misrepresented by detractors as a means to prevent regulation. For example, CBA is often criticized for promoting de-regulation because the costs are not measured in a way that is comparable with the benefits. Another criticism is that it doesn't yield a "fair" result. Finally, CBA is criticized for discounting effects because it is believed to "de-value" human life and health (33).

The perceived ethical issues associated with discounting benefits are very similar to the concerns with monetizing benefits. In both cases, information is reduced to a calculation or a number. Discounting helps evaluate the costs and benefits of policies whose effects occur in the future or extend over a long period of time. Some of the controversies derive from the selection of an appropriate discount rate. With a high discount rate, future costs, and benefits of a policy or project become insignificant. The controversy is mostly about how the discount rate affects benefits of averting long term, but potentially catastrophic problems, such as global warming, nuclear waste disposal, or long-latency cancers. However, once costs and benefits are monetized, what is being discounted is money, not lives (90).

For all the reasons above, transparency in policy formulation and the peer review process in CBA and other studies such as risk assessment are very important. Increasing the transparency of analyses and more explicitly addressing uncertainty and the quality of the information that underlies them may be part of the process for improving public acceptability.

6.3 Impact of Management Standards

Management system standards, such as ISO 9000, 14000, and 45000, as well as ANSI Z-10, are based on the think-do-check-act paradigm, and are designed to manage risk. In these standards, risk is defined as a combination of likelihood of occurrence and magnitude of effect. In his book (91), former OSHA Assistant Secretary, David Michaels, recommends that corporations, businesses, and government entities formulate their own specific hazard abatement plan and then be required to adhere to it. The type of risk assessment methodology set forth in management system standards would facilitate this integrated approach to risk assessment and risk management. Thresholds based on dose–response curves would be a part of this integrated approach, but hazards for which there is no threshold would be as important a part of the risk assessment as those for which an exposure limit exists.

Management system standards are constantly evolving. Newer iterations of ISO 9000, 14000, and ANSI Z10 as well as the recently published ISO 45000, Occupational Safety and Health Management System Standard, emphasize the importance of systems thinking. Risk applies to the organization as a whole as well, as to specific concerns, such as workplace health or financial outcomes, within the organization.

The current ISO definition of risk is "the effect of uncertainty on objectives." In this context, risk can be either positive or negative. Traditionally human health risk assessment identifies risk as negative and something to be avoided. Using this methodology exclusively, risk should be reduced.

7 REACTION TO RISK

7.1 Physiological and Psychological Basis of Risk

How we see the world influences everything we do, including how people perceive risk. What we think and how we perceive the world is intimately connected to our bodies, particularly our endocrinological and neurological systems.

The paleocortex regulates bodily function in general such as blood pressure, breathing rate, movement of food through the intestines, heart rate, sweating in response to heat, shivering in response to cold, anxiety responses, and vegetative states. Typically, these reactions are classified as subconscious. The subconscious part of the brain consists of the brain stem and limbic. The brain stem and limbic system begin processing information even before the cognitive areas are aware that it exists.

The brain stem and limbic system receive input from the senses such as touch, sight, and taste as well as from internal body functions such as the digestive tract and the cardiovascular system (92, 93). Some of the information may never reach the cortex and never be integrated into conscious thought. Subconscious effects on decision-making and risk-taking arise from several sources including (i) physiological states related to, for example, hunger, thirst, tiredness; (ii) remembered emotions such as anger, fear, reward, and punishment; and (iii) emotions associated with the current situation such a pain, depravation, disasters. In many cases, these subconscious effects operate quickly and effectively without any cortical, or conscious, recognition, or control.

In birds and mammals, the older system of coordination is overlain with cortex, a newer layer of neurons, and connecting fibers called the neocortex. Typically this is where seeing, hearing, talking, thinking, and reasoning occurs. The neocortex is considered the seat of rational

thinking, planning, and complex analysis and deliberation. "Thinking Fast and Slow" by Daniel Kahneman (94) roughly identifies the paleocortex with thinking fast and the neocortex with thinking slow.

Decision-making, associated with the pre-frontal cortex, is often a balancing act with risk-taking, associated with the limbic system. In fact, making decisions in the face of ambiguity involves at least 24 separate areas of the brain (as identified by functional Magnetic Resonance Imaging, fMRI), more areas than are involved in making decisions in the face of risk (95, 96). Decision-making is also influenced by many other inputs including trust, loss aversion, and mental models (anticipatory schemes).

Decision-making and risk taking are affected not only by the subconscious brain but also by hormones. This may be a generalized effect on the somatic state of the individual, or a more specific effect such as how testosterone modulates risk aversion (97). Oxytocin, a polypeptide protein produced in the hypothalamus which is another part of the limbic system strongly promotes trust between and among humans. Oxytocin is released during intimate human activity such as intercourse and breast-feeding, as well as during positive social interactions like hugging. Experimental use of oxytocin significantly increases pro-social behavior (98) possibly by reducing activity in the limbic system (amygdala) associated with fear and anxiety (99). Subjects given a whiff of oxytocin are more likely to give their money to an investor than those not exposed to oxytocin (100).

Even though the subconscious, by definition, is not consciously perceived, it is an integral and powerful part of decision-making. It may be described as "gut" feelings independent of cognitive thought. It relies on somatic states, both remembered and currently being experienced or imagined. It is reactive, emotion-based and, for better or worse, how human make most decisions in their daily lives.

Research continues on how other areas of the brain participate in decision-making, as well as how hormones affect human perception and decision-making. The amygdala has a major role in incorporating emotions into decision-making and "processing emotionally salient stimuli related to threat, danger, and aversion (101)." The signaling among the amygdala, the orbitofrontal cortex, and the striatum appears to be especially important when there is increased uncertainty during risky decision-making (95). Whitson and Galinsky (102) report increased activity in the amygdala of individuals who lacked control over their situation. These individuals are also more likely to perceive patterns in random or unrelated stimuli (auditory or visual). Whitson and Galinsky (102) further postulate that individuals who cannot gain control objectively are more likely to create control perceptually.

8 RESOURCES

The following is a list of useful risk resources:

1. Current Intelligence Bulletin 69: NIOSH Practices in Occupational Risk Assessment. *Suggested Citation:* NIOSH (2020). Current intelligence bulletin 69: NIOSH practices in occupational risk assessment. By Daniels RD, Gilbert SJ, Kuppusamy SP, Kuempel ED, Park RM, Pandalai SP, Smith RJ, Wheeler MW, Whittaker C, Schulte PA. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. DHHS (NIOSH) Publication No. 2020-106, (revised 03/2020), https://doi.org/10.26616/NIOSHPUB2020106revised032020. *Weblink:* https://www.cdc.gov/niosh/docs/2020-106
2. *NIOSH Chemical Carcinogen Policy: Suggested Citation* – NIOSH (2016). Current intelligence bulletin 68: NIOSH chemical carcinogen policy. By Whittaker C, Rice F, McKernan L, Dankovic D, Lentz TJ, MacMahon K, Kuempel E, Zumwalde R, Schulte P, on behalf of the NIOSH Carcinogen and RELs Policy Update Committee. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2017-100. *Weblink:* https://www.cdc.gov/niosh/docs/2017-100
3. *EPA Risk Assessment Guidelines:* EPA has a series of manuals and guidelines that they have developed and posted to their website. All the documents linked on this site are relevant. *Weblink:* https://www.epa.gov/risk/risk-assessment-guidelines
4. Society for Risk Analysis (www.sra.org) – has a trilogy of documents that outline the essentials of risk analysis.
   (a) *Risk Analysis: Fundamental Principles. Weblink:* https://www.sra.org/wp-content/uploads/2020/04/SRA-Fundamental-Principles-R2.pdf
   (b) *Core Subjects of Risk Analysis. Weblink:* https://www.sra.org/risk-analysis-overview/core-subjects
   (c) *Society for Risk Analysis Glossary. Weblink:* https://www.sra.org/risk-analysis-overview/glossary
5. The Occupational Environment – Its Evaluation and Control, 3rd Edition aka "The White Book", Edited by Daniel H. Anna, ISBN: 978-1-935082-15-6, American Industrial Hygiene Association, Fairfax, VA (2011).
6. Mathematical Models for Estimating Occupational Exposure to Chemicals, 2nd Edition, Keil CB, Simmons CE and Anthony TR editors, American

Industrial Hygiene Association, ISBN: 978-1-935082-10-1, Fairfax, VA (2009).
7. Risk Assessment Principles for the Industrial Hygienist, American Industrial Hygiene Press, ISBN: 0-932626-9708, 2700 Prosperity Avenue, Fairfax, VA, May, 2000.
8. A Strategy for Assessing and Managing Occupational Exposure, American Industrial Hygiene Press, ISBN: 0-935082-46-0, 3141 Fairview Park Drive, Suite 777, Falls Church, VA 22042, 2015.

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REFERENCES

1. Food & Drug Administration (FDA) (2020). The FDA's evolving regulatory powers, Part I: The 1906 Food and Drugs Act and its enforcement. https://www.fda.gov/about-fda/fdas-evolving-regulatory-powers/part-i-1906-food-and-drugs-act-and-its-enforcement (accessed 17 September 2020).
2. Stokstad, E. (2009). Putting chemicals on a Path to Better risk Assessment. *Science* **325**: 694–695.
3. Lehman, A.J. and Fitzhugh, O.G. (1954). 100-fold margin of safety. *Assoc Food Drug Off USQ Bull* **18**: 33–35.
4. Dourson, M.L. and Stara, J.F. (1983). Regulatory history of experimental support of uncertainty (safety) factors. *Regul Toxicol Pharmacol* **3**: 224–238.
5. Merrill, R.A. (1997). Regulatory toxiciology. In: *Cassarett and Doull's Toxicology, the Basic Science of Poisons* (ed. C.D. Klaassen), 1011–1023. New York: McGraw Hill.
6. American Conference of Governmental Industrial Hygienists (ACGIH) (2009). www.acgih.org.
7. Paustenbach, D.J. (1990). Health risk assessment and the practice of industrial hygiene. *Am Ind Hyg Assoc J* **51**: 339–351.
8. Faustman, E.M. and Omenn, G.S. (1997). Risk assessment. In: *Cassarett and Doull's Toxicology, the Basic Science of Poisons* (ed. C.D. Klassen), 75–88. New York: McGraw-Hill.
9. Crump, K.S. (1980). An improved procedure for low-dose carcinogenic risk assessment from animal data. *J Environ Pathol Toxicol* **5**: 675–684.
10. Paustenbach, D. (ed.) (2002). *Human and Ecological Risk Assessment: Theory and Practice*. New York: John Wiley & Sons.
11. Alice Ottoboni, M. (1997). *The Dose Makes the Poison*, 2e. New York: John Wiley & Sons.
12. Paustenbach, D.J. (1995). The practice of health risk assessment in the United States (1975-1995): how the U.S. and other countries can benefit from that experience. *Hum Ecol Risk Assess* **1** (1): 29–79.
13. Bachman, J. (2007). Will the circle be unbroken: a history of the US National Ambient Air Quality Standards. *J Air Waste Manage Assoc* **57** (6): 652–697. doi: 10.3155/1047-3289.57.6.652.
14. EPA/100/R-14/001 (2014). *Framework for human health risk assessment to inform decision making*. Office of the Science Advisor, Risk Assessment Forum, www.epa.gov/raf, April 2014.
15. NRC (2009). Science and decisions: advancing risk assessment, Consensus Study Report, National Research Council, National Academies Press.
16. Doull, J., Klaassen, C.D., and Amdur, M.O. (ed.) (1980). *Cassarett and Doull's Toxicology*, 2e. New York: Macmillan Publishing Co, Inc.
17. Mausner, J.S. and Kramer, S. (1985). *Mausner & Bahn Epidemiology – An Introductory Text*, 2e. Philadelphia: W.B. Saunders Company.
18. National Research Council (NRC) (1994). *Science and Judgment in Risk Assessment*. Washington, DC: National Academy Press.
19. National Research Council (NRC) (1983). *Risk Assessment in the Federal Government: Managing the Process – Working Papers*. Washington, DC: National Academy Press.
20. Environmental Protection Agency (EPA) (2004). *Risk Assessment Principles and Practices, Office of the Science Advisor*. Washington, DC: EPA.
21. Anderson, E.L. (1983). Quantitative approaches in use to assess cancer risk. *Risk Anal* **3** (4): 277–295.
22. Armitage, P. and Doll, R. (1957). A two-stage theory of carcinogenesis in relation to the age distribution of human cancer. *Br J Cancer* **11**: 161–169.
23. DOE (2020). The Risk Assessment Information System (RAIS), sponsored by the U.S. Department of Energy (DOE). https://rais.ornl.gov/home/glossary.html#H (accessed 16 September 2020).
24. NIOSH (2016). Current intelligence bulletin 68: NIOSH chemical carcinogen policy. By Whittaker C, Rice F, McKernan L, Dankovic D, Lentz TJ, MacMahon K, Kuempel E, Zumwalde R, Schulte P, on behalf of the NIOSH Carcinogen and RELs Policy Update Committee. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS(NIOSH) Publication No. 2017-100.
25. Jayjock, M.A., Lewis, P.G., and Lynch, J.R. (2001). Quantitative level of protection offered to workers by ACGIH

threshold limit values (TLV®) occupational exposure limits. *Am Ind Hyg Assoc J* **62**: 4–11.

26. National Academy of Sciences (1991). *Human Exposure Assessment for Airborne Pollutants – Advances and Opportunities*. Washington, DC: National Academy of Sciences/National Research Counsel, Commission on Geoscience, Environmental, and Resources.
27. Jayjock, M.A., Chaisson, C.F., Arnold, S., and Dederick, E.J. (2007). Modeling Framework for Human Exposure Assessment. *J Expo Sci Environ Epidemiol* **17**: S81–S89.
28. AIHA (2009). In: *Mathematical Models for Estimating Occupational Exposure to Chemicals*, 2e (ed. C.B. Keil, C.E. Simmons and T. Renee Anthony). Fairfax, VA: AIHA Press. ISBN: 13978-1-935082-10-1. Also, Drolet, D. a. A. T. (2018). MS Excel® workbook of deterministic and Monte Carlo Simulation mathematical models to estimate airborne concentrations of chemicalsMS Excel® workbook of deterministic and Monte Carlo Simulation mathematical models to estimate airborne concentrations of chemicals: AIHA, EASC. Retrieved from http://bit.ly/eascaiha.
29. Jayjock, M.A. (1997). Uncertainty analysis in the evaluation of exposure. *Am Ind Hyg Assoc J* **58** (5): 380–382.
30. Jayjock, M.A. (1995). Uncertainty as the Bane of the risk assessment process. Testimony before the President's Commission on Risk Assessment and Risk Management, Washington, DC, 14 September 1995.
31. Jekel, J.F., Katz, D.L., and Elmore, J.G. (2001). *Epidemiology, Biostatistics, and Preventive Medicine*, 2e, 125–127. Philadelphia: W.B. Saunders Company (Harcourt health Science).
32. Ruckelshaus, W.D. (1984). Risk in a free society. *Environ Law Reporter* **14**: 10190.
33. Sunstein, C.R. (2002). *Risk and Reason: Safety, Law, and the Environment*, 124. New York, NY: Cambridge University Press. ISBN: 0-521-79199-5.
34. Groeneweg, J. (1996). *Controlling the Controllable. The Management of Safety*, 3e. Leiden, The Netherlands: DSWO Press (Leiden University). ISBN: 9066951303.
35. Bernstein, P.L. (1996). *Against the Gods: The Remarkable Story of Risk*. New York, NY: John Wiley & Sons. ISBN: 0-471-12104-5.
36. Jayjock, M. (2020). Risk Assessment 101, Rohm and Haas Company, Presentation. http://www1.udel.edu/ccr/risk/jayjock/download/risk12.pdf.PDF (accessed 17 September 2020).
37. NIOSH (2018). *Mini-Symposium on Cumulative Risk Assessment*. https://blogs.cdc.gov/niosh-science-blog/2018/11/26/cra (accessed 17 September 2020).
38. EPA/630/P-02/001F (2003). U.S. Environmental Protection Agency's Risk Assessment Forum, Framework for Cumulative Risk Assessment. https://www.epa.gov/sites/production/files/2014-11/documents/frmwrk_cum_risk_assmnt.pdf.
39. National Academy of Sciences (1983). *Risk Assessment in the Federal Government: Managing the Process*. Washington, DC: Committee on the Institutional Means for Assessment of Risks to Public Health, National Research Council. ISBN: 10: 0-309-03349-7.
40. Barnthouse, L.W. and Suter, G.W. (1986). *User's Manual for Ecological Risk Assessment*. Oak Ridge National Laboratory, ORNL-6251.
41. EPA/600/9-91-050 (1992). Safeguarding the future: credible science, credible decisions. Environmental Protection Agency (USEPA), The Report of the Expert Panel on the Role of Science at EPA, Washington, DC.
42. Suter, G.W. and Barnthouse, L.W. (1993). *Ecological Risk Assessment*. Boca Raton, FL: CRC Press, LLC. ISBN: 0-87371-875-5.
43. Lehrer, J. (2009). *How We Decide*. Boston, MA: Houghton Mifflin Company. ISBN: 13/EAN: 9780618620111.
44. Lubchenco, J. (1998). Entering the century of the environment: a new social contract for science. *Science* **79**: 491–497.
45. Wilson, E.O. (1998). *Consilience: The Unity of Knowledge*. New York, NY: Alfred A. Knopf. ISBN: 0-679-45077-7.
46. National Research Council (1991). *Animals as Sentinels of Environmental Health Hazards*. Washington, DC: Board on Environmental Studies and Toxicology, NRC, National Academy Press. ISBN: 0-309-04046-9.
47. Burkhart, J.G. and Gardner, H.S. (1997). Non-mammalian and environmental sentinels in human health: back to the future? *Hum Ecol Risk Assess* **3**: 309–328.
48. Sheffield, S.R., Matter, J.M., Rattner, B.A., and Guiney, P.D. (1998). Fish and wildlife as sentinels of environmental endocrine disruptors. In: *Principles and Processes for Evaluating Endocrine Disruption in Wildlife* (ed. R.J. Kendall, J.P. Giesy, R.L. Dickerson and W. Suk), 369–430. Pensacola, FL: Society of Environmental Toxicology and Chemistry, SETAC Press. ISBN: 13: 9781880611173.
49. Stahl, R.G. (1997). Can mammalian and non-mammalian "sentinel species"; data be used to evaluate the human health implications of environmental contaminants? *Hum Ecol Risk Assess* **3**: 329–335.
50. ISO (2020). ISO was founded with the idea of answering a fundamental question: "what's the best way of doing this?" https://www.iso.org/benefits-of-standards.html (accessed16 September 2020).
51. Williams, E.S., Panko, J., and Paustenbach, D.J. (2009, Review Article). The European Union's REACH regulation: a review of its history and requirements. *Crit Rev Toxicol* **39** (7): 553–575.
52. ECHA (2020). https://echa.europa.eu (accessed 16 September 2020).
53. Adkins, C., Booher, L., Culver, D. et al. (2009). Updating PELs: is now the time? *Synergist* **20** (9).
54. Jahn, S., Bullock, W.H., and Ignacio, J.S. (ed.) (2015). *A Strategy for Assessing and Managing Occupational Exposures*, 4e. Fairfax, VA: AIHA.
55. Hewitt, P., Logan, P., Mulhausen, J. et al. (2006). Rating exposure control using Bayesian decision analysis. *J Occup Environ Hyg* **3**: 568–581.
56. Logan, P., Gurumurthy, R., Mulhausen, J., and Hewett, P. (2009). Occupational exposure decisions: can limited data interpretation training help improve accuracy? *Ann Occup Hyg* **53**: 311–324.
57. ACGIH (2008). Control banding: issues and opportunities. ACGIH Exposure/Control Banding Task Force, 21 February 2008.
58. Sussman, R.G. (2009). Criteria for OEL development. Presented at AIHCE, Science Symposium 2009, Toronto, Canada.

59. Boelter, F.W. and Redinger, C.F. (2018). *Risk in the Healthy Place of Work: Improve Risk Analysis through Structured Decision Making*, 30–33. The AIHA Synergist https://synergist.aiha.org/201812-risk-in-the-healthy-place-of-work (accessed 17 September 2020).
60. Kromhout, H., Symanski, E., and Rappaport, S.M. (1993). A comprehensive evaluation of within- and between-worker components of occupational exposure to chemical agents. *Ann Occup Hyg* **37**: 253–270.
61. Arnold, S.F., Stenzel, M., Drolet, D., and Ramachandran, G. (2016). Using checklists and algorithms to improve qualitative exposure judgment accuracy. *J Occup Environ Hyg* **13** (3): 159–168. doi: 10.1080/15459624.2015.1053892.
62. Kephalopoulos, S, A. Arvanitis, M.A. Jaykock (2005). Source characterization, transport and fate. Global CEM Net Report of the Workshop no. 2, Intra (Italy), 20–21 June 2005.
63. Van Doren, C. (1991). *A History of Knowledge: The Invention of the Scientific Method*. New York, NY: Random House Publishing Group. ISBN: 0-345-37316-2.
64. U.S. Department of Health and Human Services (2016). Office of the Assistant Secretary for Planning and Evaluation, guidelines for regulatory impact analysis. https://aspe.hhs.gov/pdf-report/guidelines-regulatory-impact-analysis (accessed 17 September 2020).
65. John D. Graham (2008). Saving lives through administrative law and economics, 157 U. Pa. L. Rev. 395.
66. Kofi Asante-Duah, D. (2002). *Public Health Risk Assessment for Human Exposure to Chemicals*, 62. Kluwer Academic Publishers.
67. Griffiths, C.W., Dockins, C., Owens, N. et al. (2002). What to do at low doses: a bounding approach for economic analysis. *Risk Anal* **22** (4): 679–688.
68. Jaynes, E.T. (2003). *Probability Theory: the Logic of Science*, 100. Cambridge University Press.
69. Federal Reserve Bank of San Francisco (2020). What is the difference between private and social costs, and how do they relate to pollution and production? https://www.frbsf.org/education/publications/doctor-econ/2002/november/private-social-costs-pollution-production (accessed 17 September 2020).
70. Vose, D. (1996). *Quantitative Risk Analysis: A Guide to Monte Carlo Simulation Modeling*. West Sussex, England: John Wiley & Sons Ltd.
71. Morgan, G. (1990). Choosing and managing technology induced risk. In: *Readings in Risk* (ed. T.S. Glickman and M. Gough), 20. Washington, DC: Resources for the Future.
72. Leigh, J.P., Markowitz, S.B., Fahs, M., and Landrigan, P.J. (2000). *Costs of Occupational Injuries and Illness*. Ann Arbor, MI: University of Michigan Press.
73. CDC (2020). Cost of Illness: what is cost of illness analysis? Associate Director for Policy and Strategy, Centers for Disease Control and Prevention. https://www.cdc.gov/policy/polaris/economics/cost-of-illness.html (accessed 17 September 2020).
74. Yabroff, K.R., Davis, W.W., Lamont, E.B. et al. (2007). Patient time costs associated with cancer care. *J Natl Cancer Inst* **99** (1), 14–23. doi: 10.1093/jnci/djk001.
75. Viscusi, W.K. and Aldy, J.E. (2003). The value of a statistical life: a critical review of market estimates throughout the world. *J Risk Uncertain* **27** (1): 5–76.
76. Merrill D. (2017). No One Values Your Life more than the Federal Government. Bloomberg LP [US], 19 October 2017. Sources: Handbook of the Economics of Risk and Uncertainty, U.S. agencies. https://www.bloomberg.com/graphics/2017-value-of-life (accessed 17 September 2020).
77. Adler, M.D. (2006). QALYs and policy evaluation: a new perspective. *Yale J Health Policy Law Ethics* **6**: 1, 27 January 2010, AEI-Brookings Joint Center Working Paper No. 05-01, U of Penn, Inst for Law & Econ Research Paper No. 05-08, U of Penn Law School, Public Law Research Paper No. 61, 10.2139/ssrn.655865 (accessed 17 September, 2020).
78. Bauer, M.D., Rudebusch, G.D. (2020). The rising cost of climate change: evidence from the bond market. Federal Reserve Bank of San Francisco Working Paper 2020-25. 10.24148/wp2020-25 (accessed 17 September 2020).
79. Gerstman, B. (1998). *Epidemiology Kept Simple: An Introduction to Traditional and Modern Epidemiology*. Wiley, John & Sons, Inc.
80. Kendall, R.J., Bens, C.M., Cobb, G.P. et al. (2007). Aquatic and Terrestial Ecotoxicology. In: *Casarett and Doull's Toxicology, the Basic Science of Poisons* (ed. C.D. Klaassen), 883–905. New york: McGraw-Hill.
81. U.S.EPA (1992). *Risk Assessment Forum: Framework of Ecological Risk Assessment*. EPA/630R-92-019. Washington, DC: EPA.
82. Bascietto, J., Hinckley, D., Platkin, J., and Slimak, M. (1990). Ecotoxicity and Ecological Risk Assessment. *Environ Sci Technol* **24**: 10–15.
83. Barabasi, A.-L. and Albert, R. (1999). Emergence of scaling in random networks. *Science* **286**: 509–512.
84. Barabasi, A.-L. (2009). Scale-free networks: a decade and beyond. Emergence of scaling in random networks. *Science* **325**: 412–413.
85. Bascompt, J. (2009). Disentangling the web of life. *Science* **24**: 416–419.
86. Ostrom, E. (2009). A general framework for analyzing sustainability of social-ecological systems. *Science* **24**: 419–422.
87. ACGIH Threshold Limit Values. www.acgih.org.
88. Calabrese, E.J. and Kenyon, E.M. (1991). *Air Toxics and Risk Assessment*, 480. Chelsea, MI: Lewis Publishers, Inc. ISBN: 0-87371-165-3.
89. Mendeloff, J.M. (1988). *The Dilemma of Toxic Substance Regulation: How Overregulation Causes Underregulation*, 174. Cambridge: MIT Press. https//mit.press.mit.edu.
90. Sunstein C. and Rowell, A. (2005). On discounting regulatory benefits, risk, money, and intergenerational equity. AEI Brookings, Joint Center for Regulatory Studies, Working Paper 05-08. The University of Chicago Law and Economics. Olin Working Paper No. 252. page 8.
91. Michaels, D. (2008). *Doubt is Their Product: How Industry's Assault on Science Threatens Your Health*. Oxford: Oxford University Press.
92. Venkatramen, A., Edlow, B.L., and Immordino-Yang, M.H. (2017). The Brainstem in Emotion: A Review. *Front Neuroanat* **11**: 1–12.

93. Balogh, K.N., Mayes, L.C., and Potenza, M.N. (2013). Risk-taking and decision-making in youth: relationships to addiction vulnerability. *J Behav Addict* **2** (1): 1–14.
94. Kahneman, D. (2011). *Thinking, Fast and Slow.* New York, Farrar, Straus and Giroux.
95. Hsu, M., Bhatt, M., Adolphs, R. et al. (2005). Neural systems responding to degrees of uncertainty in human decision-making. *Science* **310**: 1680–1683.
96. Rustichini, A. (2005). Emotion and reason in making decisions. *Science* **310**: 1624–1625.
97. Sapienza, P., Zingales, L., and Maestripieri, D. (2009). Gender differences in financial risk aversion and career choices are affected by testosterone. *PNAS* 8 September 2009, **106** (36): 15268–15273. doi: 10.1073/pnas.0907352106.
98. Kosfeld, M., Heinrichs, M., Zak, P.J. et al. (2005). Oxytocin increases trust in humans. *Nature* **435**: 673–676.
99. Kirsch, P., Esslinger, C., Chen, Q. et al. (2005). Oxytocin modulates neural circuitry for social cognition and fear in humans. *J Neurosci* **25** (49): 11489–11493.
100. Baumgartner, T., Heinrichs, M., Vonlanthen, A. et al. (2008). Oxytocin shapes the neural circuitry of trust and trust adaptation in humans. *Neuron* **58**: 639–650.
101. Oya, H., Kawasaki, H., Howard, M.A., and Adolphs, R. (2002). Electrophysiological responses in the human amygdala discriminate emotion categories of complex visual stimuli. *J Neurosci* **22**: 9501–9512.
102. Whitson, J.A. and Galinsky, A.D. (2008). Lacking control increases illusory patter perception. *Science* **322**: 115–117.

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