# 1. GENERAL INTRODUCTION

C.J. VAN LEEUWEN

## 1.1 INTRODUCTION

Over the last few decades there has been considerable activity in the field of risk assessment. This has mainly taken place in international bodies such as the Organization for Economic Co-operation and Development (OECD), the World Health Organization (WHO) - especially in the context of its International Programme on Chemical Safety (IPCS) - the European and Mediterranean Plant Protection Organization (EPPO), the Council of Europe and the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) [1-10]. Various directives and regulations in which risk assessment plays a crucial part have been issued by the European Community [11-14] and similar activities are taking place in other parts of the world, e.g., the U.S., Canada and Japan. Most of these developments would not have taken place without the contributions of many expert advisory bodies and individual scientists.

Historically, risk assessments have primarily focused on risks to human beings. It has gradually become apparent, however, that the ecological implications of large-scale environmental pollution should also receive attention. A situation has now been reached whereby detrimental ecological effects, caused e.g., by deforestation, food production (agriculture), excessive energy consumption, as well as the production and use of chemicals, have begun to threaten biological diversity and ecosystem integrity, and thus humanity's very existence. Accidents such as that at Chernobyl, the Sandoz disaster on the river Rhine, and recent cases of massive river pollution in China with benzene and cadmium, have increased awareness of the ecological and economic consequences inherent in such disasters.

Risk assessment is a central theme in the control of chemicals. Despite the role of risk assessment as the scientific foundation for many national and international regulatory guidelines, the phrase "risk assessment" means different things to different people and is often surrounded by misunderstandings and controversy. Some points of controversy involve the interpretation of scientific studies. Others have to do with science policy issues. Still others centre on definitions and on the distinctions between risk assessment and risk management. Some important definitions are given in Table 1.1.

The scope and nature of risk assessments range widely, from broadly based scientific analyses of air pollutants affecting a nation as a whole, to site-specific studies concerning chemicals in a local water supply. Some assessments are retrospective, focusing on the effects of a pollution incident, for example, the risks posed by a particular chemical dump site. Others seek to anticipate or predict possible future harm to human health or the environment, for example of a newly developed pesticide approved for use on food crops. In short, risk assessment takes many different forms, depending on its intended scope and purpose, the available data and resources, and other factors [15].

Risk management decisions may have local, regional or national consequences, but measures taken by a single country may also have world-wide consequences. Pollution does not recognize national borders. That is why the risk management of chemicals has become an important issue on the international agenda.

The development and international harmonization of risk assessment methodologies is recognized to be a great challenge. In Agenda 21 of the United Nations Conference on Environment and Development (UNCED), chapter 19 was entirely devoted to the management of chemicals [16]. The first recommendation of UNCED was to expand and accelerate the international assessment of chemical risks (Table 1.2), which requires mutual acceptance of hazard and risk assessment methodologies. Mutual acceptance of hazard and risk assessment methodologies (Figure 1.1) is considered to be the second essential step in the risk management process of chemicals, after international agreement was reached on the mutual acceptance of data by the member countries of the OECD [17]. The implementation of Agenda 21 is a long-term commitment. Therefore, it is no coincidence that chemicals were again high on the agenda of the World Summit on Sustainable Development in Johannesburg in 2002.


Figure 1.1. Mutual acceptance of data (cf. words) and hazard or risk assessment methodologies (cf. grammar) is essential to arrive at mutually accepted risk reduction measures (cf. language).



*C.J. van Leeuwen and T.G. Vermeire (eds.), Risk Assessment of Chemicals: An Introduction*, 1–36.

Table 1.1. Definitions of terms commonly used in the field of risk assessment and management.

| |
|---|
| *Hazard* is the inherent capacity of a chemical or mixture to cause adverse effects in man or the environment under the conditions of exposure |
| *Risk* is the probability of an adverse effect on man or the environment occurring as a result of a given exposure to a chemical or mixture |
| *Risk assessment* is a process which entails some or all of the following elements: hazard identification, effects assessment, exposure assessment and risk characterization |
| *Hazard identification* is the identification of the adverse effects which a substance has an inherent capacity to cause, or in certain cases, the assessment of a particular effect |
| *Effects assessment*, or more precisely, dose-response assessment is the estimation of the relationship between dose or level of exposure to a substance, and the incidence and severity of an effect |
| *Exposure assessment* is the determination of the emissions, pathways and rates of movement of a substance and its transformation or degradation in order to estimate the concentrations/doses to which human populations or environmental compartments are or may be exposed |
| *Risk characterization* is an estimate of the incidence and severity of the adverse effects likely to occur in a human population or environmental compartment due to actual or predicted exposure to a substance, and may include "risk estimation", i.e., the quantification of that likelihood |
| *Risk management* is a decision-making process that entails weighing political, social, economic, and engineering information against risk-related information to develop, analyse and compare regulatory options and select the appropriate regulatory response to a potential health or environmental hazard |
| *Risk reduction* is taking measures to protect man and/or the environment from the risks identified |
| *Safety* is defined as the strong probability that adverse effects will not result from the use of a substance under specific conditions, depending on quantity and manner of use |

In this chapter a description is given about the risk management process in general. In Section 1.2 the 8 different steps are described. They reflect the current regulatory practice in most countries, where the work is mainly done by the public authorities. In Section 1.3 a number of changes are described that reflect recent developments such as the focus on risk reduction and responsible care *(reversal of the burden of proof)*, risk communication, the importance of stakeholder participation in all stages of the risk management process, risk assessment policy and integration in risk assessment. In Section 1.4 disciplines, roles and responsibilities in the risk management process are described. How risks are expressed is explained in Section 1.5 and risk perception is described in Section 1.6. Section 1.7 focuses on uncertainty, variability and precaution and Section 1.8 provides some concluding remarks. Finally, Section 1.9 gives a more detailed overview of the different chapters of the entire book.

## 1.2 THE RISK MANAGEMENT PROCESS

Risk encompasses impacts on public health and on the environment, and arises from exposure and hazard. Risk does not exist if exposure to a harmful substance or situation does not or will not occur. Hazard is determined by whether a particular substance or situation has the potential to cause harmful effects. The risk management process is triggered by concerns about the risks of particular uses of a chemicals or particular situations.

Table 1.2. Environmentally-sound management of toxic chemicals as recommended by UNCED [16].

| |
|---|
| a. Expanding and accelerating the international assessment of chemical risks |
| b. Harmonization of classification and labelling of chemicals |
| c. Information exchange on toxic chemicals and chemical risks |
| d. Establishment of risk reduction programmes |
| e. Strengthening of national capabilities and capacities for management of chemicals |
| f. Prevention of illegal traffic in toxic and dangerous products |


Figure 1.2. The conventional wisdom is that risk management should not influence the processes and assumptions made in risk assessment. Regulatory practice, however, shows that the two elements depend on each other like Yin and Yang.

Risk assessment and risk management are closely related but different processes, with the nature of the risk management decision often influencing the scope and depth of a risk assessment [15]. In simple terms, risk assessors ask "How risky is this situation?" and risk managers then ask "What are we willing to accept?" and "What shall we do about it?" Risk assessment is usually seen as the objective/scientific part of the process and risk management as the subjective/political part. The distinction between these two components is important, though controversial. The conventional wisdom - which needs rethinking (Figure 1.2) - is that risk management should not influence the processes and assumptions made in risk assessment: the two functions should be kept conceptually and administratively separate [18]. Risk assessment provides *information* based on the analysis of scientific data which describe the form, magnitude, and characteristics of a risk, i.e. the likelihood of harm to humans or the environment. Although risk assessment is mainly a scientific task, political decisions are required on matters such as: "What are we trying to protect and to what extent should it be protected?" Endpoints, unacceptable effects, magnitude of uncertainty factors are controversial topics and based on implicit political choices. Questions about risk often have no scientific answers or the answers are multiple and contestable.

Risk management is about taking *measures* based on risk assessments and considerations of a legal, political, social, economic, and engineering nature. It is mainly a political process, although science is involved in the gathering of technical, social or economic information. The entire risk management process consists of eight steps (Figure 1.3), in which steps 1-4 belong to the risk assessment phase, while steps 5-8 are in the domain of risk management.

### 1.2.1 Hazard identification (step 1)

Hazard identification is the identification of the adverse effects that a substance has an inherent capacity to cause. It is the likelihood of harm due to exposure that distinguishes risk from hazard. Hazard identification involves gathering and evaluating data on the types of health effects or disease that may be produced by a chemical and exposure conditions under which environmental damage, injury or disease will be produced. For example, a toxic chemical that is hazardous to human health does not constitute a risk unless humans are exposed to it. The observed effects in humans may include reproductive defects, neurological defects or cancer. Ecological hazards include lethal effects, such

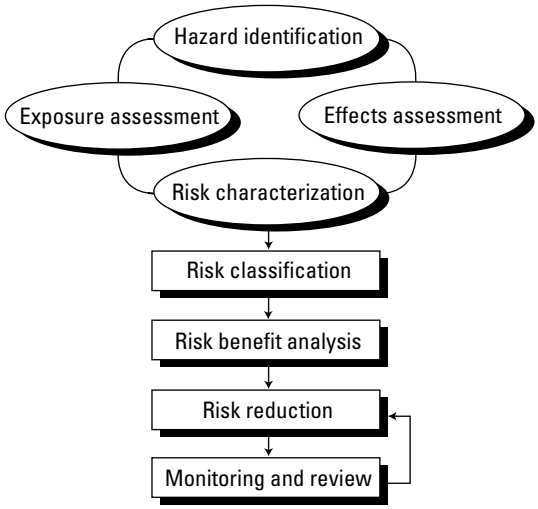


Figure 1.3. Steps in the risk management process.

as fish or bird mortality and sub-lethal effects on the growth and reproduction of various populations. This information may come from experimental laboratory studies, accidents or from other sources such as measured residues in fish or high concentrations detected at the workplace.

Hazard identification may also involve characterization of the behaviour of a chemical within the body and its interactions with organs, cells, or genetic material. The principal question is whether data from populations in which toxic effects and exposure occur suggest a potential problem for other populations under similar exposure conditions. Once a hazard (potential risk) has been identified, a number of other steps become important.

### 1.2.2 Exposure assessment (step 2)

Exposure can be assessed by measuring exposure concentrations, once chemicals are produced, used and emitted. With new chemicals, exposure assessments can only be predictions. This involves estimating emissions, pathways and rates of movement of a substance and its transformation or degradation in order to obtain concentrations or doses to which human populations or environmental compartments are or may be exposed. It involves describing the nature and size of the populations or compartments exposed to a substance, and the magnitude and duration of their exposure. The evaluation may concern past or current exposures, or anticipated future exposures. Multimedia exposure models are often used, especially in environmental exposure assessment (Chapter 4). Exposure assessment is also an uncertain part of risk assessment because of the lack of information on emission factors during the production of chemicals *(point-source pollution)*, and about the use of chemicals in various products and their emissions *(diffuse sources of pollution)*. The enormous geographic variability caused by differences in abiotic conditions, such as climate (e.g. temperature, humidity, wind speed, and precipitation), hydrology (e.g. different dilution factors in streams, lakes and rivers), geology (e.g. soil type) and biotic conditions (differences in ecosystem structures and functions) also contribute to this uncertainty. Exposure varies with time and depends on process-technology and the safety measures taken. It is therefore not surprising that measured environmental concentrations often differ by several orders of magnitude [19]. The same applies to occupational exposure and direct exposure to consumer products. It may be concluded that measurements of actual concentrations can help to reduce uncertainties in exposure assessment, but only for existing chemicals, not for new ones!

In health risk assessment (HRA) the various exposure routes are often combined in order to determine a total daily intake, expressed as mg per kg body weight per day. In ecological risk assessment (ERA) there is no single PEC or total daily intake, in fact, there are many PECs. This complexity is often simplified by deriving PECs for single environmental compartments: water, sediment, soil and air.

### 1.2.3 Effects assessment (step 3)

Effects assessment or, more precisely, dose-response assessment, is the estimation of the relationship between dose or level of exposure to a substance, and the incidence and severity of an effect. It sometimes involves the description of the quantitative relationship between the degree of exposure to a substance and the extent of a toxic effect or disease, but reliable quantitative precision cannot always be achieved. Data are generally obtained from (quantitative) structure-activity relationships (Chapters 9 and 10), read-across and *in vitro* studies or from experimental plant and animal laboratory studies or, less frequently, from experimental field studies with plants or animals, or epidemiologic studies of ecosystems and human populations (Chapters 6 and 7) or combinations of these (Chapter 11). Different dose-response relationships may be found if a substance produces different toxic effects. For instance, short-term exposure to high concentrations of benzene may produce lethal effects (acute toxic effects), whereas cancer may

be induced as a result of long-term exposure to relatively low concentrations (chronic carcinogenic effects).

For most chemicals, no effect levels (NELs) derived from studies in laboratory animals are converted into predicted or estimated NELs (PNELs or DNELs) for humans or the environment by applying *assessment factors* usually in the range of 10-10,000 [2,20-22]. Assessment factors are numbers reflecting the estimated degree or amount of uncertainty when experimental data from model systems are extrapolated to humans or ecosystems. The rationale for assessment factors is that if no assessment factors are applied large groups of the human population or large parts of ecosystems will remain unprotected. This is because laboratory tests cover only a small part of the variety of responses that may occur in ecosystems and in human populations [2,20-22]. Experiments can yield both "false positives" and "false negatives". Extrapolation involves numerous scientific uncertainties and assumptions, which in turn involve policy choices.

In HRA, risk assessment focuses on one single species. Uncertainty is restricted to differences in sensitivity between laboratory mammals and humans, variations in exposure routes and differences in sensitivity between individuals *(intraspecies variation)*. In ERA millions of species may be exposed via a variety of routes (see Chapter 7). Therefore, many NELs can be determined. Differences in sensitivities between species *(interspecies variation)* play an important part in ERA. This complexity in ERA is often simplified by deriving predicted no effect concentrations (PNECs) for different environmental compartments: water, sediment, soil and air.

Please note that E stands for Effects in the acronym DNEL, PNEL and PNEC and for Exposure in the acronym PEC (predicted environmental concentration).

### 1.2.4 Risk characterization (step 4)

Risk characterization is the estimation of the incidence and severity of the adverse effects likely to occur in a human population or environmental compartment due to actual or predicted exposure to a substance, and may include risk estimation, i.e. the quantification of that likelihood. It generally involves the integration of the previous three steps [23]:

1. Hazard identification.
2. Effects assessment, i.e. the determination of the DNEL or PNEC.
3. Exposure assessment, i.e. the determination of the PEC or human intake or exposure.

A framework to define the significance of the risk is developed, and all the assumptions, uncertainties, and scientific judgements from the preceding three steps are considered. In many international regulatory frameworks environmental risks are often expressed as PEC/PNEC ratios, i.e. as *risk quotients* (Figure 1.4). For human risks a similar comparison between exposure and the NEL is usually made. It should be noted that these ratios or comparisons provide no absolute measure of risks. Nobody knows the real risks of chemicals where the exposure exceeds the PNEC or NEL. We only know that the likelihood of adverse effects increases as the exposure/effect level ratios increase. Thus, exposure/effect ratios are internationally accepted substitutes for risks. It should also be noted that there is no such thing as precise risk assessments and scientists will always differ in the conclusions they draw from the same set of data, particularly if they contain some implicit value judgements.

At the present level of understanding we cannot adequately predict adverse effects on ecosystems, nor can we predict what part of the human population will be affected. We are only able to assess risks in a very general and simplified manner. In fact, the best we can do is provide a *relative risk ranking*. Risk ranking enables us to compare single chemicals or groups of chemicals once the risks of the respective chemicals have been assessed in a consistent "simplified" manner. Nevertheless, relative risk ranking allows us to replace

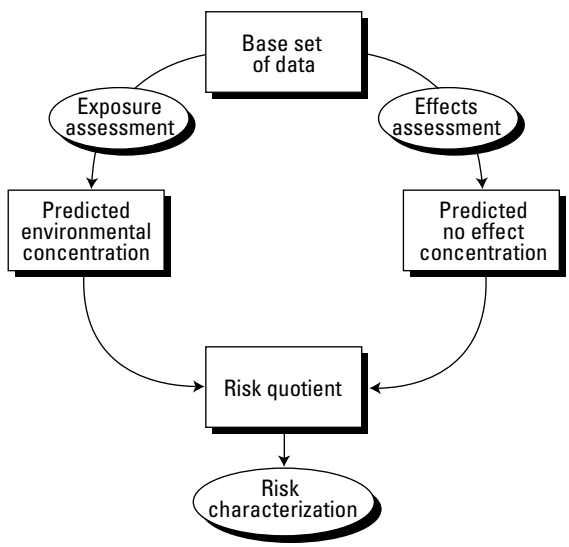


Figure 1.4. Risk characterization: a systematic procedure through estimation of exposure and effects.

dangerous processes, techniques or chemicals with safer alternatives in the risk management phase, without knowing the precise risks.

### 1.2.5 Risk classification (step 5)

Once a risk characterization has been made the focus turns to risk management. The first step in the risk management phase is the classification, i.e., the *valuation of risks* in order to decide if risk reduction is required. It is obvious that risks cannot be evaluated solely on the basis of scientific considerations, but who can decide what is acceptable? Decisions about risk classification are related to *risk acceptance* and must always be taken in a situation of some residual uncertainty. This is the field of policy-makers. According to Bro-Rasmussen [24] the term "acceptability" has become a crucial new element to be considered as a constituent part of the risk management process. The problem of defining operational criteria for "acceptable" and "unacceptable" risks is especially important in relation to the environment. Defining acceptable risk cannot be reduced to a mechanical exercise. It requires scientific knowledge as well as an appreciation of the limits of that knowledge. It requires a good understanding of the context of the risk and it requires willingness, by regulatory agencies as well as by their critics, to deal openly with these difficult, value-laden issues. Acceptability varies with time and place. What was acceptable in the past may not be acceptable in the future, and vice versa (Table 1.3). What may be acceptable in one country may be totally unacceptable in another. Cultural influences on risk management in legal and institutional frameworks are significant. It is important to realize that discussions on acceptability go back to our roots: to our youth, education and culture. In conclusion: risk classification is related to risk acceptability, which in turn is a risk-related, technical, social, cultural, political, educational and economic (conjuncture-dependent) phenomenon.

Over the past decade there has been growing support for defining two risk levels that may help to avoid lengthy debates about acceptability, because the area under discussion is restricted. These risk levels are known as:

- The upper limit, i.e. the maximum permissible level (MPL).
- The lower limit, i.e. the negligible level (NL).

These two risk limits create three zones: a black (high risk) zone, a grey (medium risk) zone and a white (low risk) zone. Actual risks in the black zone above the MPL are unacceptable and further risk management measures (RMMs) are necessary. Actual risks in the white zone below the NL (the *de minimus* level) are negligible (Figure 1.5) and further RMMs are not strictly required [25,26]. In the Netherlands, the lower limit for chemicals has generally been defined as 1% of the upper limit (Table 1.4). This approach has been adopted to take into account factors such as:

- Multiple exposure (additivity of risks and synergistic effects).
- Uncertainties in the estimates (limited testing and specific sensitivity).
- To leave a sufficient margin to distinguish between MPL and NL.

In the grey zone between the upper and lower limits, risk reduction is required based on the *ALARA* principle (as low as reasonably achievable). This is a powerful risk management principle. Managers are expected to do everything possible to reduce risks up to a limit they can justify to their organization and justify to the regulatory authorities. In general, the aim is to reduce risks until the cost of doing so is disproportionate to the benefit.

### 1.2.6 Identification and risk-benefit analysis of risk reduction options (step 6)

Once risk classification has been completed and risk reduction is thought necessary, the next consideration is the identification and analysis of options for risk reduction, and eventually selection of the most appropriate risk reduction option(s). The options for the risk reduction of chemicals range from slight adaptation of the production process or the intended use of the chemical to a complete ban on the production or use of a chemical. To that end a risk-benefit analysis *sensu lato* is carried out by drawing up of a balance sheet of the respective risks and benefits of a proposed risk-reducing intervention as compared to the baseline, i.e. the situation of not imposing risk reduction.

It is essential to remember that the result of risk classification is only one of the many aspects involved in the selection of regulatory options for risk reduction. This is the most difficult step in the risk management process, because it is a multifactorial task in which the risk manager has to consider not only the risk assessment but also other important aspects (Figure 1.6), such as:

- *Technical feasibility:* are measures technically feasible?
- *Social and economic factors:* e.g. what are the costs, do the measures affect employment or, in the case of extremely high risks, do we need to remove people from their homes?

Table 1.3. Changes in the perception of health and environmental risks and their solutions.

| 1970 | 1990 |
|---|---|
| • Sectoral (air or surface water) | • Multiple media (including soil, sediment and groundwater) |
| • Localized | • Diffuse pollution |
| • Human health and well-being | • Ecosystem health, production functions and goods |
| • Local/regional | • National/international |
| • Limited economic damage | • Great economic damage |
| • End-of-pipe solutions | • Integrated approaches |

Table 1.4. Risk limits for chemicals. From [23].

| | Maximum permissible level | Negligible level |
|---|---|---|
| Man: *individual risk* | | |
| chemicals with threshold | $10^{-6}$/y | $10^{-8}$/y |
| chemicals without threshold | PNEL | 1% of PNEL |
| Man: *cumulative risk* | | |
| chemicals without threshold | $10^{-5}$/y | $10^{-7}$/y |
| Ecosystems | PNEC[a] | 1% of PNEC |

[a] The PNEC is determined by using fixed assessment factors (little data) or variable assessment factors (adequate data set) calculated by means of a statistical extrapolation model with an arbitrary cut-off value set at a protection level of 95% of the species [24].

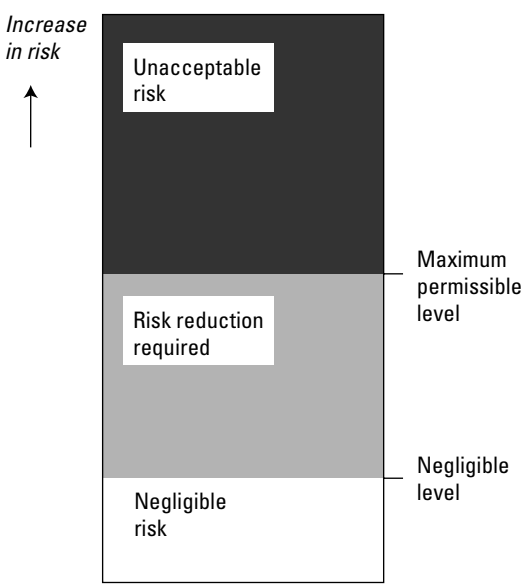


Figure 1.5. Risk limits and risk reduction.

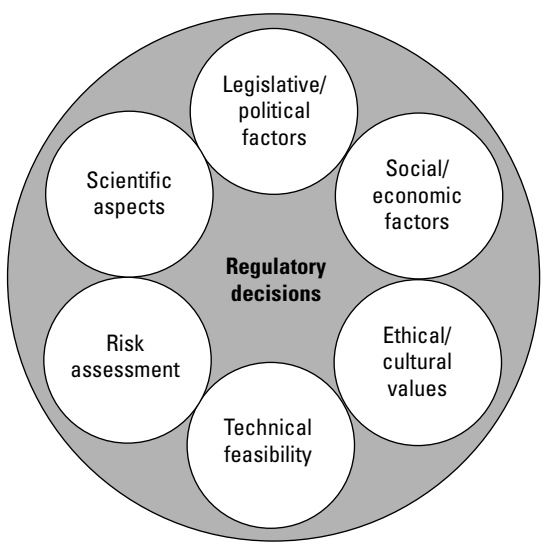


Figure 1.6. Elements in risk management. Modified from the U.S. Congress, Office of Technology Assessment [27].

- *Ethical and cultural values:* e.g. will a potential measure discriminate against specific groups in our society?
- *Legislative/political factors:* legal, regulatory, policy, and litigative constraints or risks, i.e. do we have appropriate regulatory, monitoring and enforcement tools?
- *Scientific aspects:* the limits of science are manifest at different levels; how great are the uncertainties in methodologies, measurements and other observations, extrapolations; do the risks affect mortality, morbidity or both and what assumptions have been made?

Selecting risk-reducing options will trigger "acceptability" discussions, not only about the predicted risks themselves but also about the anticipated consequences of risk reduction measures. This requires *risk communication*: a process by which stakeholders discuss risks and consequences with one another. Because the perception of risks (see Section 1.6) often differs widely, risk communication typically requires a sensitive approach and should involve genuine dialogue. The role of risk communication will be discussed in more detail in Section 1.3.2.

The use of a *cost-benefit analysis*, where the risks reduced by a proposed intervention are juxtaposed to estimate the net benefits (or net costs) to society and thus cover all major changes that will occur as a consequence of imposing a restriction compared with the baseline, is sometimes, but not always, a useful tool in risk management. To gauge benefit in an absolute sense, it is necessary to assign a value to the risk avoided (e.g. lives saved, lifetime extended). In general, the philosophy is that the greater the risk, the greater the incentive to reduce it. Estimated values of saving one additional "statistical life" can vary by at least six orders of magnitude [29,30]. Another relevant term used in this context is *cost-effectiveness* (determination of that action which maximizes the level of risk reduction per unit cost). Environmental risks are also difficult to quantify, although clean-up costs for polluted soil or sediment, as well as loss of fish stocks can be quantified. Cost-benefit analyses are useful in many contexts, certainly in ranking investments in some order of priority and effectiveness. However, this approach can only be a guideline, another input into a decision.

In conclusion, selecting the options for risk reduction using risk-benefit analysis is a multifaceted task centering on discussions about acceptability. Acceptability revolves around facts, value judgements and communication. It is this part of the risk management process in particular, where the lines between science, science policy and policy become fuzzy, that much conflict arises over where the boundary should be drawn [18]. Some of the forces at work in policymaking regarding human health and the environment are shown in Figure 1.7.

### 1.2.7 Risk reduction (step 7)

Risk reduction is taking measures to protect humans and/or the environment against the risks identified. Apart from the factors explained above, a number of additional factors should be taken into account before a risk management decision is taken, including those related to the implementation of RMMs. These considerations include: effectiveness, practicality, monitorability, equity, administrative simplicity, consistency, public acceptability, time, and the nature of the legislative mandate. There are different approaches to risk management (Chapter 2). In this Section only a brief summary will be given.

1. Classification and labelling

Notifiers of chemicals are required to provisionally classify and label dangerous substances on the basis of the intrinsic properties of the chemical. The decision on how to classify and label a substance is based on a series of criteria which themselves are based on the results of standard laboratory tests. The classification and labelling includes assigning a symbol (Figure 1.8), a risk phrase and a safety phrase [31,32]. Classification and labelling can be considered to be the first risk management tool for chemicals.

2. Safety standards

Safety or quality standards are another approach to chemicals control. Such standards are set with the intention of protecting human health and the environment. The terms criteria, guidelines, objectives, and standards, are often used. In this sequence the nature of the values moves from recommendations towards legally binding provisions. The use and interpretation of these terms varies between different agencies and countries. For the purposes of this book, these terms are defined as follows:

- *Criteria* are quality guidelines based on the evaluation of scientific data.
- *Guidelines* are numerical limits or narrative statements that are applied to support and maintain designated uses of the environment or to protect human health.
- *Objectives* are numerical limits or narrative statements that have been established to protect and maintain human health or designated uses of the environment at a particular site.

- *Standards* are fixed upper limits of exposure for certain chemicals that are laid down in enforceable laws or regulations by one or more levels of government.

Well-known examples of standards are the air, water and soil quality standards as well as the threshold limit values (TLVs) for airborne concentrations of industrial chemicals at the workplace. Environmental quality standards and TLVs are the control levels at which exposure is currently considered acceptable. They do not provide assurance of safety. Guidelines, objectives and standards for chemicals are derived from criteria, often by applying safety factors. Another example is the acceptable daily intake (ADI). The ADI is derived by applying a safety factor to no observed effect levels (NOELs) obtained from toxicological studies. An ADI is an estimate of the daily exposure dose that is unlikely to have any detrimental effects even if exposure occurs over a lifetime.

Absolute safety is a special case in safety standards. The most obvious example is the so-called Delaney clause, enacted by the U.S. Congress in 1958 as an amendment to the Food and Drug Act. This requires that no (food) additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal. The introduction of this amendment posed significant problems for the US authorities. In practice, the US authorities abandoned this approach in the mid-1980s.

3. Risk reduction measures *(sensu proprio)*

RMMs may comprise [33]:

- Technical measures such as redesign of production and use processes, closed systems, separation of man

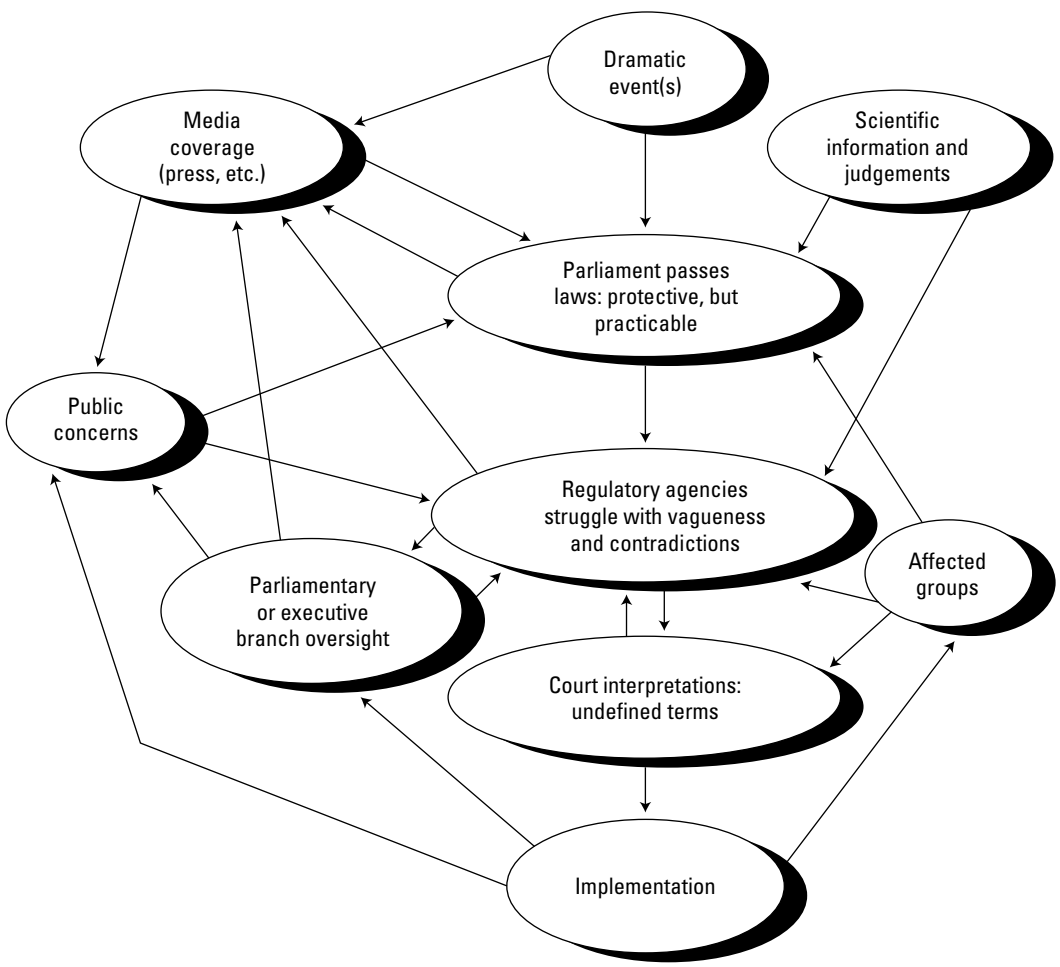


Figure 1.7. Forces in health and environmental policy-making. Modified from Lave and Malès [28]. With permission. Copyright 1989 American Chemical Society.

and sources (by construction measures), exhaustion, ventilation, separation and clarification techniques, physical, chemical and biological treatment.
- Organizational measures such as restriction to certain specific workplaces, limiting time of operation or work activities, training, monitoring and surveillance, prohibiting eating, drinking and smoking at the site.
- Instructions, information and warnings regarding normal use or safe use. This may include classification and labelling as described above.
- Personal protection measures such as gas and dust filter masks, independent air equipment, goggles, gloves and protective clothing.
- Product-substance related measures. Examples include limiting the concentration of a substance in a preparation or article.

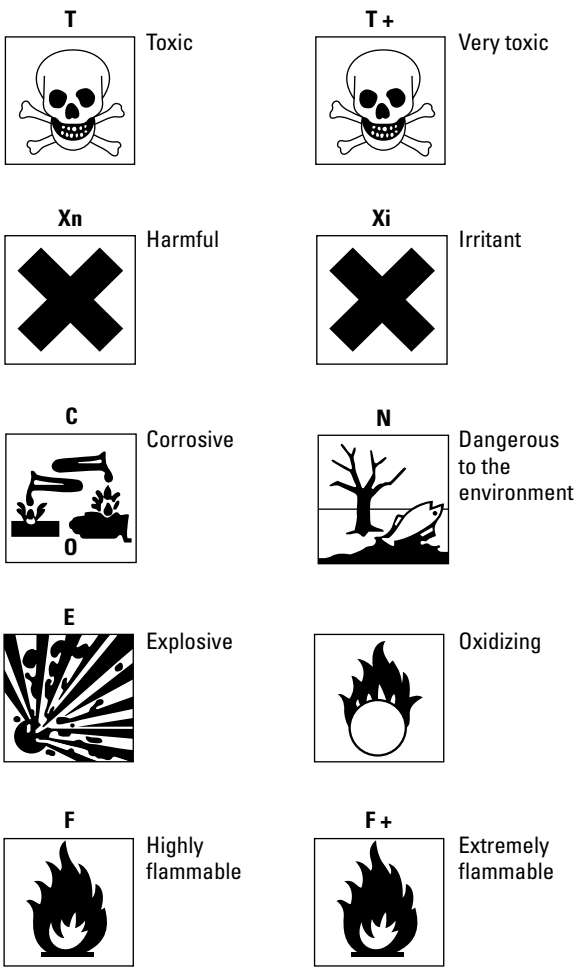


Figure 1.8. Classification and labelling of chemicals is the most frequently applied management tool in the control of chemicals.

- Instructions to limit the use of a substance or product. This can be implemented by limiting certain applications and uses and the restriction of uses with releases, etc.

### 1.2.8 Monitoring and review (step 8)

Monitoring and review is the last step in the risk management process. Monitoring is the process of repetitive observation for defined purposes of one or more chemical or biological elements according to a pre-arranged schedule over space and time, and using comparable and preferably standardized methods. Monitoring is undertaken to ensure that previously formulated standards are being met. In this sense monitoring serves an important function in enforcement (Figure 1.3), i.e. control. Monitoring serves a number of purposes [34]:
- The *control function* to verify the effectiveness of risk reduction (control) strategies and check for compliance.
- The *signal or alarm function* to be able to detect sudden (adverse) changes in human health and the environment. Ideally, the monitoring system should be designed such that the causes can be traced immediately.
- The *trend (recognition) function* to enable the prediction of future developments based on time-series analysis.
- The *instrument function* to help in the recognition and clarification of underlying processes.

Monitoring plays an important role in both environmental and health risk management. In health risk management biomonitoring is a part of the exposure-disease continuum as depicted in Figure 1.9. It can be used for consumer and occupational safety. Both biological monitoring and biochemical effect monitoring are crucial methods to help better understand the complex relationships between external and internal exposure and consequently, the potential adverse health effects that may result from exposure. Just like ambient monitoring, biological monitoring and biochemical effect monitoring should be regarded as exposure monitoring methods with high specificity for the substance being measured. Both methods give a measure of the total actual exposure regardless of the route of exposure [35]. Typical examples of biological monitoring are the determination of metals in blood or urine, unchanged substances (e.g. PCBs) in e.g. adipose tissue or blood, specific metabolites of a chemical in urine or volatile compounds in exhaled

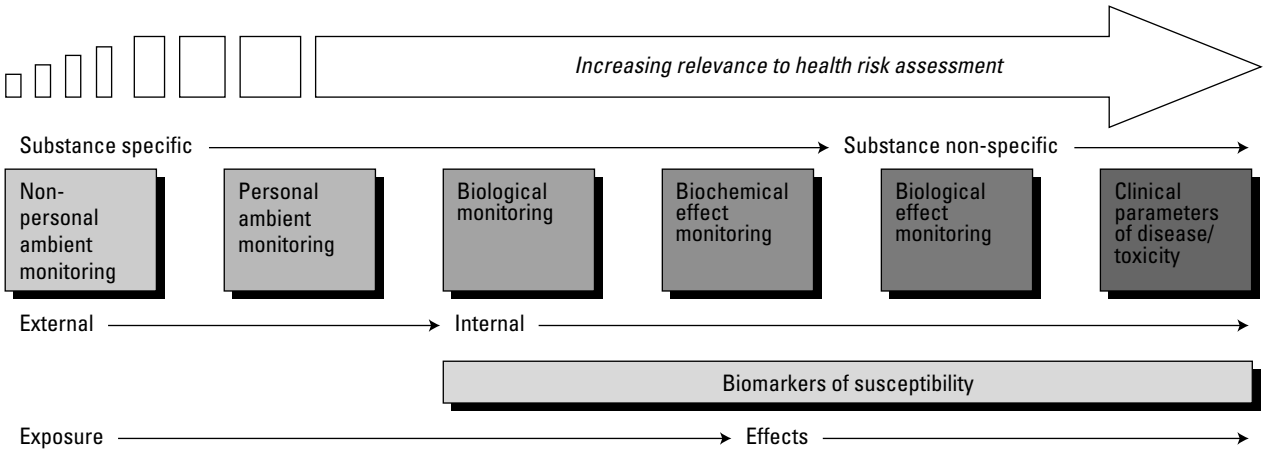


Figure 1.9. Monitoring techniques as part of the exposure-disease continuum according to ECETOC [35]. Non-personal external (ambient) monitoring includes static air monitoring, monitoring of soil, drinking, ground or surface water monitoring, and "food basket" monitoring. Personal external monitoring includes personal air monitoring and dermal exposure monitoring. With permission.

breath. Biochemical effect monitoring includes the determination of adducts of a specific chemical to DNA or a protein, or increased or decreased levels of specific enzyme activities.

Besides monitoring there are many other ways to review environmental and health management measures such as: audits and inspections, voluntary agreements and programmes, reporting (e.g. in case of voluntary agreements), market investigations, economic instruments, product registers, technology assessments, performance measurements and indicators for human health and sustainable development. These are equally important tools used to arrive at sustainable patterns of production, use and disposal of chemicals [36-39].

## 1.3 FURTHER DEVELOPMENTS IN THE RISK MANAGEMENT PROCESS

Section 1.2 described the different steps in the risk management process. These steps reflect the current practices of risk assessment and risk management. Compared to the first version of our book published in 1995, many developments have taken place and a number of them need to be highlighted in this new edition. They are crucial elements in the REACH legislation [40]. The major changes are shown in Table 1.5.

First of all, in the context of the REACH legislation [40], the focus has shifted from risk assessment to risk management, i.e. the implementation of RMMs, and from the principle of the authorities identifying and regulating the risks to industry taking its own responsibility for doing the assessments and implementing the necessary control measures to adequately control the risks.

Secondly, the risk management process has been put in a much wider context. The planning of risk assessments, the problem formulation phase, risk communication and stakeholder participation have all become more important. Communication with all the stakeholders at all stages in the process is crucial. In this respect the report of the US Presidential/Congressional Commission on risk assessment and risk management [41] and the guidelines for ecological risk assessment [42] have had a substantial impact.

The third major development is the inclusion of risk assessment policy as a specific component of risk management, as advocated by the Codex Alimentarius Commission [43]. This particular inclusion can help us to understand disagreements arising from differences in up-stream framing assumptions [43].

The fourth relevant development is the need for further integration between human health and

Table 1.5. Major changes in the risk management process during the last decade.

| |
|---|
| 1. Focus on risk reduction and responsible care |
| 2. Risk communication and stakeholder participation |
| 3. Risk assessment policy and the role of science |
| 4. Integration in risk assessment |

environmental risk assessment [44-48]. These major trends and paradigm shifts will be discussed here in Section 1.3.

### 1.3.1 Focus on risk reduction and responsible care

Under the REACH legislation [40] emphasis will be placed on industry taking its own responsibility for the safe use of chemicals. This will take the form of a formal requirement to draw up *exposure scenarios*. These scenarios will be used as a tool to indicate what risk management measures (RMMs) will be used under what operational conditions to ensure that risks are adequatly controlled during the manufacture and use of chemicals. According to REACH, exposure scenarios will be developed for manufacturing processes and for identified uses of the substance on its own or in a preparation and for all life-cycle stages resulting from these uses.

Exposure scenarios are essential for risk management at the various life-cycle stages to ensure safe handling and adequate control of risks related to human health (workers, consumers and the general population exposed via the environment) and the environment. To be able to make realistic estimates of the exposures, it is important, as a first step, to determine which RMMs are already in place. These measures are an integral part of the overall process of developing exposure scenarios for identified uses of a substance on its own or in a preparation and the life-cycle stages resulting from these uses. How to arrive at appropriate exposure scenarios is an iterative process described in more detail in Chapters 2 and 12. Although a manufacturer or importer is not required to be proactive in seeking information on the uses of their chemicals, it will be beneficial to be so. It would allow them to develop a Chemicals Safety Assessment (CSA) covering all identified uses. Thus, already early in the process of developing the CSA, the manufacturer or importer should identify the uses of their chemicals and obtain sufficient information to develop exposure scenarios, e.g. by approaching customers, to be able to adequately control risks. Relevant RMMs should therefore be taken as a starting point for the development of exposure scenarios under the assumption that the described and recommended measures are implemented.

While in the past the entire risk management process, as described in Figure 1.3, was the responsibility of authorities (except for the implementation of risk reduction), the responsibility has now shifted to industry (manufacturers and importers in collaboration with their downstream users). Furthermore the focus has changed from risk assessment to risk management. These are fundamental changes by which the main policy objectives of REACH are achieved, i.e., the *reversal of the burden of proof* from the authorities to industry for testing and risk assessment and a shift in the focus on identification and implementation of RMMs to controlling the risks of chemicals. In this way REACH could be considered a legal instrument for implementing "responsible care".

Little experience has so far been obtained with exposure scenarios and these new iterative approaches to reduce risks. This redesign of the risk management and the practical tools approach needed to implement "responsible care" or "risk reduction first" will be developed further over the next few years following a stakeholder participation process that will be described in more detail in the next section.

### 1.3.2 Risk communication and stakeholder participation

Risk communication is an essential interactive process among the stakeholders, i.e. risk managers, risk assessors, and those who may directly or indirectly be affected by the risk management decision. The general principles of risk management decision-making are given in Box 1.1. Risk communication is the link between risk assessment and risk management. Stakeholders who could potentially be included in any particular risk assessment are representatives of industry, public and occupational health professionals, public pressure groups, academic experts, specific consumer groups and private citizens. These stakeholders can participate in a number of ways, including assisting in the development of management goals, proposing assessment endpoints, providing valuable insight and information, and reviewing assessment results. Timely engagement of all the stakeholders will help to ensure that different technical perspectives, public values, perceptions, and ethics are considered [33,41,42].

Although the circumstances of stakeholder involvement will vary widely between risk assessments (depending on the regulatory and management context of the assessment), active stakeholder participation helps to ensure understanding and acceptance of assessment results and management actions.

Stakeholder participation and risk communication are key elements in a broad framework for risk management that was developed by the US Presidential/Congressional Commission [41]. This general framework was designed to help all types of risk managers - government officials, private sector business, and individual members of

**Box 1.1. General principles for risk management decision-making [41]**

A good risk management decision:

- Addresses a clearly articulated problem in its public health and ecological context.
- Emerges from a decision-making process that elicits the views of those affected by the decision, so that differing technical assessments, public values, knowledge, and perceptions are considered.
- Is based on a careful analysis of the weight of evidence that supports conclusions about a problem's potential risks to human health and the environment.
- Is made after examining a range of regulatory and non-regulatory risk management options.
- Reduces or eliminates risks in ways that:
  - Are based on the best available scientific, economic, and other technical information.
  - Account for their multisource, multimedia, multichemical, and multirisk contexts.
  - Are feasible, with benefits reasonably related to their costs.
  - Give priority to preventing risks, not just controlling them.
  - Use alternatives to command-and-control regulation, where applicable.
  - Are sensitive to political, social, legal and cultural considerations.
  - Include incentives for innovation, evaluation, and research.
- Can be implemented effectively, expeditiously, flexibly, and with stakeholder support.
- Can be shown to have a significant impact on the risks of concern.
- Can be revised and changed when significant new information becomes available, while avoiding "paralysis by analysis."

the public - make good risk management decisions. This Commission also broadened the definition of risk management. In their view risk management is "the process of identifying, evaluating, selecting, and implementing actions to reduce risks to human health and to ecosystems", whereas the goal of risk management was defined as "scientifically sound, cost-effective, integrated actions that reduce or prevent risks while taking into account social, cultural, ethical, political, and legal considerations". The framework consists of six consecutive stages:

1. Define the problem and put it in context.
2. Analyze the risks associated with the problem in context.
3. Examine the options for addressing the risks.
4. Make decisions about which option to implement.
5. Take actions to implement the decision.
6. Conduct an evaluation of the actions.

Every stage of this framework (Figure 1.10) relies on defining risks in a broader context, involving stakeholders, and repeating the process, or part of it, when needed. The problem formulation phase is the most important step. It establishes the goals, breadth, and focus of the assessment. It is a systematic planning step that identifies the major factors to be considered, linked to the regulatory and policy context of the assessment [42]. This step requires an intensive dialogue between all stakeholders to define the goals of the assessment (Box 1.2). The importance of problem formulation was also highlighted in the USEPA guidelines for ecological risk assessment [42]. Shortcomings consistently identified were: (1) absence of clearly defined goals, (2) endpoints

**Box 1.2. Defining the problems and putting them in a context [41]**

1. Identifying and characterizing an environmental health problem, or a potential problem, caused by chemicals or other hazardous agents or situations.
2. Putting the problem into its public health and ecological context.
3. Determining risk management goals.
4. Identifying risk managers with the authority or responsibility to take the necessary actions.
5. Implementing a process for engaging stakeholders.

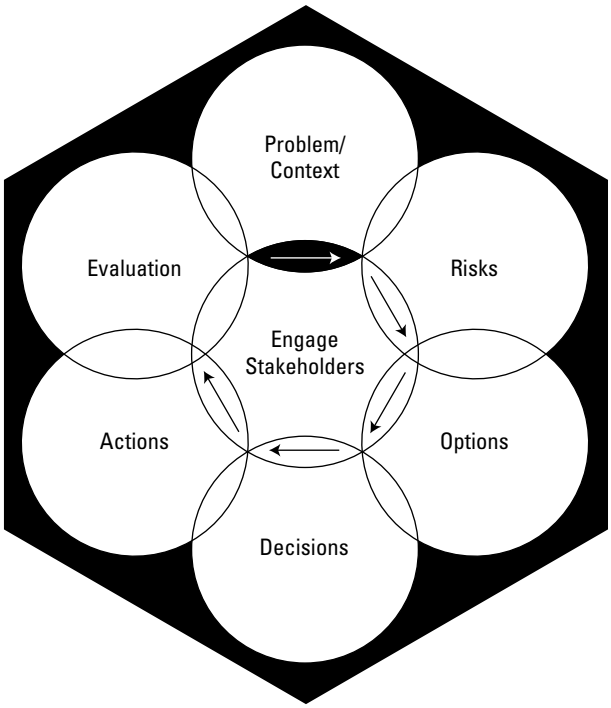


Figure 1.10. Framework for risk management according to the US Presidential/Congressional Commission [41].

that were ambiguous and difficult to define and measure, and (3) failure to identify important risks. These and other shortcomings can be avoided through rigorous development of the products of problem formulation as described by the USEPA [42].

The identification of "what" needs to be assessed is also known as the determination of the *assessment endpoints*. Further dialogue and interaction between risk managers and all other stakeholders will subsequently lead to a scientific and technical way of "how" to measure risk. This is the identification of the *measurement endpoints*. Essentially, this second step is a translation from higher-level decision criteria from the manager to the assessors by formulating evaluation questions with specific assessment and measurement endpoints and a testable hypothesis [49]. It is also during the problem formulation phase that the nature and extent of integration must be defined [45-47]. The involvement of stakeholders at all stages in the risk management process has great advantages (Box 1.3).

### 1.3.3 Risk assessment policy and the role of science

**Risk assessment policy**

A Dutch State-Secretary of science once said that science does not play a decisive role in important political decisions. Whether you agree or not, there is a growing recognition that science, on its own, cannot settle policy questions (see also Sections 1.2 and 1.7), and consequently that policy-makers need to take both scientific considerations and other legitimate factors into account (Figure 1.6). A common approach on the part of the policy-makers and their advisors [50] was to represent these deliberations and policy-making processes in terms of a model that did not acknowledge prior framing judgements. An important part of these framing assumptions concern what the Codex Alimentarius Commission (CAC) calls "risk assessment policy" [43]. According to the CAC *risk assessment policy* comprises documented guidelines on the scope of the assessment, the range of options (and associated judgements for their application) at appropriate decision points in the risk assessment such that the scientific integrity of the process is maintained [43]. Very often, the key difficulty facing risk managers, expert advisors and policy analysts has been to understand how, within the policy-making process, scientific considerations and other relevant factors can be distinguished and separated from each other and yet ultimately brought together to arrive at informed, systematic, complete, unbiased and

**Box 1.3. Seven benefits of engaging stakeholders [41]**

1. Supports democratic decision-making.
2. Ensures that public values are considered.
3. Develops the understanding needed to make better decisions.
4. Improves the knowledge base for decision-making.
5. Can reduce the overall time and expense involved in decision-making.
6. May improve the credibility of agencies responsible for managing risks.
7. Should generate better accepted, more readily implemented risk management decisions.

transparent decisions. The relevance of risk assessment policy has been demonstrated in a critical analysis of trade disputes [50]. The study showed that:

1. Different judgements were made about what the breadth and scope of scientific risk assessments should be.
2. Different judgements were made about the ways uncertainties should be handled by risk assessors, and the significance that should be ascribed to them.
3. Different judgements were made about the benchmarks by reference to which the available evidence is interpreted.
4. Different judgements were made about the "chosen level of protection" i.e. the extent to which risks and uncertainties are socially acceptable.

These *prior framing assumptions* [50], may have to do with very practical questions related to the management context, identification of the assessment and measurement endpoints, or to specific questions related to the data and the risk assessment methodologies [49,50]. Just to mention a few:

1. What management decisions will the risk assessment support?
2. What are the time constraints on performing the risk assessment?
3. What is the budget for the risk assessment, including the collection and generation of additional data and/or modelling?
4. Is there going to be more than 1 assessment (i.e. more than 1 alternative to be examined)?
5. What is the maximum level of uncertainty that will still allow for a decision to be made, and how should uncertainties be handled?
6. What are the reference conditions against which possible adverse effects or risks will be compared?
7. Which impacts are deemed to be within the scope of the assessment and which are outside it?
8. What kind of evidence can be included and what can be discounted?
9. How should the available evidence be interpreted?
10. How much of different kinds of evidence would be necessary or sufficient to justify different judgements?

In conclusion, risk assessment policy judgements have routinely played a key role in risk policy-making processes, but they have often remained implicit, unacknowledged and unexamined [50]. As a result, the CAC [43] concluded that: "the determination of risk assessment policy should be included as a specific component of risk management. Risk assessment policy should be established by risk managers in advance of risk assessment, in consultation with risk assessors and all other interested parties. The procedure aims at ensuring that the risk assessment process is systematic, complete, unbiased and transparent…Where necessary, risk managers should ask risk assessors to evaluate the potential changes in risk resulting from different risk management options."

**The role of science**

Further to the increased emphasis on risk communication and stakeholder participation different levels of scientific involvement can be distinguished. The first type of approach articulated by policy-officials can be encapsulated in what is termed a *technocratic model*. A technocratic model assumes that risk policy can and should be decided solely by reference to scientific considerations and expert advice. In short it is "on, and only on, the basis of sound science" [50]. This reflects the thinking of the 1980s, but has its roots in the 1890s. [51] The technocratic model is incapable of explaining how to make decisions in conditions of acknowledged scientific uncertainties and neglects many other relevant factors, as given in Figure 1.6.

In response to the inadequacies of the technocratic model, an increasingly large portion of public policy-makers and their advisors now represent the processes in which they participate as a *decisionist model* [50]. This closely corresponds to the model described in Figure 1.3. It assumes that risk policy is, and should be, the product of a two-stage process, the first of which is purely scientific (risk assessment) and a second one that includes economic, social, technical, political and other considerations, often called risk management. This model reflects the thinking of the early 1990s. The decisionist model assumes that the risk assessment phase is entirely independent on any and all risk management considerations and judgements which, of course, it is not (Figure 1.2). For instance, every mandatory risk assessment of a chemical starts with an explicit political decision about the core set of data - the basis - on which a risk assessment will be performed. These discussions have been dominated by politicians, not only decades ago, e.g. in discussions about minimum data requirements (pre-marketing set of data or base set in the OECD and the EU respectively), but also more recently in the context of the political discussion about REACH.

The results of the study of trade disputes [50] can effectively be incorporated in a third model on how science and governance should interact. This third model

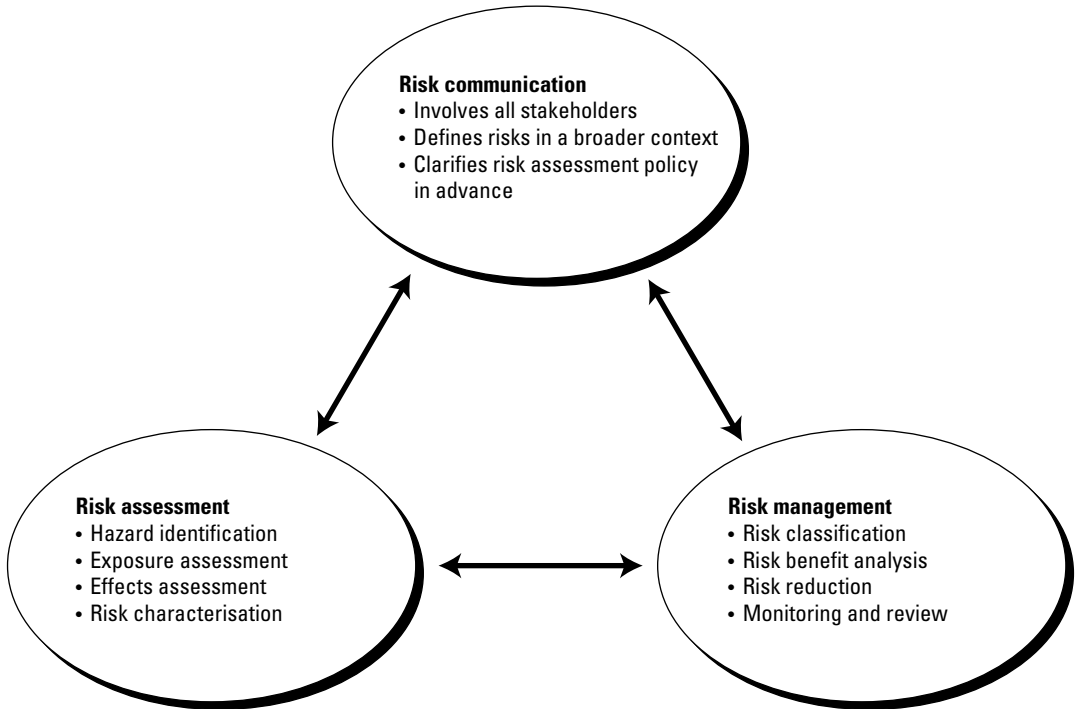


Figure 1.11. Risk analysis. Future processes of risk management should focus on risk communication in an interactive dialogue with all stakeholders and clarification of risk assessment policy at all stages [41-43].

emphasises the importance of risk assessment policy as given by the CAC [43]: "risk assessment policy should be established by risk managers in advance of risk assessment, in consultation with risk assessors and all other interested parties." This third model, the *transparent model* [50], assumes that not just science-based risk assessments play a role in policy-making processes, but that the risk assessments are also influenced by the socio-economic, cultural and political contexts in which they are developed. The transparent model assumes that non-scientific considerations play a distinctive up-stream role in setting the framing assumptions that shape the ways in which risk assessments are performed. It implies that rather than leaving those assumptions implicit, and leaving risk assessors to take responsibility for non-scientific judgements, risk managers should provide their risk assessors with explicit upstream framing guidance. In this way the transparent model can be considered as a three-stage iterative process (Figure 1.11) encompassing:

1. Risk communication over the entire process embedded in an iterative dialogue engaging all stakeholders at all phases (Figure 1.10) with a focus on risk assessment policy in advance of the actual risk assessment [41-43,50]. This phase is dominated by legislative, socio-economic and political considerations, particularly in relation to public and occupational health and environmental protection.
2. Risk assessment, (steps 1-4 in Figure 1.3) dominated by scientific considerations.
3. Risk management decision-making (steps 5-8 in Figure 1.3) based on technical, economic and social information.

Does this mean that the role of science in the overall risk management process has decreased over time? First of all, the process of risk assessment has not changed fundamentally in the past 25 years [41,52]. Secondly, scientists will continue to play a crucial role in the problem formulation and dialogue with risk managers in the development of risk assessment methodologies, in making explicit what we want to protect and at what levels, and in providing clarity about the uncertainties in assessments that were made [41,42,47,49]. The real change is the increased awareness that scientists are part of an overall risk management process in which the role of other stakeholders (Box 1.3) has increased. This new way of thinking is gradually implicitly, and sometimes explicitly, finding its way into current practice. Examples include the development of the REACH legislation [40], the development of Technical Guidance Documents [22] and other REACH implementation projects [33,53]. It is

obvious that further work is necessary to provide clarity on the quality of the input (data), testing/assessment strategies, risk assessment models and their assumptions, simple tools to quantify uncertainties, guidance about acceptable levels of uncertainty and further practical guidance concerning the risk characterisation/risk management interface.

The debate on how to use and implement scientific expertise continues! The role of scientific expertise in EU policy making remains under discussion. In multiple scientific committees, experts provide guidance to regulators and decision-makers about the potential risks to human health and the environment. Proponents of a "technocratic" approach claim the credibility problem of supranational regulation caused by extensive politicization. They want to provide far-reaching delegation of powers to independent experts. Representatives of a "democratic" approach argue for a more socially inclusive use of expertise by providing a broader participatory mechanism for a variety of stakeholders as described above [54,55]. These views are conflicting. Gaps remain in the scope of the operational guidelines for the inclusion of scientific evidence in the legislative process, and in relation to information quality, the interpretation of evidence and the reporting of results. There is a lack of institutional mechanisms to ensure the integrity, quality, and effective operation of the scientific advisory system. In a recent review it was concluded that there are weaknesses in the effective use of scientific evidence in policy-making and regulatory decision-making processes by the European Union and a structured programme of reform has been proposed [56,57].

A further focus on risk assessment policy as advocated by the CAC [43] will allow us to arrive at considerable improvements regarding informed, systematic, complete, unbiased and transparent decision-making. A recent bulletin of the US Office of Management and Budget [58] contains clear proposals to make the risk assessment process better understood, more transparent and more objective. It also broadens the set of circumstances in which risk assessment needs to be done. The purpose of this proposed risk assessment bulletin is to enhance the technical quality and objectivity of risk assessments prepared by federal agencies in the USA by establishing uniform, minimum standards. Under the REACH legislation [40] emphasis will be placed on industry's own responsibility for the safe use of chemicals. Once uniform, minimum standards have been formulated and internationally agreed, correct implementation by regulatory agencies, as well as industries, will enhance the scientific and technical quality of the risks assessments. It will foster international collaboration on risk assessments of chemicals *(sharing the burden)*. It will facilitate communication about risks and it will embed risk assessment more deeply in the decision-making process.

### 1.3.4 Integration in risk assessment

As indicated above, it is important to deal with both human health risks and environmental risks. Let us first look at the effects part of the risk equation, i.e., the toxicological and ecotoxicological effects. From a scientific viewpoint, studies into the mechanism of toxicity should be a central element of risk. This is because the mechanism of toxicity is often similar across a wide range of species, even though the observed endpoints may vary [44,46,59]. The most obvious benefits of integrated assessment come from the sharing of information and even collaboration in the generation of hazard information by health and ecological risk assessors. Successful integration of human health and environmental (ecological) risk assessment must begin with the recognition that, for pragmatic rather than scientific reasons, the strategies for these areas have developed independently of one another. This is despite the fact that in many situations human health risk and environmental risks are interdependent. For many uses of chemicals there is a legal requirement that an assessment be made for the risks to both human and ecological health, but commonly these assessments are conducted separately [44].

What has been said about the integration of toxicological effects also applies to the exposure part of risk assessment. First of all, the same process may cause exposure to both workers and the environment and controlling worker exposure to exhaust ventilations, for example, may cause an environmental problem. Human and environmental exposure assessment are therefore linked by the same "determinants of exposure". Secondly, when developing exposure scenarios these must be based on integrated thinking in order to avoid or reduce problem shifting.

This integration of human and ecological risk assessment, both effects assessment and exposure assessment, can provide better input for decision-making. The move towards integration to achieve more fully informed decisions must come from the realization that decisions are currently not always fully informed [46] and often are not made in a cost effective manner [59]. Integration has been one of the major

Table 1.6. Types of integration in the risk management process and why they are needed [45-48].

**Exposure and effects** – This is the most fundamental type of integration in risk assessment, i.e. the interaction of exposure estimates with estimates of the relationship between exposure and effects to estimate risks.

**Multiple agents** – Assessments should integrate risks to humans and the environment from all agents that are relevant to the decision.

**Multiple routes** - Assessments should integrate risks to human health and the environment from all routes of exposure relevant to the decision.

**Multiple endpoints** – Assessments should consider all potentially significant endpoints for both human health and ecological receptors that are relevant to the decision.

**Multiple receptors** – Assessments should consider all classes of human and ecological receptors that are relevant to the decision.

**Multiple scales in dimensions** – Extrapolations in risk assessment can occur in various dimensions including time (short to long term), place (one site to other sites), space (local to regional), biological scale (small species to larger ones), or mechanisms (molecular processes to physiology and responses at individual to population level).

**Life cycle** - Assessments may need to integrate the risks from the entire life cycle of the chemical or product.

**Normal use, accidents and incidents.** Risk assessments tend to focus on normal uses and permitted discharges of e.g. waste-water as a result of production. Extreme events such as peak discharges, accidents and uses that are not permitted or illegal may dominate ecological and health risks and should be integrated into health and ecological risk assessments.

**Management alternatives** – When decisions are based on comparison of alternatives, assessments should consider the risks from relevant alternatives in an integrated manner.

**Socio-economics and risks** – The actual level of protection provided depends on the relative acceptability to society of the costs and benefits. Currently, the integration of social sciences into risk assessments is largely limited to weighing the costs of a regulated party against the benefits to the public.

**Stakeholder participation** – Integration of active stakeholder participation will help to improve the risk assessment and acceptance of management actions (see Box 1.3).

trends in environmental risk assessment. This increase in integration is predictable, as narrowly focused assessments often have failed to provide adequate answers in the past [45-47]. Apart from the integration of human health and environmental effects and exposure assessments, there are a variety of other types of integration that should be explored further to improve risk-based decision-making. This integrative thinking will also help to focus efforts and resources in the risk assessment and risk management process. These types of integration are given in Table 1.6.

## 1.4 DISCIPLINES, ROLES AND RESPONSIBILITIES IN RISK MANAGEMENT

The assessment of risks associated with the production, use and disposal of chemicals is a task that cannot be undertaken without adequate knowledge of chemistry (including process technology), toxicology and biology (Figure 1.12). Yet, the complexity of the subject requires the involvement of other disciplines: mathematics, statistics and informatics. These disciplines play an essential part in disentangling, analyzing and quantifying the complex interactions between substances, species

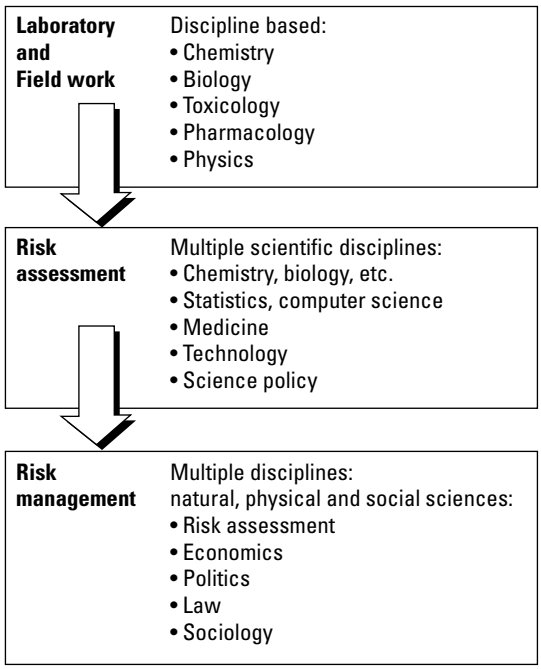


Figure 1.12. Disciplines involved in the risk management process. Modified from Patton [15].

and systems, often using models. These complex systems may be either ecosystems with numerous species and functions to be protected, or "human environments" or "technospheres", in which attention is focused on only one species: man. Human populations may be exposed directly, i.e. at the workplace (occupational exposure) and through consumer goods such as detergents, or indirectly via the environment. Of course, other disciplines are involved as well, including physics, medicine, geology, hydrology, and epidemiology.

The feature distinguishing risk assessment from the underlying sciences is this: after evaluating standard practices within the discipline, the most relevant information from each of these areas is brought together to describe the risk. This means that individual studies, or even groups of studies, from a single discipline, may be used to develop risk assessments, although they are not, in themselves, generally regarded as risk assess-ments nor can they alone generate risk assessments [15]. In other words, risk assessment is multi-disciplinary team work (Figures 1.12). Risk management is also a multi-disciplinary process. It draws on data, information, and principles from many other disciplines and specialists with different kinds and levels of expertise representing many different organizations and interested parties (Figures 1.11 and 1.12). Risk communication is a vital part of the process of involving, informing and advising people about how they can manage potential risks. Risk communication requires an understanding by manufacturers and importers of the information needs of users. The development of appropriate risk-based communication systems, including the provision of complementary information using, for example, websites and educational campaigns, should be pursued. Roles and responsibilities of the different stakeholders are different. In conclusion:

- Scientific experts need independence so that they are willing to speak "truth to power". However, they should not be involved in decision-making and used only as providers of input to regulatory decision-making. Persson [55] stated it very clearly: "it is essential to distinguish the role of the expert from the role of the decision-maker." Scientific experts inform and decision-makers/regulators should: (a) manage the overall risk management process, (b) decide on the risk management options, and (c) take their responsibility as they are accountable.
- Involving stakeholders and incorporating their recommendations where possible, re-orients the decision-making process from one dominated by regulators to one that includes those who must live with the consequences of the decision. This not only fosters successful implementation, but can also promote greater trust in government institutions [41].

## 1.5 HOW RISKS ARE EXPRESSED

Risk can be defined as the probability of an adverse effect in an organism, system or (sub)population caused under specified circumstances by exposure to an agent. Risk has three characteristic variables: the type, magnitude and probability of the hazard. In quantitative terms, risks are often expressed in terms of probability estimates ranging from zero (harm will not occur) to one (absolute certainty that harm will occur). A distinction is made between *chemicals with and without threshold levels*. In the case of *chemicals without threshold levels*, e.g. many carcinogens, often a linear relationship is assumed between exposure (dose) and effect (incidence of cancer). This means that, in a statistical sense, it is always possible that an effect will occur. In such cases, the risk number represents the *probability* of additional cancer cases occurring. For example, an estimate for chemical X might be expressed as $1 \times 10^{-6}$, or simply $10^{-6}$. This figure can also be written as 0.000001, or one in a million, which means that one additional case of cancer is projected in a population of one million

people exposed to a certain level of chemical X over their lifetimes. Similarly, smoking 1 packet of cigarettes a day produces a potential risk of lung cancer of 5 x $10^{-3}$ per year (Table 1.7) or 1 in 200 per year. These risks signify additional cases to the background incidence of cancer in the general population. The American Cancer Society has published statistics that indicate that the background incidence of cancer in the general population is 1 in 3 over a lifetime [15]. It should be noted that not all carcinogens cause non-threshold effects and that non-carcinogenic effects may also be non-threshold.

Not all chemicals present non-threshold cancer risks, but they may affect developmental, reproductive, neurobehavioural, and other body functions. Such effects are often associated *with a threshold level* and a non-linear S-shaped relationship between dose and effect. There is a threshold level below which there is no effect, albeit that the precise level of this threshold will vary between individuals. In other words, unlike chemicals with non-threshold effects, risk is not assumed to be present in all doses or concentrations. Typically, such substances are regulated by determining NELs in test species by applying a predetermined or calculated assessment factor (AF) to arrive at an ADI or DNEL for man [21,45] or PNEC for ecosystems [2,45,60] :

$$\text{ADI or DNEL or PNEC} = \text{NEL} / \text{AF} \qquad (1.1)$$

An ADI or DNEL is a rough estimate of the daily exposure to which human populations (including sensitive subgroups) may be subjected that is not likely to cause harm during a lifetime. For chemicals with threshold levels, values are not typically given as probability of occurrence, but rather as *levels of exposure* estimated to be without harm. These values are typically expressed in mg (of the chemical) per kg of body weight per day. A PNEC is a rough estimate of the exposure level at which ecosystems will suffer no harm. PNECs are typically expressed as mg/L air or water or as mg/kg soil or sediment.

The uncertainty in a DNEL, PNEC or ADI may be one of several orders of magnitude (i.e. powers of 10). As exposures typically vary over time and space, and plant and animal species vary widely in their susceptibility to toxicants, the question may be asked: can effects, exposures and risks be expressed by a single figure or do we need to provide ranges of concentrations? Let's look at a carcinogenic compound. The statement for a carcinogenic compound that the risk of a specified exposure concentration is A x $10^{-B}$ is actually shorthand for the general truth that "we are Y% sure that the risk is no more than A x $10^{-B}$ for Z% of the population". Real risks cannot be given for chemicals which pose a threat at certain thresholds (Section 1.2.4). Where the PEC/PNEC ratio is less than 1, we are V% sure that the exposure concentration does not exceed the NEC for W species which were tested for ecosystem X, comprising a total of Y species at time Z. Where the PEC/PNEC ratio is greater than 1, it is not at all clear what the risks is. Absolute certainty in risk assessment is impossible.

Patton [15] stresses a number of other important points. Firstly, the numbers themselves do not tell the whole story. For instance, even though the numbers are identical, a cancer risk value of $10^{-6}$ for the "average exposed person" (perhaps exposed through the food supply) is not the same thing as a cancer risk of $10^{-6}$ for a "most exposed individual" (perhaps someone exposed because he lives or works in a highly contaminated area). It is important to know the difference. By omitting the qualifier "average" or "most exposed" the risk is incompletely described, which would mean a failure in risk communication.

Secondly, numerical estimates are only as good as the data is they are based on ("garbage in, garbage out"). Just as important as the quantitative aspect of risk characterization (the risk numbers) then, are the qualitative aspects. How extensive is the database supporting the risk assessment? Does it include human epidemiological data as well as experimental data? Does the laboratory data base include test data on more than one species? If multiple species are tested, do they all respond similarly to the test substance? Are extrapolations being made from more or less sensitive varieties, species and endpoints? What are the data gaps, the missing pieces of the puzzle? What are the scientific uncertainties? What science-policy decisions are made to address these uncertainties? What working-assumptions underlie the risk assessment? What is the overall confidence level in the risk assessment? All of these qualitative considerations are essential to deciding what reliance to place on a number and to determining potential risk.

## 1.6 PERCEPTION OF RISKS

The perception of risks (and benefits) varies between individuals and public, business, labour, and other stakeholders. Moreover, they change with time (Table 1.3) and across cultures. People continually assess situations and decide whether the risks associated with a particular action can be justified. In certain circumstances, harmful effects are clearly attributable

Table 1.7. Annual mortality rate associated with certain occurrences and activities in the Netherlands [25].

| Activity/occurrence | Annual mortality rate | |
|---|---|---|
| Drowning as a result of dike collapse | $10^{-7}$ | 1 in 10 million |
| Bee sting | $2x10^{-7}$ | 1 in 5 million |
| Struck by lightning | $5x10^{-7}$ | 1 in 2 million |
| Flying | $1.23x10^{-6}$ | 1 in 814,000 |
| Walking | $1.85x10^{-5}$ | 1 in 54,000 |
| Cycling | $3.85x10^{-5}$ | 1 in 26,000 |
| Driving a car | $1.75x10^{-4}$ | 1 in 5,700 |
| Riding a motorbike | $2x10^{-4}$ | 1 in 1,000 |
| Smoking cigarettes (1 packet a day) | $5x10^{-3}$ | 1 in 200 |

to a particular course of action. However, in other cases, the impact of such effects may be uncertain and need not be immediately obvious. People use different methods to evaluate their own individual risks and environmental risks. In some cases the perception of a group of people may alter the priorities assigned to reducing competing risks. Risks that are involuntary or "novel" seem to arouse more concern than those that are voluntary or "routine", i.e. accepted. Environmental risks are largely of an involuntary nature. "Natural" contaminants and toxins in food may be considered acceptable even though they may cause illness, while food additives whose introduction (or identification) in foodstuffs is to assist in preservation may not be acceptable to some people [61].

Hazards that are delayed in their effect, such as extinction of populations or species caused by long-term accumulation of persistent pollutants in food webs, are usually difficult to observe, assess and control. As a result, hazards of this type are often regarded as being more serious than those that happen immediately. Others, such as Lovell [53], state that "outcomes which are rare, unpredictable, and catastrophic, such as chemical plant explosions, are viewed as more disturbing than those that are common, regular, and small in size, such as road accidents, even if the overall cost in human life and suffering may be similar. There seems to be a "dread" component to people's perception of certain types of risks".

Table 1.7 gives examples of the various risks to which man can be exposed. The risks inherent in these activities give some indication of the magnitude of the risk added to natural circumstances due to human interference. Some are *voluntary* risks, e.g. smoking, others are of an *involuntary* nature, e.g. being struck by lightning. Although the risks of, say, smoking and driving a car are comparatively great, they are widely accepted. On the other hand, even the presence of minute quantities of (natural) carcinogenic substances in food is not readily accepted by the public at large. Although the risk-benefit equation should be a major determinant, both the risk and the benefit are frequently not fully understood and people develop irrational fears [62].

## 1.7 UNCERTAINTY, VARIABILITY AND PRECAUTION

### 1.7.1 Uncertainty and variability

Risk assessment controversies often revolve around disagreements regarding the nature, interpretation, and justification of methods and models used to evaluate incomplete and uncertain data. When science is used for regulatory purposes, decision-makers need to be informed not only of the available scientific knowledge but also of relevant uncertainties and lacunae in the knowledge base. We need to distinguish between uncertainty and variability. Uncertainty can often be reduced by obtaining or generating more information. This is one of the reasons why we apply tiered testing and assessment strategies. Variability is a natural phenomenon and cannot be reduced (Box 1.4). The aim of uncertainty analysis is to identify major sources of uncertainty in either hazard or exposure assessment. Any risk assessment carries uncertainty with it. An evaluation of uncertainty therefore should assist in communicating these uncertainties to improve decision-making in the light of the uncertainty associated with the outcome of the risk assessment [33,63]. The probability that any given chemical presents a hazard to man and/or the environment can be difficult to determine, but it is essential that rigorous scientific methods be used in any such assessment. Mathematical approaches to risk

**Box 1.4. Risk assessment according to Aristotle**

***"It is the mark of an instructed mind to rest easy with the degree of precision which the nature of the subject permits and not to seek an exactness where only an approximation of the truth is possible."***

assessment help to expose a problem to logical analysis, and to identify areas of uncertainty. This type of analysis provides an intellectual basis for decision-making or determining further research needs. In other words: risk assessment is driven by doubt, not by certainty.

Mathematical analysis can, unfortunately, be used for hiding inconvenient information or muddled thinking behind a façade of apparent technical and scientific expertise [64]. It is important to realize that mathematical assumptions are still assumptions and require estimates of the errors implicit in them. Using ranges of values rather than only a central estimate is a necessary adjunct to risk assessment and forms the basis of a sensitivity analysis, which tests how general the findings of an assessment may be. Risk assessment in practice is far from ideal and is hampered by four types of uncertainty:

1. Lack of information.
Very often basic data are lacking or inadequate to make precise predictions. Where essential data are lacking the use of expert judgement, estimation methodologies or even default values becomes necessary. This lack of basic data [65,66] applies to toxicological data (Table 1.8) and is likely to be even greater for data on emissions, fate and exposure concentrations. The data situation for lower volume chemicals is even worse! This general lack of data applies to the 100,000 chemicals on the European Inventory of Existing Commercial Chemical Substances (EINECS). For new chemicals, plant protection products and biocides, the actual situation may be slightly better because basic information is required for notification and registration.

Table 1.8. Estimation of available toxicological data (%) for about 2500 High Production Volume Chemicals [66].

| | |
|---|---|
| Acute oral toxicity | 77 |
| Repeated dose toxicity | 58 |
| Genetic toxicity *in vivo* | 38 |
| Genetic toxicity *in vitro* | 67 |
| Reproductive toxicity | 26 |
| Teratogenicity | 32 |
| Acute ecotoxicity (fish and daphnids) | 68 |
| Short-term toxicity (green algae) | 45 |
| Effects on soil organisms | 30 |

2. Measurement uncertainties.
Measurement uncertainties include low statistical power due to insufficient observations, difficulties in making measurements, inappropriateness of measurements, and human error (incorrect measurements, misidentifications, data recording errors and computational errors).

3. Observation conditions.
Uncertainties related to conditions of observation include spatiotemporal variability in climate, soil type, sensitivity, ecosystem structure, differences between natural and laboratory conditions, and differences between tested or observed species and species of interest for risk assessment.

4. Inadequacies of models.
Inadequacies of models include a fundamental lack of knowledge concerning underlying mechanisms, failure to consider multiple stresses, responses of all species, extrapolation beyond the range of observations, and instability of parameter estimates. In fact two related types of uncertainties can be distinguished: quantifiable uncertainties (the "known unknowns") and undefined uncertainties that cannot be described or quantified (the "unknown unknowns"). The PEC/PNEC approach is an example of such "unknown unknowns" (Sections 1.2.4 and 1.5). The same is true for laboratory-based soil quality criteria because there is a fundamental lack of knowledge about the differences in the bioavailability of the chemical between the laboratory and the field.

Suter [64] distinguishes between three types of uncertainty, i.e. stochasticity, error and ignorance, whereas Ricci et al. [67] identify six elements:

1. Scientific judgements and defaults that are imposed on stakeholders by regulators when scientific evidence is contradictory and causation is unknown.
2. Misspecified models that exclude key variables or wrongly or incompletely formulate the relationships between them
3. Statistical uncertainties that combine aspects of model misspecification and choice of model with estimation and inference, heterogeneities of statistical

and physiological parameters, confounders, effect modifiers, measurement errors and missing or censored data.
4. Deterministic representations where the formal description of physical processes gives an illusion of complete and certain knowledge of future outcomes and their magnitude.
5. Probabilistic representations where the analysis concerns assessing events that have not yet occurred.
6. Statistical representations where the analysis concerns inference about a population's parameters from observed exposures and outcomes determined from experimental or observational study.

In risk assessment reports of chemicals, generally two ways of dealing with uncertainty can be seen: a *deterministic* approach and a *probabilistic* approach [68]. In the deterministic approach, uncertainty is not explicitly addressed by the application of "reasonable worst-case assumptions" in hazard and exposure assessments. The advantage of the simple deterministic approach is that it is quick and easy to apply and takes uncertainties into account without having to specify uncertainty about elements in the assessment that are difficult to estimate. It also avoids the problem of communicating risks in terms of probability and statistics that are often difficult to follow for non-experts. Therefore it has proven to be very efficient in taking regulatory decisions. The disadvantage of the deterministic approach to uncertainty is that several reasonable worst-case assumptions can be combined leading to unrealistic assessment outcomes and outcomes that are not transparent [33,68,69]. The deterministic approach gives a false sense of accuracy and ignores variability in the population [68].

Uncertainties occur throughout the different steps of the risk assessment and should thus be addressed as an integral part of the work during the assessment and not as an add-on in the reporting at the end of the assessment.

### 1.7.2 Quantifying uncertainty and validation

**Quantifying uncertainty**

Quantifying estimates of uncertainty, as is sometimes done in *probabilistic risk assessments* (PRA), may help in making more rational decisions on the risk of toxic substances and can help to achieve a better balance between assessment, uncertainty and safety [33,68,70]. The advantage of a quantitative treatment of uncertainty is that assumptions about variability and uncertainty must be backed up by explicit information [71]. The application of uncertainty analysis to decision-making is far from routine as virtually all decisions are still based on point estimates of exposure and effects. As sources and magnitude of uncertainties will differ between chemicals, it means that some substances can be assessed with greater confidence than others, as illustrated in Figure 1.13. The disadvantages of PRA are obvious. Additional information is needed to estimate the uncertainty in hazard and exposure assessment that may be difficult, time-consuming or expensive to generate [72,73]. Examples of PRA [74-76] show that it is also more complex and more difficult to communicate. Furthermore, no scientific consensus exists about standard methods and their validation. There seems to be a guarded interest in uncertainty analysis, but currently it does not receive high priority. There seems to be a gap between the scientist and the risk manager [68]. Perhaps this is related to the fact that there are many sources of uncertainty. Some of these uncertainties can be quantified, whereas sometimes major sources of uncertainty are simply non-quantifiable. This may create a false sense of security and certainty. An additional disadvantage of PRA is that regulators need to decide on an acceptable risk level for the outcome of the risk assessment [33].

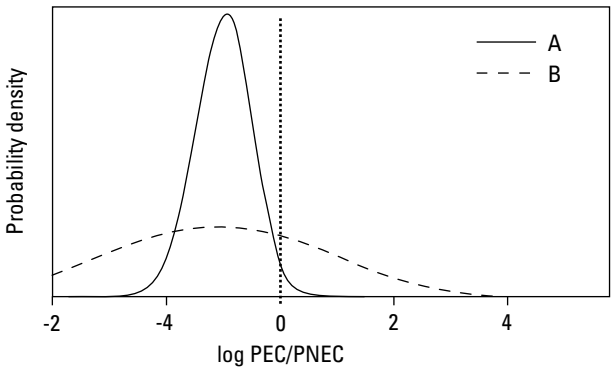


Figure 1.13. Probability distributions of two hypothetical chemicals with the same median PEC/PNEC ratio. Redrawn from Jager et al [68]. With permission. Copyright Elsevier.

The current state of science is that some elements of uncertainty analysis and some probabilistic approaches are already part of the guidance on effects assessment [22]. Similar approaches are not routinely applied in the areas of exposure assessment and risk characterisation. Jager et al. [68] have tried to list the options that are currently available to revise risk assessments in order to deal with uncertainties in the risk characterization stage (Figure 1.14). They arrived at three options in order of preference:

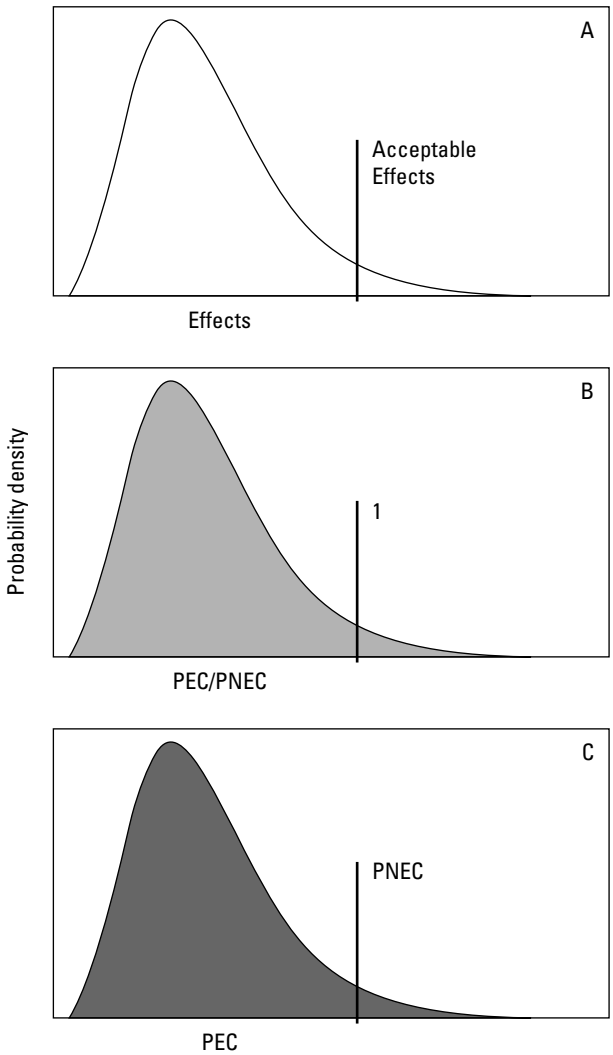


Figure 1.14. Options for uncertainty in risk characterization. Redrawn from Jager et al [68]. With permission. Copyright Elsevier.

A. Establish a dose-effect relationship for human populations and ecosystems. The result of the risk characterization stage will be a probability distribution of effects. Decisions can be based on an acceptable level of effects.
B. Revise the assessment factors in the effects assessment to yield a median, or most likely, PNEC Instead of a conservative estimate and attaching uncertainty to these factors (e.g. instead of a factor of 1000 use an assessment factor of 100 with a factor of 10 uncertainty)
C. Leave the effects assessment as it is now. In that case, only uncertainty in the exposure estimate needs to be quantified. The result of the risk characterization will be a probability that the PEC exceeds a fixed, worst-case PNEC.

Further discussions and developments are needed to improve transparency and to address variability and uncertainty [76-78]. Recently, pragmatic proposals have been made to use three ways of getting to grips with uncertainty in risk assessments that have different levels of complexity, resource intensity (time and money) and data needs [33]. With a view to developing maximum workability, a tiered strategy has been developed:

Tier 1: Qualitative uncertainty assessment. Uncertainty assessment using a deterministic approach linked to scenario analysis.
Tier 2: Simple (semi-quantitative) analysis. This is a simple semi-quantitative probabilistic analysis providing insight into the influence of uncertainty on the risk quotient or risk characterization ratio (RCR).
Tier 3: Full quantitative PRA.

Such a system can be applied in a pragmatic manner following the principle of: “as simple as possible and as complex as needed.”

**Validation**

Risk assessments are generally performed by applying risk assessment models, such as EUSES [79]. These models are crucial as they increase transparency and predictability. They play an important role in risk communication and risk acceptance. The more specific models are, the more data are needed and the more difficult they are to generalize. On whatever scale we use models - biological models such as the zebra fish or rat, local or multi-compartment exposure models, or risk assessment models - they remain a distortion of the truth and their output is input-dependent. Users must be confident that their models actually correspond with the systems being studied. The process of obtaining this confidence has been referred to as model validation. Model validation can be defined as any process that is designed to assess the correspondence between the model and the system. The purpose of validation is to improve the credibility and reliability of predictive methods. Validation must be viewed as an iterative process in which predictions are tested, models are refined, and then new predictions are tested [80].

Risk assessment is a broad term that encompasses a variety of analytical techniques that are used in different situations, depending upon the nature of the hazard, the available data, and needs of the decision-makers.

As a consequence it is essential to realize that (model) validation is also context-specific, i.e. validation needs to be placed in the context of the risk management decision to be made. Models for priority setting of chemicals for future evaluation or a safety evaluation of a specific chemical require different data to be assessed using different models with different input and output qualities. Too much focus on model validation without putting the whole exercise in a broader regulatory context may lead to "validation paralysis" or "paralysis by analysis". At least three kinds of studies can contribute to validation:

- Improved measurements of specific quantities and testing of assumptions.
- Experimental testing of models under reasonably realistic conditions.
- Monitoring of effects or other investigations to determine the level of agreement between predictions and the actual observations.

Using a model to quantify risks and their uncertainties would, in principle, permit more useful risk assessments, but if the model itself is a poor representation of reality, the results might be totally meaningless. Furthermore, it should be stressed that although uncertainties in effects data, exposure data and methodologies in risk assessment are important, uncertainties and prior framing assumptions in risk policy may be even more important. Transparency in this area is of the utmost importance in order to improve decision-making (see Section 1.3 and Figures 1.6, 1.7 and 1.11).

### 1.7.3 Precaution

Taking regulatory action on the basis of *the precautionary principle* is sometimes interpreted as an alternative to taking action based on an assessment of risks [81]. In practice, however, many references in international law to the precautionary principle refer to the use of this approach when there are threats of serious irreversible damage, but there is a lack of conclusive scientific evidence. For instance, in the Rio Declaration of 1992 principle 15 states: "in order to protect the environment, the precautionary approach shall be widely applied by States according to their capability. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation." Some people have argued that this definition is legally unenforceable [67], whereas others say it is enforceable and have defended the precautionary principle against five common charges, namely that it is: (1) ill-defined, (2) absolutist, (3) leads to increased risk-taking, (4) is a value-judgement or an ideology and (5) is unscientific or marginalizes the role of science. Those who defend the precautionary principle argue that, in principle, it is no more vague or ill-defined than other decision principles and that it can be made precise through elaboration and practice [81-83]. According to Kriebel et al. [83] the precautionary principle has four central components:

1. Taking preventive action in the face of uncertainty.
2. Shifting the burden of proof to the proponents of an activity.
3. Exploring a wide range of alternatives to possibly harmful actions.
4. Increasing public participation in decision-making.

They argue that a shift to more precautionary policies creates opportunities and challenges for scientists to think differently about the ways they conduct health and environmental studies and communicate results. According to these authors the precautionary principle highlights this tight, challenging link between science and policy, which is in line with the observations made in Sections 1.3 and 1.4.

In 2000, the European Commission published a Communication on the precautionary principle [84] providing a general framework for its use in EU policy (see Box 1.5). The aim was to outline the Commission's approach to using the precautionary principle, to establish guidelines for it, to build a common understanding of how to assess, manage and communicate risk that science is not yet able to evaluate fully, and to avoid unwarranted recourse to the precautionary principle as a disguised form of protectionism [84]. The precautionary principle is a cornerstone of the REACH legislation [40] and of EU health and environmental management in general [84,85]. In the Communication of the Commission it is clearly stated that the precautionary principle should be considered as part of a structured approach to the analysis of risk which comprises three elements: risk assessment, risk management and risk communication, as shown in Figure 1.11. The precautionary principle is particularly relevant to the management of risk. In the Commission Communication four elements need to be highlighted in the context of this book.

1. The precautionary principle is based on the assumption that a thorough scientific evaluation of the risks is performed which is as objective and complete as possible prior to decision-making: "the implementation of an approach based on the precautionary principle should start with a scientific evaluation, as complete as possible, and where possible, identifying at each stage the degree of scientific uncertainty."

**Box 1.5. The precautionary principle according to the European Commission [84]**

Where action is deemed necessary, measures based on the precautionary principle should be, *inter alia:*

1. **Proportional** to the chosen level of protection.
2. **Non-discriminatory** in their application.
3. **Consistent** with similar measures already taken.
4. **Based on an examination of the potential benefits and costs** of action or lack of action (including, where appropriate and feasible, an economic cost/benefit analysis).
5. **Subject to review,** in the light of new scientific data.
6. **Capable of assigning responsibility for producing the scientific evidence** necessary for a more comprehensive risk assessment.

**Proportionality** means tailoring measures to the chosen level of protection. Risk can rarely be reduced to zero, but incomplete risk assessments may greatly reduce the range of options to risk managers. A total ban may not be a proportional response to a potential risk in all cases. However, in certain cases, it is the sole response to a given risk.

**Non-discrimination** means that comparable situations should be treated differently, and that different situations should be treated in the same way, unless there are objective grounds for doing so.

**Consistency** means that measures should be of comparable scope and nature to those already taken in equivalent areas in which all scientific data are available.

**Examining costs and benefits** entails comparing the overall cost to the Community of action and lack of action, in both the short and long term. This is not simply an economic cost-benefit analysis: its scope is much broader, and includes non-economic considerations, such as the efficacy of possible options and their acceptability to the public. In the conduct of such an examination, account should be taken of the general principle and the case of law of the Court such that the protection of health takes precedence over economic considerations.

**Subject to review** in the light of new scientific data, means measures based on the precautionary principle should be maintained as long as scientific information is incomplete or inconclusive, and the risk is still considered too high to be imposed on society, in view of the chosen level of protection. Measures should be periodically reviewed in the light of scientific progress, and amended as necessary.

**Assigning responsibility for producing scientific evidence** is already a common consequence of these measures. Countries that impose a prior approval (marketing authorization) requirement on products that they deem dangerous *a priori* reverse the burden of proving injury, by treating them as dangerous unless and until businesses do the scientific work necessary to demonstrate that they are safe.

Where there is no prior authorization procedure, it may be up to the user or to public authorities to demonstrate the nature of a danger and the level of risk of a product or process. In such cases, a specific precautionary measure might be taken to place the burden of proof on the producer, manufacturer or importer, but this cannot be made a general rule.

2. The second relevant element in the Communication of the Commission is the separation of roles and responsibilities between scientist and decision-makers: “decision-makers need to be aware of the degree of uncertainty attached to the results of the evaluation of the available scientific information. Judging what is an “acceptable” level of risk for society is an eminent political responsibility. Decision-makers faced with an unacceptable risk, scientific uncertainty and public concerns have a duty to find answers. Therefore, all these factors have to be taken into account”.
3. The third relevant element is related to risk communication: “the decision-making procedure

should be transparent and should involve as early as possible and to the extent reasonably possible all interested parties".

4. Actions taken under the precautionary principle must in certain cases include a clause reversing the burden of proof and placing it on the producer, manufacturer or importer: "measures based on the precautionary principle may assign responsibility for producing the scientific evidence necessary for a comprehensive risk evaluation."

These views are comparable to the views expressed in the policy paper "Premises for Risk Management" published by the Dutch Ministry of the Environment in 1989 [25] and the US Presidential/Congressional Committee in 1997 [41] as discussed in Section 1.3.2. The Commission has added a number of important elements and conditions to make the precautionary principle more operational [84]. These are given in Box 1.5. In reviewing the role of the precautionary principle in the EU risk assessment process on industrial chemicals [81] it was concluded that the main reason for doing so was the uncertainties in the risk assessment (or the underlying effects or exposure data), which were, according to the scientific experts, so high that a "normal" level of certainty could not be obtained. In the next decade it will be a scientific, legal, and political challenge to make the precautionary principle a legally enforceable and practical tool in health and environmental management. As stated above, the precautionary principle is a cornerstone of REACH. Further general guidance or rules need to be developed that will support policy-makers in their decisions as to whether this uncertainty is so large that action is warranted or whether it is acceptable to wait until further information becomes available.

## 1.8 CONCLUDING REMARKS

It is not uncommon that during the selection of options for risk reduction, fundamental questions about the principles of risk assessment are raised. It is also not uncommon that discussions on risk reduction re-open discussions on data needs and risk assessment methodologies; zinc is an example [73]. Risk assessment is an important tool, but not if it is used to postpone decision-making *("paralysis by analysis")* or as a cover for a deregulatory agenda [86-88]. Risk assessors need to know:

- Their science.
- The multiple uncertainties in risk assessment.
- The multiple media and many spatial levels of risk assessment (Table 1.3).
- The limited relevance of science, i.e., the science underlying most risk assessments is inconclusive [88].
- The limited information content of effects and exposure data, including monitoring data [89-90].
- The limitations of risk assessment in general (Box 1.4).
- The difference between data, information and knowledge (Figure 1.15).
- That information must be credible and verifiable.
- That information for decision-making should be timely and affordable to those who need it and should be communicated in a manner which is understandable, efficient, and transparent [91].
- The limitations on how risks can be expressed (Section 1.5).
- The importance of risk communication in general (Section 1.3).
- The stakeholders and the context in which they are working (Figure 1.6).
- The forces in health and environmental decision-making (Figure 1.7).
- The consequences assessments may have in terms of follow-up risk reduction measures.
- The different roles and responsibilities in risk management (Section 1.4).
- The different perceptions of risk (Section 1.6).

It has become common to distinguish between: (1) data, (2) information, and (3) knowledge and wisdom. *Data* can be defined as basic observations or measurements. Data can be transmitted, combined and analyzed using a variety of tools such as EUSES [79]. *Information* refers to the products of analysis and interpretation, such as a risk assessment report. Knowledge is created by accumulating information by e.g. interacting, aggregation, filtering and transmission to the risk manager for example. *Knowledge* is internalized; it is information in the mind, in a context, based on personal perceptions and experiences allowing it to be transformed into action. It is familiarity gained by experience. *Wisdom* concerns interaction with stakeholders, management of the bigger picture (Figure 1.6), re-applied knowledge and experience from lessons learned, prudence, good judgement and reflection.

A few concluding remarks will be made using this distinction between data, information, knowledge and wisdom as shown in Figure 1.15.

1. Data

In fact, roughly three tiers of data (testing and measurements) can be distinguished, from initial to comprehensive (Table 1.9). Very few chemicals are in the

Table 1.9. Stages in risk assessment and required effects and exposure information.

| Tiers | Stages | Effects data | Exposure data |
|---|---|---|---|
| Tier-1 | initial or preliminary | short-term toxicity | basic physicochemical data, equilibrium partitioning |
| Tier-2 | refined | chronic toxicity | steady-state model predictions |
| Tier-3 | comprehensive | more chronic, epidemiological and field data | measurements and (non)steady-state model predictions |

data-rich category [65,66]. Risk management decisions can be postponed where tier 3 testing and measurement is seen as the decisive level (Figure 1.16). Tier 3 data (Figure 1.17) is costly, time-consuming and not always necessary. Rather than taking the defensive approach by generating more data about a chemical to prove that its risks are acceptable, a proactive approach may be taken by looking for harmless substitutes, for which tier 1 data may suffice. For example, the replacement of a persistent toxic chemical by a readily biodegradable toxic compound can take place on the basis of tier 1 data. That is why classification and labelling (Figure 1.8) is such an important risk management tool.

2. Information

Risk assessments tend to be uncertain and highly variable and their quality varies considerably [58]. This is also true of socio-economic, financial and technical projections about the consequences of risk reduction. Risk assessment can be a very a time-consuming activity [73], complex and difficult to communicate despite the availability of international guidance [22,33] and risk assessment models [79]. "Paralysis by analysis" may be a realistic threat to the future risk assessment and management of chemicals. Our current ability to generate new data often exceeds our ability to evaluate it [89]. In my view, further simplifications of information and information-flows are necessary in order to manage chemicals in the near future. Simple methodologies such as relative risk ranking on the basis of tier 1 data will not lose their relevance [93]. The implementation of REACH [40] will require a pragmatic and target-oriented approach to manage risks. Government agencies, the regulated community, and stakeholders face the challenges of generating and interpreting data for risk assessments in a cost-effective and efficient manner [94]. Chapman [95] has recently made a plea for simpler approaches to regulating chemicals. She suggested moving away from risks and assessing the riskiness of chemicals, i.e., (1) their capacity to cause harm, (2) their novelty (a matter of the degree to which something is different from what we know), (3) their persistence and (4) their mobility.

3. Wisdom and knowledge

It is difficult to predict which methodologies will be implemented in the near future to speed-up the assessment and management process, but the key will be further simplification based on Aristotle's knowledge and wisdom about risk assessment (Box 1.4). In the regulatory process, risk assessment will never provide "the correct answer" and risk management will never provide "absolute" solutions. To assume otherwise would

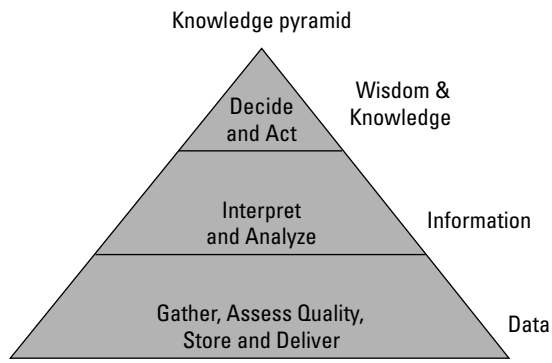


Figure 1.15. The knowledge pyramid. Modified from [91].

be to accept that there will be no further changes in the knowledge, views, values, rights and duties accepted by society and its individual members over time [61]. The multiple uncertainties in risk assessment mean that it is possible for its conclusions to be attacked from both sides. Arguments over whether or not assumptions in risk assessments are scientifically valid often amounts to debate about whether it is better to err on the side of "false positives" (if there is an error, it is more likely to be a false indication of danger) or "false negatives" (if there is an error, it is more likely to be a false indication of safety). Those who might be harmed by the substance being assessed will generally favour false positives; those who would gain from the substance will generally favour false negatives [18]. Different groups often interpret the results from the same study in different ways [95].

Risk assessment can be most useful when those who rely on it to inform the risk management process understand the context, its nature and its limitations, and use it accordingly. This means that decision-makers must at least understand that the process is assumption and value laden; that they are aware what assumptions were used in the assessment in question, and what values they reflect. They must also be aware that the risk estimate is expressed as a range, with a given certainty that the true average lies within that range; that variability is expressed to the degree that it is known; and that uncertainties can be reduced but often at high cost. Managing risks implies *management of the simplicity-complexity dilemma* (Figure 1.17). Risk managers must take all these factors into account when making a decision, along with political and economic factors which are not related to the risk assessment (Figure 1.6). Wisdom and knowledge are a prerequisite for *informed decision-making*.

Risk management of chemicals is an international challenge. Frameworks differ in scope and depth and continue to undergo dramatic changes [96]. New challenges will continue to arrive [40,97].

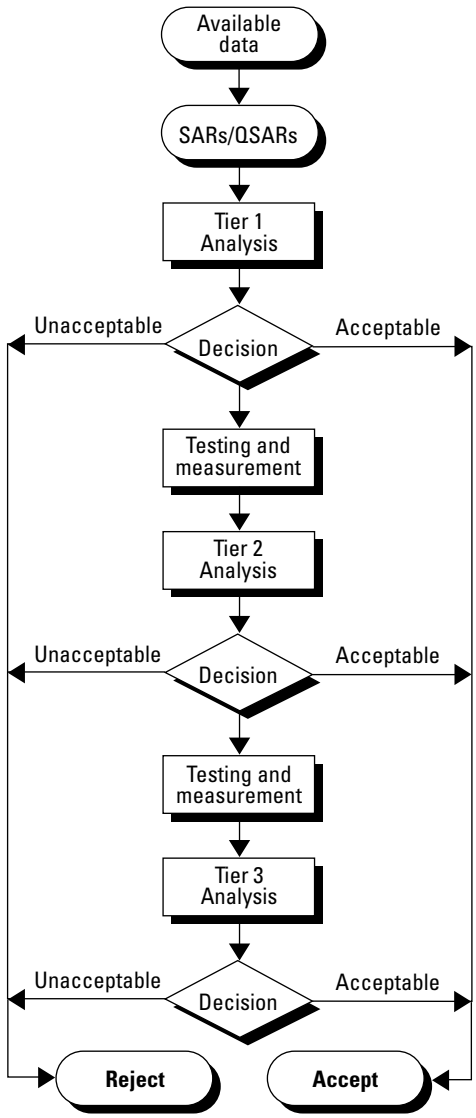


Figure 1.16. Diagram of the risk assessment process. Modified from Cairns Jr., Dickson and Maki [92].

## 1.9 CONTENTS OF THE BOOK

Applying risk assessment techniques to analyse the risks of chemicals to man and the environment is the subject of this book (Figure 1.18). It provides basic information to understand the process of risk assessment of chemicals arising from normal production, their use and disposal. Risk assessment for major accidental releases is not dealt with. The same applies to the various monitoring techniques that can be used for the enforcement of risk reduction measures. The contents of the book fall into 5 main sections.

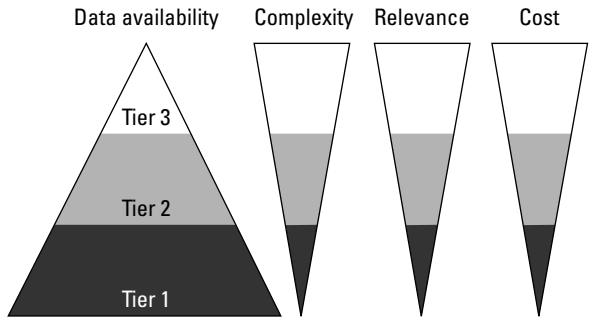


Figure 1.17. The simplicity-complexity dilemma.

- Part I deals with general issues in the risk management of industrial chemicals (Chapter 1).
- Part II is about exposure assessment. It starts with sources and emissions (Chapter 2), transport, accumulation and transformation processes (Chapter 3) and two chapters on exposure assessment, i.e., environmental and human exposure assessment (Chapters 4 and 5).
- Part III is related to human health and ecological effects assessment and risk characterization (Chapters 6 and 7).
- Part IV is about data and data estimation. It describes aspects of data needs, sources and quality evaluation (Chapter 8), the prediction of physicochemical properties and fate (Chapter 9), and the prediction of endpoints of toxicity and ecotoxicity (Chapter 10). Chapter 11 is devoted to so-called "Intelligent Testing Strategies".
- Part V is about risk assessment and management of industrial chemicals in the EU (REACH), USA, Japan and Canada (Chapters 12-15), whereas the OECD chemicals programme to support international cooperation on the assessment and management of chemicals is presented in Chapter 16. Most chapters, where relevant, include a section on further reading and a list of references for those who want more information about data, methodologies or processes.
- In addition, the book contains a glossary of the major key issues and terminology. Risk terminology is difficult and may cause confusion as risk assessors may disagree on terminology [98,99]. We have tried to be consistent with the risk terminology because without a common set of definitions, a meaningful discussion of this complex subject area is impossible.

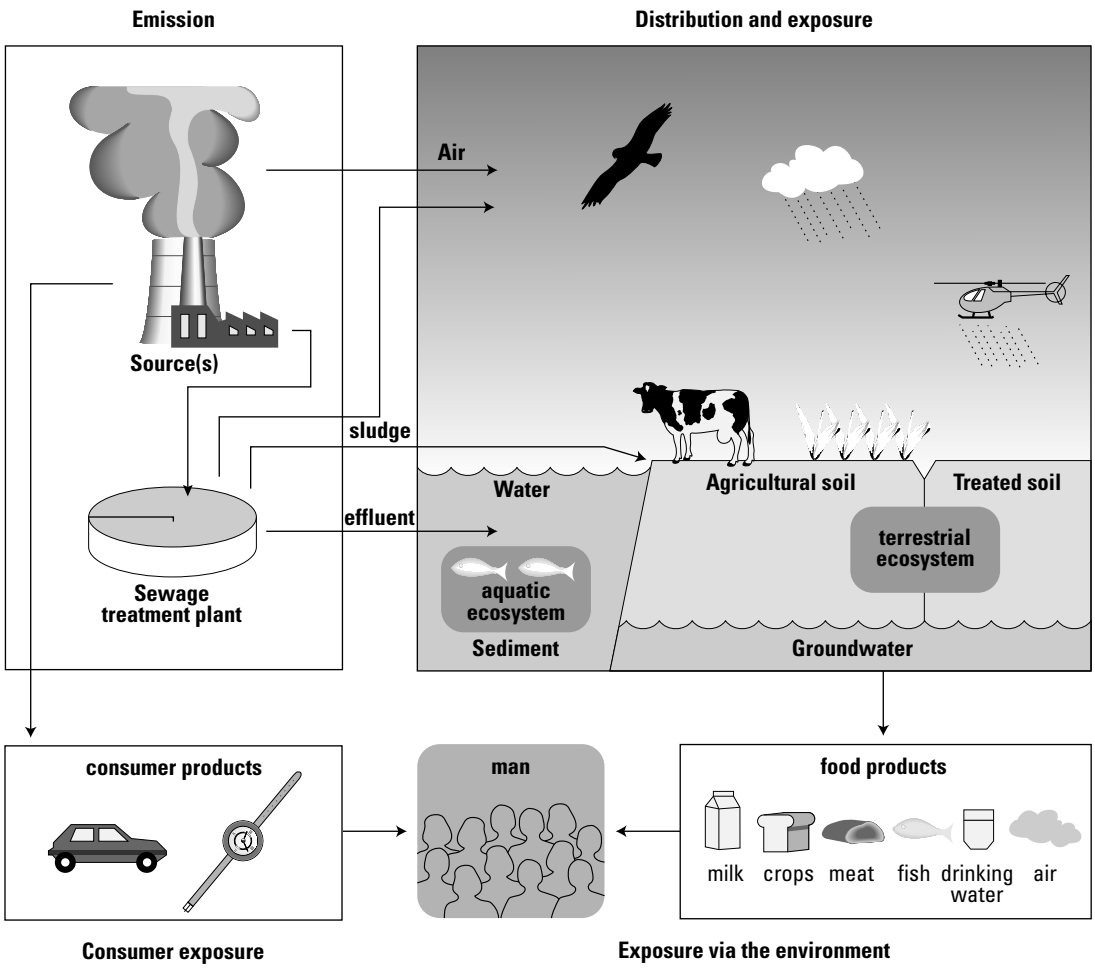


Figure 1.18. Elements of the European Union System for the Evaluation of Substances covered in this book [79]. The evaluation system comprises man, ecosystems (both aquatic and terrestial) and micro-organisms in sewage treatment plants.

The 16 chapters are summarized below.

*Chapter 1. General introduction.*
This chapter covers the general principles of risk assessment and risk management. It describes the role of risk assessment and other socio-economic and policy factors which contribute to the overall process of risk management of chemicals. Important definitions are given which are used in this field.

*Chapter 2. Emissions of chemicals to the environment.*
This chapter deals with the sources and emissions of chemicals into the environment, the life cycles of chemicals, point and diffuse sources of pollution and the classification of chemicals into main, industrial and use categories, as well as the development of "exposure scenarios". This provides important information for estimating emissions.

*Chapter 3. Transport, accumulation and transformation processes.*
This chapter highlights the transport, transformation and accumulation processes, e.g. advection, dispersion, volatilization, sorption, sediment transport, wet and dry deposition, bioaccumulation and biomagnification. Biotic and abiotic transformation processes are also included.

*Chapter 4. Environmental exposure assessment.*
The central theme of this chapter is environmental exposure assessment, i.e. the determination of exposure concentrations. It reviews compartmental models for surface water, groundwater, soil and air, as well as multimedia approaches.

*Chapter 5. Human exposure assessment.*
The central theme of this chapter is (external) human exposure assessment, i.e. the determination of exposure concentrations as a result of (a) exposure through the environment. It also highlights (b) consumer exposure assessment and (c) occupational exposure.

*Chapter 6. Toxicity testing for human health risk assessment.*
The main theme of this chapter is the assessment of health effects in man. It describes short and long-term toxicity, reproductive toxicity, mutagenicity, carcinogenicity, sensitization and irritation. Extrapolation methodologies and assessment factors are given which are used for the determination of DNELs for man.

*Chapter 7. Ecotoxicological effects.*
This chapter deals with ecotoxicological effects assessment for the aquatic and terrestrial environments. It describes single-species tests with aquatic and terrestrial species as well as multi-species studies. Extrapolation methodologies and safety factors are given which can be used to derive PNECs for ecosystems. It also examines the issue of mixture toxicity and the assessment of PBT and vPvB chemicals.

*Chapter 8. Data: needs, availability, sources and evaluation.*
This chapter addresses the input of any risk assessment, i.e. the data related to releases of chemicals, fate, exposure and effects. The focus of this chapter is on effects data.

*Chapter 9. Predicting fate-related physicochemical properties.*
This chapter describes basic physicochemical properties such as water solubility, melting point, boiling point, Henry's law constant, vapour pressure ($P_v$), the octanol-water partition coefficient ($K_{ow}$). Structure-activity relationships (SARs) and quantitative structure-activity relationships (QSARs) are given for various physicochemical parameters, (bio)accumulation and (bio)degradation.

*Chapter 10. Predicting toxicological and ecotoxicological endpoints.*
This chapter is about SARs and QSARs for basic toxicological and ecotoxicological properties. The application of SARs and QSARs can help to overcome the problem of data gaps and reduce animal testing.

*Chapter 11. Intelligent Testing Strategies.*
This chapter brings together the previous chapters on exposure and effects assessment. It describes testing strategies combining use and exposure information and effects information obtained from QSARs, read-across methods, thresholds of toxicological concern (TTCs), and *in vitro* tests prior to *in vivo* testing, as this is a more rapid, efficient, and cost-effective way of performing a risk assessment of chemicals.

*Chapter 12. The management of industrial chemicals in the EU.*
This chapter is about REACH. It summarizes the main features and requirements of the REACH legislation.

*Chapter 13. The management of industrial chemicals in the USA.*
This chapter is about the Toxic Substances Control Act in the USA It summarizes the main features and requirements of the legislation of industrial chemicals in the USA, including voluntary initiatives such as the Challenge Programme on High Production Volume Chemicals.

*Chapter 14. The management of industrial chemicals in Japan.*
This chapter is about chemicals management in Japan. It summarizes the main features and requirements of the legislation of industrial chemicals in Japan. It describes how risk assessment is applied in this regulatory context.

*Chapter 15. The assessment and management of industrial chemicals in Canada.*
This chapter summarizes the main features and requirements of the legislation of industrial chemicals in Canada, including the methodology of selecting priority chemicals. The relevant elements of how risk assessments are performed in Canada are included as well.

*Chapter 16. The OECD chemicals programme.*
This chapter describes the OECD activities relevant for the testing, assessment and management of industrial chemicals.

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