6.1: Introduction - The Essence of Risk Assessment

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Learning Objectives

After this module, you should be able to:

- explain the terms risk, hazard, risk assessment, risk management and solution-focused risk assessment ;
- explain the different steps of the risk assessment process, the relation between these steps and how the principle of tiering works;
- give an example of a risk indicator;
- indicate the most important advantages and disadvantages of the risk assessment paradigm.

Key words

Risk, hazard, tiering, problem definition, exposure assessment, effect assessment, risk characterization

Introduction

We assess risks on a daily basis, although we may not always be aware of it. For example, when we cross the street, we - often implicitly - assess the benefits of crossing and weigh these against the risks of getting hit by a vehicle. If the risks are considered too high, we may decide not to cross the street, or to walk a bit further and cross at a safer spot with traffic lights.

Risk assessment is common practice for a wide range of activities in society, for example for building bridges, protection against floods, insurance against theft and accidents, and the construction of a new industrial plant. The principle is always the same: we use the available knowledge to assess the probability of potential adverse effects of an activity as good as we can. And if these risks are considered too high, we consider options to reduce or avoid the risk.

Terminology

Risk assessment of chemicals aims to describe the risks resulting from the use of chemicals in our society. In chemical risk assessment, risk is commonly defined as "the probability of an adverse effect after exposure to a chemical". This is a very practical definition that provides natural scientists and engineers the opportunity to quantify risk using "objective" scientific methods, e.g. by quantifying exposure and the likelihood of adverse effects. However, it should be noted that this definition ignores more subjective aspects of risk, typically studied by social scientists, e.g. the perceptions of people and (dealing with) knowledge gaps. This subjective dimension can be important for risk management. For example, risk managers may decide to take action if a risk is perceived as high by a substantial part of the population, even if the associated health risks have been assessed as negligible by natural scientists and engineers.

Next to the term "risk", the term "hazard" is often used. The difference between both terms is subtle, but important. A hazard is defined as the inherent capacity of a chemical (or agent/activity) to cause adverse effects. The labelling of a substance as "carcinogenic" is an example of a hazard-based action. The inherent capacity of the substance to trigger cancer, as for example demonstrated in an *in vitro* assay or an experiment with rats or mice, can be sufficient reason to label a substance as "carcinogenic". Hazard is thus independent of the actual exposure level of a chemical, whereas risk is not.

Risk assessment is closely related to risk management, i.e. the process of dealing with risks in society. Decisions to accept or reduce risks belong to the risk management domain and involve consideration of the socio-economic implications of the risks as well as the risk management options. Whereas risk assessment is typically performed by natural scientists and engineers, often referred to as "risk assessors", risk management is performed by policy makers, often referred to as "risk managers".

Risk assessment and risk management are often depicted as sequential processes, where assessment precedes management. However, strict separation of both processes is not always possible and management decisions may be needed before risks are assessed. For example, risk assessment requires political agreement on what should be protected and at what level, which is a risk management issue (see Section on Protection Goals). Similarly, the identification, description and assessment of uncertainties in the assessment is an activity that involves risk assessors as well as risk managers. Finally, it is often more efficient to define alternative management options before performing a risk assessment. This enables the assessment of the current situation and alternative

management scenarios (i.e., potential solutions) in one round. The scenario with the maximum risk reduction that is also feasible in practice would then be the preferred management option. This mapping of solutions and concurrent assessment of the associated risks is also known as solution-focused risk assessment.

Risk assessment steps and tiering

Chemical risk assessment is typically organized in a limited number of steps, which may vary depending on the regulatory context. Here, we distinguish four steps (Figure1):

1. Problem definition (sometimes also called hazard identification), during which the scope of the assessment is defined;
2. Exposure assessment, during which the extent of exposure is quantified;
3. Effect assessment (sometimes also called hazard or dose-response assessment), during which the relationship between exposure and effects is established;
4. Risk characterization, during which the results of the exposure and effect assessments are combined into an estimate of risk and the uncertainty of this estimate is described.

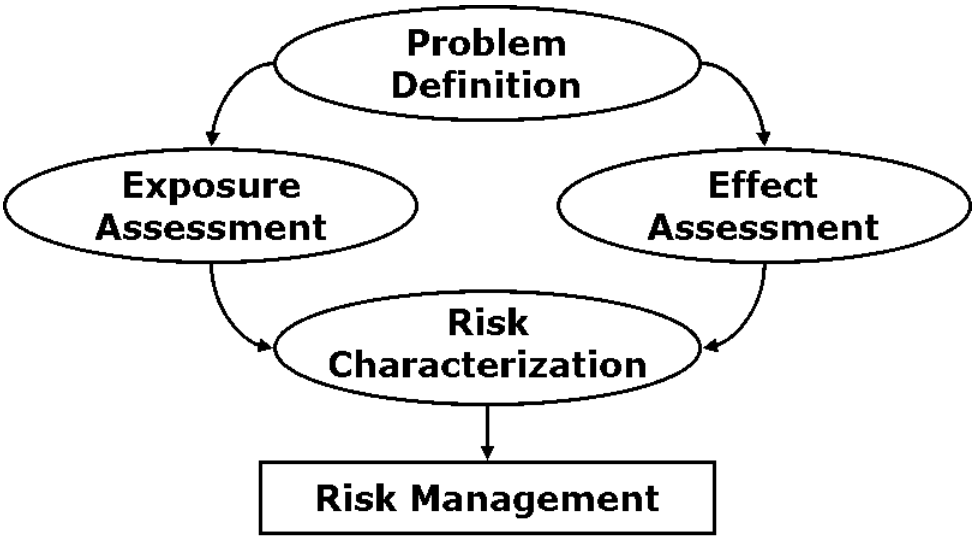

Figure 1. Risk assessment consists of four steps (problem definition, exposure assessment, effect assessment & risk characterization) and provides input for risk management.

The four risk assessment steps are explained in more detail below. The four steps are often repeated multiple times before a final conclusion on the acceptability of the risk is reached. This repetition is called tiering (Figure 2). It typically starts with a simple, conservative assessment and then, in subsequent tiers, more data are added to the assessment resulting in less conservative assumptions and risk estimates. Tiering is used to focus the available time and resources for assessing risks on those chemicals that potentially lead to unacceptable risks. Detailed data are gathered only for chemicals showing potential risk in the lower, more conservative tiers.

The order of the exposure and effect assessment steps has been a topic of debate among risk assessors and managers. Some argue that effect assessment should precede exposure assessment because effect information is independent of the exposure scenario and can be used to decide how exposure should be determined, e.g., information on toxicokinetics can be relevant to determine the exposure duration of interest. Others argue that exposure should precede effect assessment since assessing effects is expensive and unnecessary if exposure is negligible. The current consensus is that the preferred order should be determined on a case-by-case basis with parallel assessment of exposure and effects and exchange of information between the two steps as the preferred option.

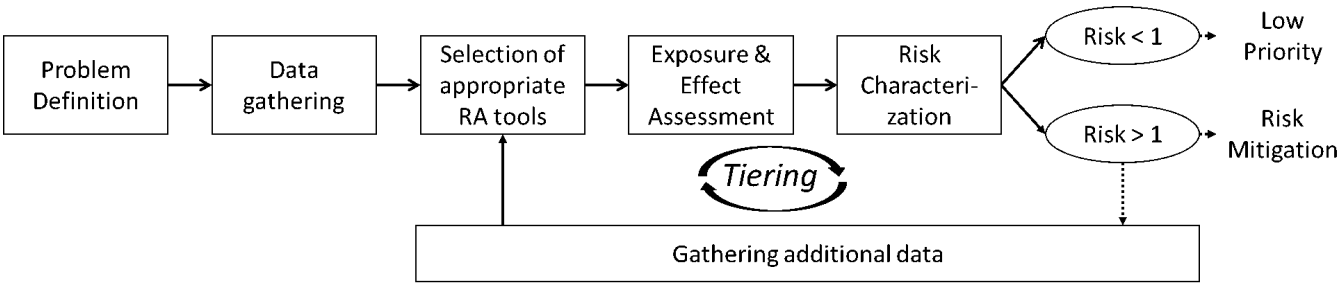

Figure 2: The principle of tiering in risk assessment. Initially risks are assessed using limited data and conservative assumptions and tools. When the predicted risk turns out unacceptable (Risk >1; see below), more data are gathered and less conservative tools are used.

Problem definition

The scope of the assessment is determined during the problem definition phase. Questions typically answered in the problem definition include:

- What is the nature of the problem and which chemical(s) is/are involved?
- What should be protected, e.g. the general population, specific sensitive target groups, aquatic ecosystems, terrestrial ecosystems or particular species, and at what level?
- What information is already available, e.g. from previous assessments?
- What are the available resources for the assessment?
- What is the assessment order and will tiering be applied?
- What exposure routes will be considered?
- What is the timeframe of the assessment, e.g. are acute or (sub)chronic exposures considered?
- What risk metric will be used to express the risk?
- How will uncertainties be addressed?

Problem definition is not a task for risk assessors only, but should preferably be performed in a collaborative effort between risk managers, risk assessors and stakeholders. The problem definition should try to capture the worries of stakeholders as good as possible. This is not always an easy task as these worries may be very broad and sometimes also poorly articulated. Risk assessors need a clearly demarcated problem and they can only assess those aspects for which assessment methods are available. The dialogue should make transparent which aspects of the stakeholder concerns will be assessed and which not. Being transparent about this can avoid disappointments later in the process, e.g. if aspects considered important by stakeholders were not accounted for because suitable risk assessment methods were lacking. For example, if stakeholders are worried about the acute and chronic impacts of pesticide exposure, but only the acute impacts will be addressed, this should be made clear at the beginning of the assessment.

The problem definition phase results in a risk assessment plan detailing how the risks will be assessed given the available resources and within the available timeframe.

Exposure assessment

An important aspect of exposure assessment is the determination of an exposure scenario. An exposure scenario describes the situation for which the exposure is being assessed. In some cases, this exposure situation may be evident, e.g. soil organisms living a contaminated site. However, especially when we want to assess potential risks of future substance applications, we have to come up a typical exposure scenario. Such scenarios are for example defined before a substance is allowed to be used as a food additive or before a new pesticide is allowed on the market. Exposure scenarios are often conservative, meaning that the resulting exposure estimate will be higher than the expected average exposure.

The exposure metric used to assess the risk depends on the protection target. For ecosystems, a medium concentration is often used such as the water concentration for aquatic systems, the sediment concentration for benthic systems and the soil concentration for terrestrial systems. These concentrations can either be measured or predicted using a fate model (see Section 3.8) and may or may not take into account bioavailability (see Section 3.6). For human risk assessment, the exposure metric depends on the exposure route. An air concentration is often used to cover inhalation, the average daily intake from food and water to cover oral exposure, and uptake through skin for dermal exposure. Uptake through multiple routes can also be combined in a dose metric for internal

exposure, such as Area Under the Curve (AUC) in blood (see Section 6.3.1). Exposure metrics for specific wildlife species (e.g. top predators) and farm animals are often similar as those for humans. Measuring and modelling route-specific exposures is generally more complex than quantifying a simple medium concentration, because it does not only require the quantification of the substance concentration in the contact medium (e.g., concentration in drinking water), but also quantification of the contact intensity (e.g., how much water is consumed per day). Especially oral exposure can be difficult to quantify because it covers a wide range of different contact media (e.g. food products) and intensities varying from organism to organism.

Effect assessment

The aim of the effect assessment is to estimate a reference exposure level, typically an exposure level which is expected to cause no or very limited adverse effects. There are many different types of reference levels in chemical risk assessment; each used in a different context. The most common reference level for ecological risk assessment is the Predicted No Effect Concentration (PNEC). This is the water, soil, sediment or air concentration at which no adverse effects at the ecosystem level are being expected. In human risk assessment, a myriad of different reference levels are being used, e.g. the Acceptable Daily Intake (ADI), the oral and inhalatory Reference Dose (RfD), the Derived No Effect Level (DNEL), the Point of Departure (PoD) and the Virtually Safe Dose (VSD). Each of these reference levels is used in a specific context, e.g. for addressing a specific exposure route (ADI is oral), regulatory domain (the DNEL is used in the EU for REACH, whereas the RfD is used in the USA), substance type (the VSD is typical for genotoxic carcinogens) or risk assessment method (the PoD is typical for the Margin of Safety approach).

What all reference levels have in common, is that they reflect a certain level of protection for a specific protection goal. In ecological risk assessment, the protection goal typically is the ecosystem, but it can also be a specific species or even an organism. In human risk assessment, the protection goal typically comprises all individuals of the human population. The definition of protection goals is a normative issue and it therefore is not a task of risk assessors, but of politicians. The protection levels defined by politicians typically involve a high level of abstraction, e.g. "the entire ecosystem and all individuals of the human population should be protected". Such abstract protection goals do not always match with the methods used to assess the risks. For example, if one assumes that one molecule of a genotoxic carcinogen can trigger a deathly tumour, 100% protection for all individuals of the human population is feasible only by banning all genotoxic carcinogens (reference level = 0). Likewise, the safe concentration for an ecosystem is infinitely small if one assumes that the sensitivity of the species in the system follows a lognormal distribution which asymptotically approaches the x-axis. Hence, the abstract protection goals have to be operationalized, i.e. defined in more practical terms and matching the methods used for assessing effects. This is often done in a dialogue between scientific experts and risk managers. An example is the "*one in a million lifetime risk estimated with a conservative dose response model*" which is used by many (inter)national organizations as a basis for setting reference levels for genotoxic carcinogens. Likewise, the concentration at which the no observed effect concentration (NOEC) for only 5% of the species is being exceeded is often used as a basis for deriving a PNEC.

Once a protection goal has been operationalized, it must be translated into a corresponding exposure level, i.e. the reference level. This is typically done using the outcomes of (eco)toxicity tests, i.e. tests with laboratory animals such as rats, mice and dogs for human reference levels and with primary consumers, invertebrates and vertebrates for ecological reference levels. Often, the toxicity data are plotted in a graph with the exposure level on the x-axis and the effect or response level on the y-axis. A mathematical function is then fitted to the data; the so-called dose-response relationship. This dose-response relationship is subsequently used to derive an exposure level that corresponds to a predefined effect or response level. Finally, this exposure level is extrapolated to the ultimate protection goal, accounting for phenomena such as differences in sensitivity between laboratory and field conditions, between tested species and the species to be protected, and the (often very large) variability in sensitivity in the human population or the ecosystem. This extrapolation is done by dividing the exposure level that corresponds to a predefined effect or response level by one or more assessment or safety factors. These assessment factors do not have a pure scientific basis in the sense that they account for physiological differences which have actually been proven to exist. These factors also account for uncertainties in the assessment and should make sure that the derived reference level is a conservative estimate. The determination of reference levels is an art in itself and is further explained in sections 6.3.1 for human risk assessment and 6.3.2 for ecological risk assessment.

Risk characterization

The aim of risk characterization is to come up with a risk estimate, including associated uncertainties. A comparison of the actual exposure level with the reference level provides an indication of the risk:

$$Risk\ Indicator = \frac{Exposure\ Level}{Reference\ Level}$$

If the reference level reflects the maximum safe exposure level, then the risk indicator should be below unity (1.0). A risk indicator higher than 1.0 indicates a potential risk. It is a "potential risk" because many conservative assumptions may have been made in the exposure and effect assessments. A risk indicator above 1.0 can thus lead to two different management actions: (1) if available resources (time, money) allow and the assessment was conservative, additional data may be gathered and a higher tier assessment may be performed, or (2) consideration of mitigation options to reduce the risk. Assessment of the uncertainties is very important in this phase, as it reveals how conservative the assessment was and how it can be improved by gathering additional data or applying more advanced risk assessment tools.

Risks can also be estimated using a margin-of-safety approach. In this approach, the reference level used has not yet been extrapolated from the tested species to the protection goal, e.g. by applying assessment factors for interspecies and interindividual differences in sensitivity. As such, the reference level is not a conservative estimate. In this case, the risk indicator reflects the "margin of safety" between actual exposure and the non-extrapolated reference level. Depending on the situation at hand, the margin-of-safety typically should be 100 or higher. The main difference between the traditional and the margin-of-safety approach in risk assessment is the timing for addressing the uncertainties in the effect assessment.

Reflection

Figure 3 illustrates the risk assessment paradigm using the DPSIR chain (Section 1.2). It illustrates how reference exposure levels are being derived from protection goals, i.e. the maximum level of impact that we consider acceptable. The actual exposure level is either measured or predicted using estimated emission levels and dispersion models. When measured exposure levels are used, this is called retrospective or diagnostic risk assessment: the environmental is already polluted and the assessor wants to know whether the risk is acceptable and which substances are contributing to it. When the environment is not yet polluted, predictive tools can be used. This is called prospective risk assessment: the assessor wants to know whether a projected activity will result in unacceptable risks. Even if the environment is already polluted, the risk assessor may still decide to prefer predicted over measured exposure levels, e.g. if measurements are too expensive. This is possible only if the pollution sources are well-characterized. Retrospective (diagnostic) and prospective risk assessments can differ substantially in terms of problem definitions and methods used, and are therefore discussed in separate sections in this online book.

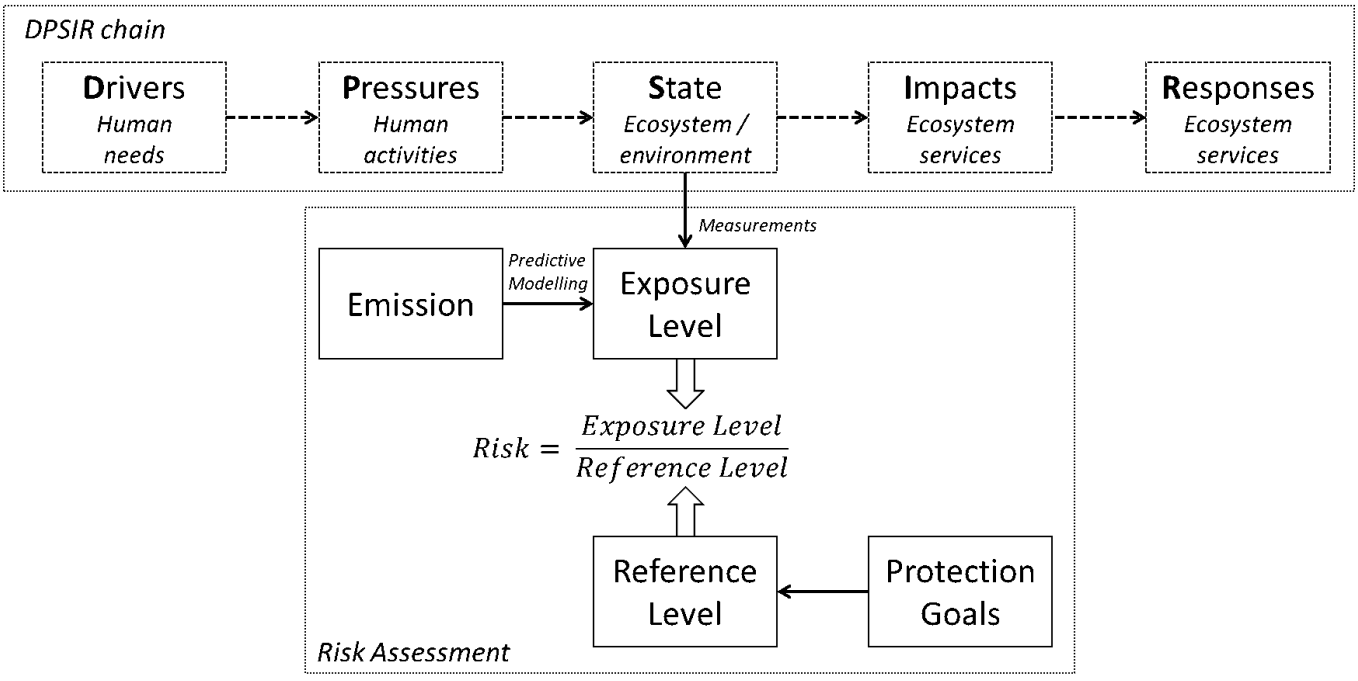

Figure 3: The risk assessment paradigm and the DPSIR chain.

Figure 3 can also be used to illustrate some important criticism on the current risk assessment paradigm, i.e. the comparison between the actual exposure level and a reference level. In current assessments, only one point of the dose-response relationship is being used to assess risk, i.e. the reference level. Critics argue that this is suboptimal and a waste of resources because the dose-

response information is not used to assess the actual risk. A risk indicator with a value of 2.0 implies that the exposure is twice as high as the reference level but this does not give an indication of how many individuals or species are being affected or of the intensity of the effect. If the dose-response relationship would be used to determine the risk, this would result in a better-informed risk estimate.

A final critical remark that should be made, is the fact that risk assessment is often performed on a substance-by-substance basis. Dealing with mixtures of chemicals is difficult because each mixture has a unique composition in terms of compounds and concentration ratios between compounds. This makes it difficult to determine a reference level for mixtures. Mixture toxicology is slowly progressing and several methods are now available to address mixtures, i.e. whole mixture methods and compound-based approaches (Section 6.3.6). Another promising development are effect-based methods (Section 6.4.2). These methods do not assess risk based on chemical concentration, but on the toxicity measured in an environmental sample. In terms of DPSIR, these methods are assessing risks on the level of impacts rather than the level of state or pressures.

6.1. Question 1

Imagine the herbicide glyphosate would be banned based on its carcinogenic properties. Would this intervention be risk-based or hazard-based?

6.1. Question 2

Indicate whether the following activities should involve risk assessors, risk managers/politicians and/or stakeholders:

1. Determination of a safe dose level based on established protection goals;
2. Determination of protection goals;
3. Determination of intervention options;
4. Demarcation of the risk assessment problem;
5. Translation of abstract protection goals into operational goals.

6.1. Question 3

Indicate whether the following risk assessments are retrospective or prospective:

1. Determining the adverse impacts of a contaminated area on human health and the environment;
2. Quantifying the human health risk of current air pollution levels;
3. Determining whether the risks associated with a new pesticide are acceptable;
4. Predicting the risk of chemicals based on current emission levels.

6.1. Question 4

A risk assessment was performed for two different substances, i.e. A and B. The risk indicator value of substance A was 1.5 and that of substance B was 2.0. A risk manager proposes to first address substance B and subsequently substance A. Do you agree? Motivate your answer.
