Universidade do Algarve

Faculdade de Ciências e Tecnologia

2023

RISK MANAGEMENT

RELATÓRIO de UNIDADE CURRICULAR

Luís Miguel Nunes

UNIVERSIDADE DO ALGARVE

Faculdade de Ciências e Tecnologia

Relatório Pedagógico da Unidade Curricular

no âmbito de Provas Púbicas de Agregação

na Universidade do Algarve:

Risk Management

Assinado por: **Luís Miguel de Amorim Ferreira Fernandes Nunes**
Num. de Identificação: 08480966
Data: 2023.07.12 15:58:51+01'00'

CHAVE MÓVEL

Luís Miguel Nunes

Faro, 2023

(contra-capa para impressão sustentável)

O presente documento constitui o relatório pedagógico da unidade curricular de "Risk Management" (2 ECTS) apresentado no âmbito de Provas Púbicas de Agregação na Universidade do Algarve, de acordo com o estabelecido no artigo 5º, alínea b) do Decreto-Lei (DL) nº 239/2007, de 19 de junho: as provas de agregação são constituídas "pela apresentação, apreciação e discussão de um relatório sobre uma unidade curricular, grupo de unidades curriculares, ou ciclo de estudos, no âmbito do ramo do conhecimento ou especialidade em que são prestadas as provas".

O texto é apresentado em língua inglesa, uma vez que diz respeito a uma disciplina com o mesmo nome lecionada no Mestrado Erasmus Mundus em *Chemical Innovation and Regulation*, e por aprovação Reitoral de 17 de novembro de 2022. Esta disciplina faz parte de um dos módulos do curso, de que sou responsável, dedicado a "Chemical Plants Safety" (6 ECTS), e de que fazem parte outras duas disciplinas complementares sobre *Chemical Reactivity Hazards* (2 ECTS) e *Chemical Process Safety* (2 ECTS), dadas por colegas da Universidade Barcelona (Daniel Sainz e Anton Vidal, respetivamente).

Luís Miguel Nunes

Faro, 04/07/2023

TABLE OF CONTENTS

1 INTRODUCTION

In this subject we will study the general framework for risk management applied to the production, storage, transport, and use of chemical substances, having humans as the target receptors.

Humans are exposed to hazardous substances through three major pathways: the environment compartments, consumer goods, and occupational activities (Figure 1). We will focus here on the environmental and consumer goods pathways. The first focus on risk analysis for substances that may reach the environment due to emissions during the production, storage, transport, or manipulation of a substance, or from a waste stream at a chemical plant. The second on risks due to exposure to hazardous substances present in the different products people use and enter in contact with in the daily live.

Following release, substances will undergo variable dispersion and degradation in the environment depending on their physical-chemical properties, and on the physical-chemical and biological conditions of the medium. We will discuss briefly the key properties affecting environmental fate and accumulation in living organisms. More details were given in a other subject in the course.

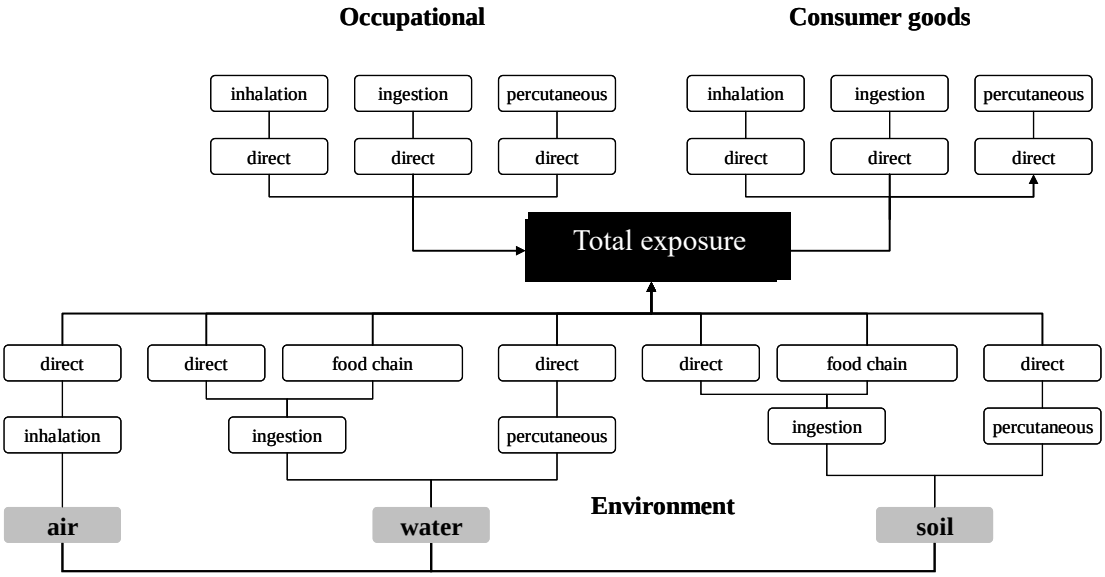

Figure 1. Major routes for human exposure (adapted from EEA, 1999)

Risk management, as set out by the Organisation for Economic Co-operation and Development (OECD, 2003) is the "decision-making process involving considerations of political, social, economic, and technical factors with relevant risk assessment information relating to a hazard to develop, analyse, and compare regulatory and non-regulatory options and to select and implement appropriate regulatory response to that hazard. it comprises three elements: risk evaluation; emission and exposure control; risk monitoring." It is the second step in *risk analysis* (Table 1), following *risk assessment*, and preceding *risk communication*. Risk management is therefore quantitatively supported by the calculations made in the risk assessment phase, justifying that we spend more time reviewing its methods. Moreover, the remaining phases and particular methods are covered by other disciplines in the course, so they are not discussed in detail here:

Structure toxicity relationship
Health and safety in chemistry
Principles of toxicological assessment
Genotoxicity assessment
Toxicology
Toxicokinetics and toxicogenetics
Health safety of nanotechnology
Environmental analysis and detection in the environment
Environmental risk of plastic material
Chemical pollutant remediation
Social perception of the chemical risk
Chemical reactivity hazards
Safety in the use of chemicals
Food regulation

Table 1. Environmental risk terminology (OECD, 2003)

Risk Analysis							
A process for controlling situations where an organism, system or (sub) population could be exposed to a hazard. The Risk Analysis process consists of three components: (1) risk assessment, (2) risk management and (3) risk communication.							
(1) Risk assessment				**(2) Risk management**			**(3) Risk communication**
A process intended to calculate or estimate the risk to a given target organism, system or (sub)population , including the identification of attendant uncertainties, following exposure to a particular agent, taking into account the inherent characteristics of the agent of concern as well as the characteristics of the specific target system. Includes four steps: hazard identification, hazard characterisation (related term: dose-response assessment), exposure assessment, and risk characterization. It is the first component in a risk analysis process.				Decision-making process involving considerations of political, social, economic, and technical factors with relevant risk assessment information relating to a hazard so as to develop, analyse, and compare regulatory and non-regulatory options and to select and implement appropriate regulatory response to that hazard. Comprises three elements: risk evaluation; emission and exposure control; risk monitoring.			Interactive exchange of information about (health or environmental) risks among risk assessors, managers, news media, interested groups and the general public.
Hazard identification	**Dose-response assessment**	**Exposure assessment**	**Risk characterization**	**Risk evaluation**	**Emission and exposure control**	**Risk monitoring**	
The identification of the type and nature of adverse effects that an agent has as inherent capacity to cause in an organism, system or (sub) population.	The qualitative and, wherever possible, quantitative description of the inherent properties of an agent or situation having the potential to cause adverse effects. This should, where possible, include a dose-response assessment and its attendant uncertainties. (aka, Dose-Effect Relationship, Effect Assessment, Dose-Response Relationship, Concentration -Effect Relationship.	Evaluation of the exposure of an organism, system or (sub) population to an agent (and its derivatives).	The qualitative and, wherever possible, quantitative determination, including attendant uncertainties, of the probability of occurrence of known and potential adverse effects of an agent in a given organism, system or (sub)population, under defined exposure conditions.	Establishment of a qualitative or quantitative relationship between risks and benefits of exposure to an agent, involving the complex process of determining the significance of the identified hazards and estimated risks to the system concerned or affected by the exposure, as well as the significance of the benefits brought about by the agent. It is an element of risk management. Risk Evaluation is synonymous with Risk-Benefit evaluation		Process of following up the decisions and actions within risk management in order to ascertain that risk containment or reduction with respect to a particular hazard is assured.	

Table 2. Definitions of risk assessment

Author	Definition of RA
Paustenbach (2002)	"The process or procedure used to estimate the likelihood that humans or ecological systems will be affected adversely by a chemical or physical agent under specific set of conditions"
US National Academy of Sciences (NAS, 1983)	"The characterization of the potential adverse health effects of human exposures to environmental hazards. Risk assessments include several elements: description of the potential adverse health effects based on an evaluation of results of epidemiologic, clinical, toxicologic, and environmental research; extrapolation from those results to predict the type and estimate the extent of health effects in humans under given conditions of exposure; judgments as to the number and characteristics of persons exposed at various intensities and durations; and summary judgements on the existence and overall magnitude of the public-health problem. Risk assessment also includes characterization of the uncertainties inherent in the process of inferring risk."
US Environmental Protection Agency (USEPA, 1992)	"The determination of the kind and degree of hazard posed by an agent, the extent to which a particular group of people have been or may be exposed to the agent, and the present or potential health risk that exists due to the agent."
UK The Royal Society (UKRS, 1992)	"The combination of the probability, or frequency, of occurrence of a defined hazard and the magnitude of the consequences of the occurrence"
Organisation for Economic Co-operation and Development (OECD, 2003)	"A process intended to calculate or estimate the risk to a given target organism, system or (sub)population , including the identification of attendant uncertainties, following exposure to a particular agent, taking into account the inherent characteristics of the agent of concern as well as the characteristics of the specific target system. The Risk Assessment process includes four steps: hazard identification, hazard characterisation (related term: dose-response assessment), exposure assessment, and risk characterization. It is the first component in a risk analysis process."
WHO's International Programme on Chemical Safety (WHO, 2004)	"A process intended to calculate or estimate the risk to a given target organism, system, or (sub)population, including the identification of attendant uncertainties, following exposure to a particular agent, taking into account the inherent characteristics of the agent of concern as well as the characteristics of the specific target system. The risk assessment process includes four steps: hazard identification, hazard characterization (related term: Dose–response assessment), exposure assessment, and risk characterization. It is the first component in a risk analysis process."

Author	Definition of RA
European Environment Agency (EEA, 1999)	"The procedure in which the risks posed by inherent hazards involved in processes or situations are estimated either quantitatively or qualitatively. In the life cycle of a chemical for instance risks can arise during manufacture, distribution, in use, or disposal process. Risk assessment of the chemical involves the identification of inherent hazards at every stage and an estimation of the risks posed by these hazards. Risk is estimated by incorporating a measure of the likelihood of the hazard actually causing harm and a measure of the severity of harm in terms of the consequences to people or the environment." The author also defines Environmental (or ecological) Risk Assessment (ERA): "the examination of risks resulting from technology that threaten ecosystems, animals, and people. It includes human health risk assessments, ecological or ecotoxicological risk assessments, and specific industrial applications of risk assessment that examine endpoints in people, biota or ecosystems".

(cont.)

Risk assessment has been seen as a rational and objective basis for priority setting and decision making in environmental policy, and so many regulators and developers advocate its use. The sequence of the various risk assessment process steps is: i) establishing the context; ii) identification; iii) analysis; iv) assessment; v) management; and vi) decision making. Despite significant differences at specific steps and in its definition (Table 2), they are generally very similar across different industries and countries. Terminology also varies, but some generic terms are widely accepted. Differences in the current approaches to risk assessment mainly come from: i) the extent to which the sequence of the risk assessment process is taken into account; ii) the explicit or implicit use of the basic risk criteria, probability of occurrence and extent of damage, in some of the process steps (expressed in quantitative, semiquantitative or qualitative terms) (Kirchsteiger, 2005).

In the following paragraphs we briefly review two risk-based models common in the industry, viz.: i) Quantitative Risk Assessment (QRA), and ii) method proposed by the National Academy of Science (NAS, 1983). These two were at the origin of all the other human and environmental risk assessment models, hence their interest.

Before going into the methods in greater detail, some definitions are needed. Specifically, what is the "hazard" included in some of the definitions of "risk", "risk analysis", "risk assessment", "risk management", and "risk communication". The definitions used here are those proposed in the wake of the IPCS/WHO/OECD (WHO, 2004). They complement those in Table 1:

Hazard is an inherent property of a substance having the potential to cause adverse effects when an organism, system or (sub) population is exposed to it.

Risk is the probability of an adverse effect in an organism, system, or (sub)population caused under specified circumstances by exposure to the substance.

Hazard identification, whereby the type and nature of adverse effects that a substance has an inherent capacity to cause in an organism, system, or (sub)population are pinpointed. It is the process of determining whether exposure to an agent can cause an increase in the incidence of a health condition (cancer, birth defect, etc.). It involves characterizing the nature and strength of the evidence of causation. Although the question of whether a substance causes cancer or other adverse health effects is theoretically a yes-no question, there are few chemicals on which the human data are definitive. Therefore, the question is often restated in terms of effects in laboratory animals or other test systems, e.g., 'Does the agent induce cancer in test animals?' Positive answers to such questions are typically taken as evidence that an agent may pose a cancer risk for any exposed humans. Information from short-term in vitro tests and on structural similarity to known chemical hazards may also be considered (NAS, 1983)." Note that this step may be the only one necessary if no hazard is found or if a regulatory agency elects to act without further analysis. Also, the model starts by identifying the hazard, which influences the scope, since regulatory agencies already know the context of the work and they can manage without the problem formulation step.

Hazard identification in the context of industrial activity refers also to the description of the type, amount, timing, and probability of a release. In many instances a description of how releases are consequences of triggering events and actions is also included. For this purpose, the following techniques are common in the industry: i) checklist,

event trees, failure mode and effect analysis (FMEA), fault trees, hazard and operability study (HAZOP), knowledge-based HAZOP, task analysis, and what-if. Checklists specify the components of a plant that require safe design, based on industry codes, accident databases, and expert judgment. Event tree analysis is an inductive process that starts with an initiating event and studies all the consequent chain of events that may lead to an accident. Failure mode and effect analysis studies the ways equipment may fail or be incorrectly operated and the consequences. It helps to develop better designs, more resilient to incorrect use and/or malfunction. Fault tree analysis is a deductive method, represented in a logic diagram that illustrates how a combination of events (e.g., failures or accidents) may lead to a failure (or accident) of interest. HAZOP is a method where deviations from design parameters are evaluated in terms of their causes, consequences and correction measures. Terms such as "higher", "lower", "more, "less", etc., are used to create scenarios. This method is very common. In knowledge-based HAZOP some or all of the evaluation terms are substituted by an industry or process-specific checklist. When other methods show that the human factor is very important, task analysis allows the detection and correction of processes where human failure risk is high. Finally, in what-if methods, a small group of experts gathers for a brainstorming meeting led by a chairman who puts questions about a specific process and what unexpected events could produce unwanted consequences.

Dose-response assessment is the process of characterizing the relation between the dose of an agent administered or received and the incidence of an adverse health effect in exposed populations and estimating the incidence of the effect as a function of human exposure to the agent. It takes account of intensity of exposure, age pattern of exposure, and possibly other variables that might affect response, such as sex, lifestyle, and other modifying factors. A dose-response assessment usually requires extrapolation from high to low dose and extrapolation from animals to humans (NAS, 1983). A dose-response assessment should describe and justify the methods of extrapolation used to predict incidence and should characterize the statistical and biologic uncertainties in these methods." Assessment endpoints here are those related to human health (morbidity and mortality).

Risk characterization is the process of estimating the incidence of a health effect under the various conditions of human exposure described in exposure assessment (NAS, 1983). It is performed by combining the exposure and dose-response assessments. The summary effects of the uncertainties in the preceding steps are described in this step."

Assessment endpoint is not of general use (WHO, 2004) but shows up with frequency in North American documentation, being the qualitative/quantitative expression of a specific factor with which a risk may be associated as determined through an appropriate risk assessment. When a contaminant crosses the external exposure surface of a receptor and is absorbed into the body, an exposure turns into a dose. From there, the contaminant can disseminate throughout the body in its original form, in a metabolized form, or both. The dose that the target internal tissue, organ, or developing embryo/foetus gets is the endpoint for exposure science; this is the site where the dose starts the toxicity pathways that result in the unfavourable outcome (USEPA, 2019). This endpoint serves as the starting point for toxicology (Pleil and Sheldon 2011). The endpoint may refer also to populations and ecosystems.

Exposure assessment (also known as exposure scenario) is a set of conditions or assumptions about sources, exposure pathways, amounts or concentrations of agent(s)involved, and an exposed organism, system, or (sub)population (i.e., numbers, characteristics, habits) used to aid in the evaluation and quantification of exposure(s) in a given situation. It is the process of measuring or estimating the intensity, frequency, and duration of human exposures to an agent currently present in the environment or of estimating hypothetical exposures that might arise from the release of new chemicals into the environment. In its most complete form, it describes the magnitude, duration, schedule, and route of exposure; the size, nature, and classes of the human populations exposed; and the uncertainties in all estimates. Exposure assessment is often used to identify feasible prospective control options and to predict the effects of available control technologies on exposure (NAS, 1983).

When analysing risk one has to answer questions such as (EEA, 1999): i) what is the object of the analysis; ii) what is the risk source; iii) is the hazard a single substance or is it a mixture; iv) is the source an individualized origin, or is it a diffuse source; v) is the analysis carried out during production, transport, use, or disposal of the substance or in all these stages; vi) what are the pathways (air, soil, water); vii) what or who are the receptors; viii) why is a risk assessment being carried out; ix) what end-points are used; x) are regulatory guides to be used as indicators of acceptable risks and of what end-points to use; and xi) where will risk assessment start and stop.

Risk assessment reports summarizing the results of the analysis are documents intended to provide risk managers (e.g., policy makers and regulators) with the pertinent information so that the best decisions can be made. These reports should assemble, critique and interpret all pertinent scientific information relating to toxicology, human

experience, environmental fate, and exposure (Paustenbach, 2002). It has been observed that under similar conditions and with the same information, risk managers may decide differently in different countries or regions according to the public perception of risk, which may change from person to person and from place to place. In fact, Starr (1985), who initiated the analysis of the relation between technological risk, social benefits, and acceptability back in 1969 (Starr, 1969), indicates that "public acceptance of any risk is more dependent on public confidence in risk management than on quantitative estimates of risk consequences, probabilities, and magnitudes". While quantitative estimates of risk consequences, probabilities, and magnitudes are important for making informed decisions about risk, people's perception of risk is often shaped by a variety of other factors, such as emotions, trust in authorities, and cultural values. For instance, people may be more willing to accept a risk if they trust that the relevant authorities are taking appropriate measures to manage and mitigate that risk. On the other hand, if there is a perceived lack of transparency or competence in risk management, people may be less willing to accept even relatively small risks. While quantitative estimates of risk are important, risk management and risk communication strategies that consider the public's perceptions and values are likely to be more effective in increased risk awareness, resulting in better preparedness and risk-prevention habits, better decision-making and environmental protection, and in general in more trust in risk management strategies.

Quantitative risk assessment (QRA) model

Quantitative Risk Assessment (Figure 3) was first applied to large technological systems in 1975 for the Assessment of Accident Risks in U.S. Nuclear Power Plants and has since been implemented in many other fields. It is worth reviewing it here because it set the framework for what later became the environmental risk assessment methods.

QRA (Kaplan and Garrick, 1981) is a specialist method used to numerically calculate environmental, individual, worker and public risk level values. These can then be compared with regulatory risk criteria. Satisfactory demonstration of acceptable risk levels is often a requirement for the approval of major hazardous plant construction plans, management of chemicals, remediation actions, etc. QRA should answer the following questions (UKEA, 2005): i) what can go wrong?; ii) how likely is it?; and iii) what are the consequences?. It is a top-down approach that proceeds as follows for technological systems (Apostolakis, 2004):

i. A set of undesirable end states (adverse consequences) is defined, e.g., in terms of risk to the public, loss of crew, and loss of the system;
ii. For each end state, a set of disturbances to normal operation is developed that, if uncontained or unmitigated, can lead to the end state. These are called initiating events (IE);
iii. Event and fault trees or other logic diagrams are employed to identify sequences of events that start with an IE and end at an end state. Thus, accident scenarios are generated. These scenarios include hardware failures, human errors, fires, and natural phenomena. The dependencies among failures of systems and redundant components (common-cause failures) receive particular attention. These scenarios answer the first question;
iv. The probabilities of these scenarios are evaluated using all available evidence, primarily past experience and expert judgment;
v. The accident scenarios are ranked according to their expected frequency of occurrence.

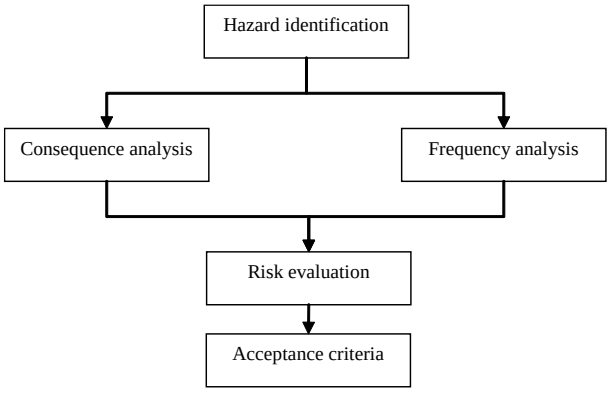

Figure 3. Quantitative Risk Assessment stages

The approach needs some alterations when applied to the evaluation of environmental contamination and consequent effects on human health. It is nevertheless interesting to look at the reasoning behind the model, even if applied to a different situation. The QRA model has the following generic stages (Figure 3): i) hazard identification; ii) consequence analysis; iii) frequency analysis; iv) risk evaluation; iv) acceptance criteria.

Risk is a function of two parameters: the likelihood that an undesired event will occur, and its consequences (equation 1) These two parameters may be calculated in sequence or simultaneously; or in iterative feedback loop processes where the result of one stage is used to alter the previous stage. See an example of a QRA procedure with such a feedback loop in Figure 4.

$$Risk = f\left(frequency \cdot consequences\right) \quad (1)$$

Before a QRA is conducted, some aspects must be reviewed, in particular the purpose of the study, so that the appropriate results are generated, the facilities and risks to be included, special reporting needs, including regulatory requirements; in addition, the methodologies that will provide the required results must be chosen. Hence, QRA may be divided in two parts (IOMC, 2006): i) preparation – where the objectives, scope, standards and methodologies are selected; and ii) implementation.

Preparatory part may be divided into six components (Figure 5): i) identify the objective; ii) specify output requirements; iii) determine scope of assessment; iv) identify data and information sources; v) identify special reporting needs; vi) select what models to apply.

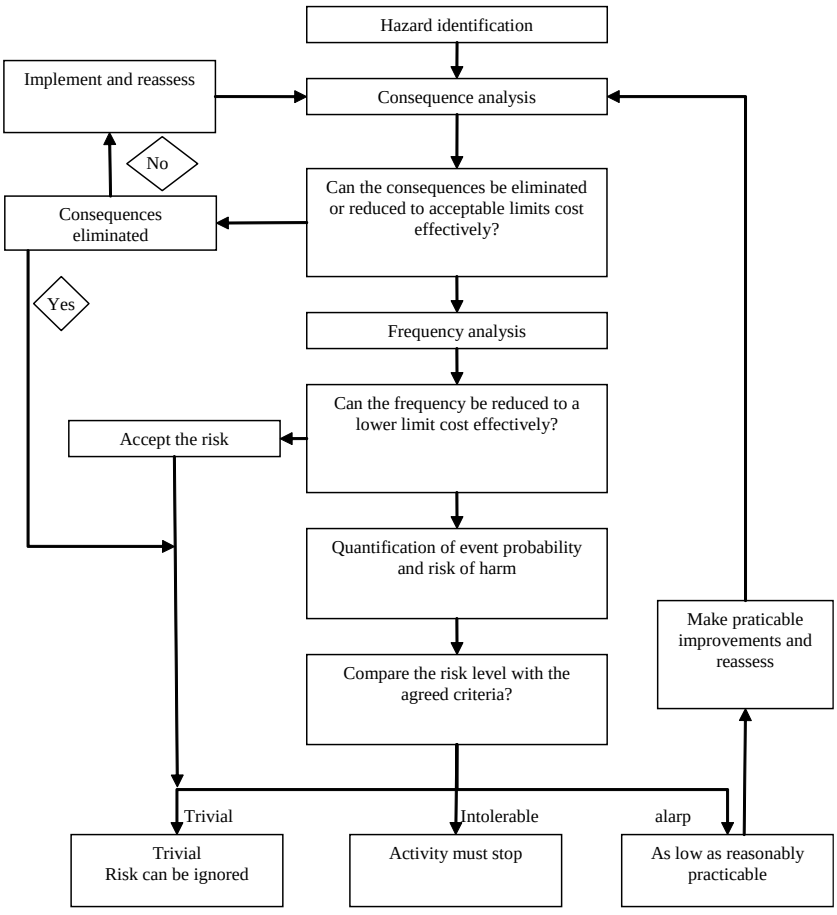

Figure 4. Example of procedure for QRA (adapted from Calow, 1998)

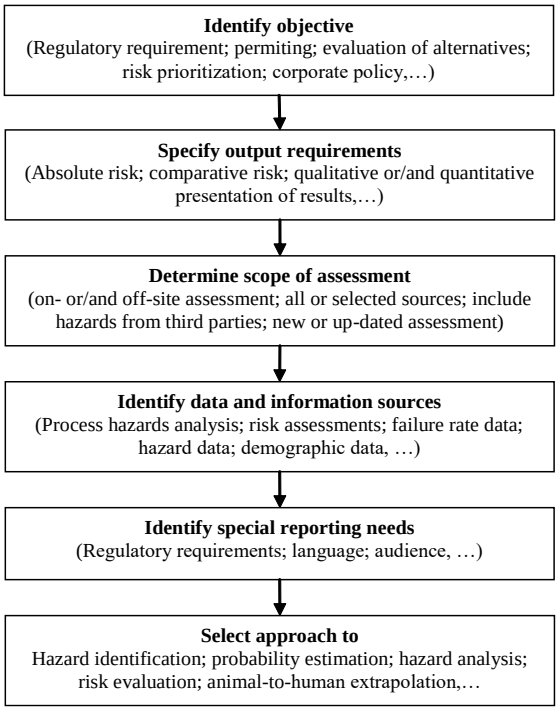

Figure 5. QRA – preparation (adapted from IOMC, 2006)

It is fundamental at the start of a QRA to clearly identify how and for what end are the results of the assessment going to be used. The purpose affects the scope of the work, the way data is processed (e.g., by modeling or spatial interpolation); the methodologies will have to be chosen to give the expected type of results. Even the format and content of the report may have to be adapted to particular requirements. Common requirements include:

i. Permitting, where the legal process sets particular requirements – it is likely that the report is submitted to a permitting authority, therefore having to follow legal specifications;
ii. regulatory requirement – in many countries (particularly in Europe), QRA process and reporting are clearly regulated (see for example the "Guidelines for Environmental Risk Assessment and Management" (DEFRA/UKEA, 2000) and the "Guidance on Requirements for Land Contamination Reports" (UKEA, 2005), both emanating from regulatory agencies in the United Kingdom, and the "Technical Guidance Document on Risk Assessment," from the European Chemical Bureau (ECB, 2003a);
iii. evaluation of alternatives, in this case the level of detail for each alternative is lower, with the analysis being concentrated on finding the differences in risks;
iv. risk prioritization, is used to rank potential hazards or system deficiencies for possible mitigation; it is a process based on a complex set of societal, economic and political considerations, in addition to human health and ecological risks, and is interdependent with risk assessment (SAIC, 1992);
v. corporate policy, may require all operations that meet a particular criterion to be subject to QRA (or, as happens in many cases, to some management tool, such as ISO 14001, where risk assessment may be useful for assessing environmental impacts);
vi. cost/benefit analysis, used to choose between risk mitigation measures for potential implementation – measures usually reduce either the likelihood of occurrence or the severity of the hazard.

Specify output requirements: These must respond to the objectives of the assessment. Examples of output requirements are (IOMC, 2006):

i. Absolute or comparative risk estimates, where the first are generally needed if there is concern about the tolerability of the risk, when the risks from different studies are to be added, or if the systems to be compared are very different; the latter are used to choose from different options when there is no question about the tolerability of the risk;
ii. qualitative or quantitative risk assessment - developing fully quantified risk assessments can be very expensive and time consuming; in many instances a qualitative study will provide sufficient data on which to base a decision; qualitative assessments are generally used for internal purposes and rely on the experience and judgment of the assessment team who will draw on their experience in

conducting rigorous quantified assessments; the results of qualitative assessments may determine the need for more rigorous QRA of certain operations; some authors identify qualitative risk assessment with only hazard identification and exposure assessment of the QRA, while quantitative risk assessment includes all four components of QRA (SAIC, 1992; WHO, 2004), though qualitative assessment may also be used for dose-response and risk characterization (ECB, 2003b,c; CCME, 2006);

iii. format of the results, where two main formats are usually used, namely spatial presentation (contours) of individual risks, and plots of consequences (e.g., fatalities or injuries) against frequency; other aspects that affect report format are the focus on individual or societal risk, interest in maximum versus average risk, focus on level of hazard or probability of injury, proximity and nature of surrounding population, fixed facility or transportation activity, and regulatory requirements.

Determine scope of assessment: Scope must meet the requirements of the assessment objectives. Examples of items to consider for scope are:

i. Single agent or multiple substance analysis, which specific endpoints, which exposure pathways, what timescales;
ii. on-site or off-site risk assessment;
iii. when more than one source is present, there may be the need to identify which one(s) is(are) to be assessed;
iv. are hazards from third parties to be included in the analysis;
v. is the assessment a new one or is it a reassessment.

Identify data and information sources: where the literature research should concentrate on existing reports (viz., HAZOP reports, FMEA studies, event/fault tree studies, etc., QRA reports, company and industry failure rate data and accident data bases, hazard data (material safety data sheets, hazardous consequence calculations, historical accident data, etc.), demographic data, and meteorological data), and databases. Where regulatory demands must be considered, the report content, detail and presentation must be adapted to the expected audience (e.g., regulatory agency and public).

Where the methods and models have to be identified (includes qualitative and quantitative ones). These include, but are not limited to (IOMC, 2006):

i. Hazard identification (HAZOP, good for complex systems or new technology; failure mode and effects analysis, used where a very detailed assessment is required; checklist, good for simple common facilities with similar designs, historical data, good for simple systems where one is confident that all possible scenarios will be revealed by historical data);
ii. Frequency analysis (fault/event trees, good for complex systems where multiple accident causes exist; historical data, good for simple common systems; layer of protection analysis, provides a consistent basis for judging whether there are sufficient independent protection layers to control risk);
iii. Hazard analysis (Simple models, used where the overall risk is not sensitive to the hazard zones or where a quick study is required; public models, required by some regulators (e.g. in the Netherlands, California); complex models, used where the overall risk is sensitive to the hazard zones or where conditions cannot be modelled using simpler approaches (for example, mixtures);
iv. Risk evaluation, where the models to be used must be identified.

QRA implementation may be divided into four principal tasks: hazard identification, frequency analysis, hazard analysis, and risk determination (IOMC, 2006). These tasks are not necessarily in the same order as presented for the QRA model, as here they represent the way the model is implemented and reflect the existence of steps in the model that may be (or may have to be) implemented simultaneously to allow iterative evaluation (Figure 6). These tasks require expert knowledge, information databases (e.g., on industrial accidents in similar plants and processes) to carry out the frequency analysis, specific modelling tools to assess hazard releases, and their effects (hazard analysis), and to help undertake risk determination.

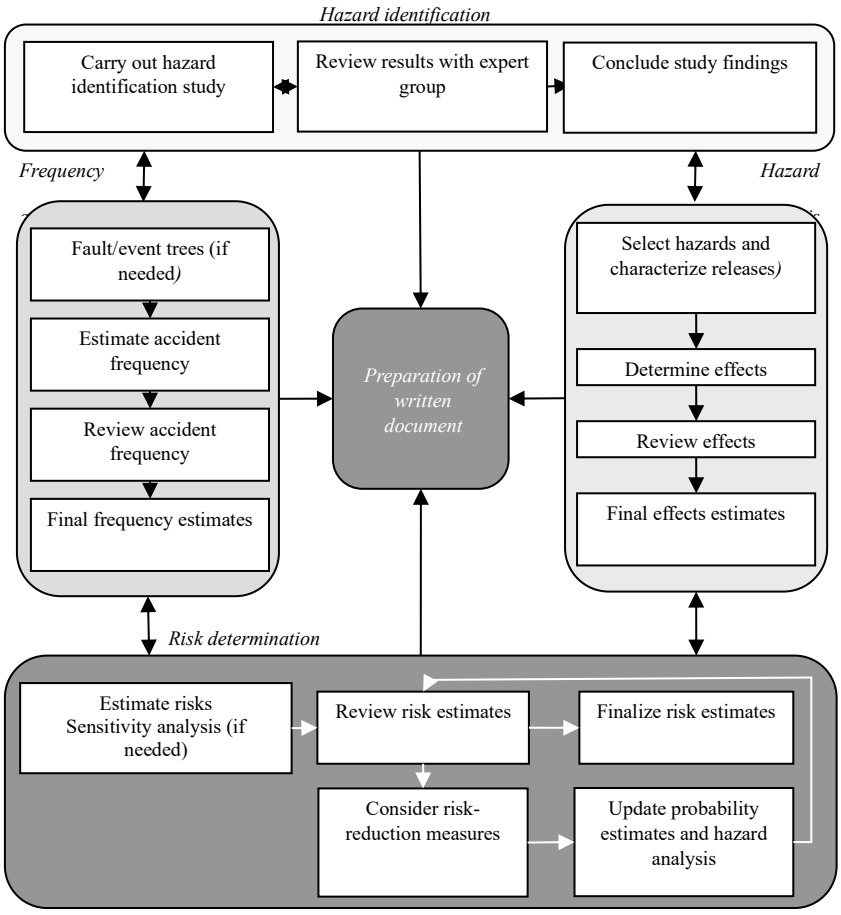

Figure 6. QRA implementation (adapted from IOMC, 2006)

National Academy of Sciences environmental risk assessment model

The model for chemical risk to human health developed by the National Academy of Sciences (NAS, 1983) in the United States in 1983 is widely used and accepted and has provided the basis for other subsequent methods. It is at the basis of legislation in the US as well as in the European Union. The model is less complex to apply than others as it does not include the quantification of the social aspects of risk (as e.g., the World Health Organization's quality-adjusted life-years, and disability-adjusted life years (WHO, 2020)).

The model includes four steps: i) hazard identification; ii) dose-response assessment; iii) exposure assessment; and iv) risk characterization (Figure 7).

The model requires the collection of some scientific information about:

1. Hazard identification (see data sources and models in the previous chapter)
    a. epidemiological data;
    b. animal bioassay data;
    c. short-term studies;
    d. comparison of molecular structure (e.g., quantitative structure-activity relationship, and quantitative structure-property relationship);
2. Dose-response assessment
    a. low-dose extrapolation;
    b. animal-to-human extrapolation;
3. Exposure assessment
4. Risk characterization.

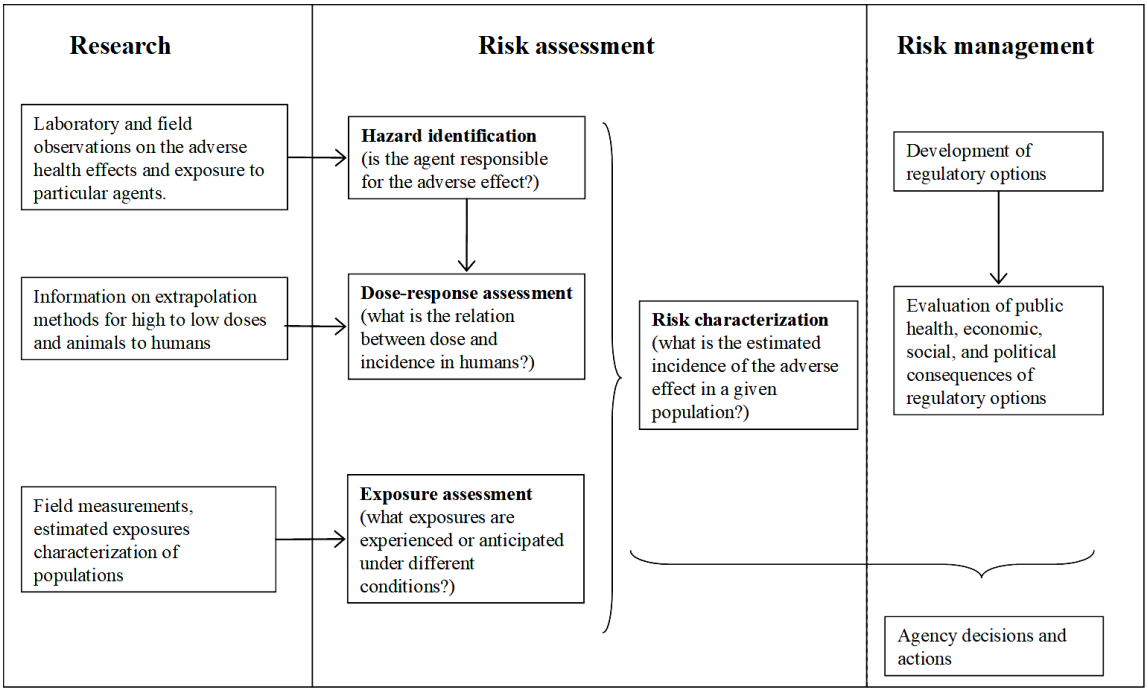

Figure 7. NAS' risk assessment model (adapted from: NAS, 1983)

International organizations, including the Organisation for Economic Co-operation and Development (OECD), World Health Organization, U.S. EPA, and the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC), recommend very similar models for assessing the risks of chemical substances. They are all based on the same principles as QRA and NAS, with the necessary adaptations according to their specific objectives. The environmental risk assessment follows the general guidelines established for risk management under ISO 31000 (ISO, 2018) with the necessary adaptations (Figure 8). For instance, *risk identification* in the ISO compares to *effect assessment* (i.e., hazard identification) in the EU's regulation (ECB, 2003b); *risk analysis* compares to *exposure assessment* and *risk characterization*, and finally *risk evaluation* compares to *risk outcome assessment* (i.e., risk evaluation, and emission and exposure control, following the OECD's terminology in Table 1).

The detailed description of risk analysis would take too long to fit here. Instead, it can be found in supporting slides for the subject and in the recommended bibliography:

Fundamental:

IPCS Risk Assessment Terminology, Part 1, IPCS/OECD key generic terms used in chemical hazard/risk assessment; Part 2. IPCS glossary of key exposure assessment terminology. World Health Organization, Geneva, 2004.

Technical guidance document on risk assessment, Part I-IV. European Chemicals Bureau, Institute for Health and Consumer Protection, Ispra, 2003. (or *Risk assessment guidance for Superfund. Volume I - Human health evaluation manual (Part A). Interim Final.* U.S. Environmental Protection Agency. Washington, D. C., 1989.)

ISO (2009, 2018 review). ISO 31000. Risk management — Principles and guidelines (2009). International Standardization Organization, Geneva, Switzerland

Complementary:

Part 1: Guidance document on characterizing and communicating uncertainty in exposure assessment. World Health Organization, Geneva, 2008.

Guidelines for Human Exposure Assessment Guidelines for Human Exposure Assessment. U.S. Environmental Protection Agency. Washington, D. C., 2019.

Paustenbach , D. J. (2002). Human and ecological risk assessment. Theory and practice. Wiley, Interscience, USA.

Links to other reference material, including exposure factors, toxicological profiles, environmental, food and consumer goods reference databases, and modelling tools are available at my website: https://sitesforprojects.wixsite.com/luismiguelnunes/riskassessment.

From ISO 31000 (2018) to Environmental Risk Assessment (ERA)

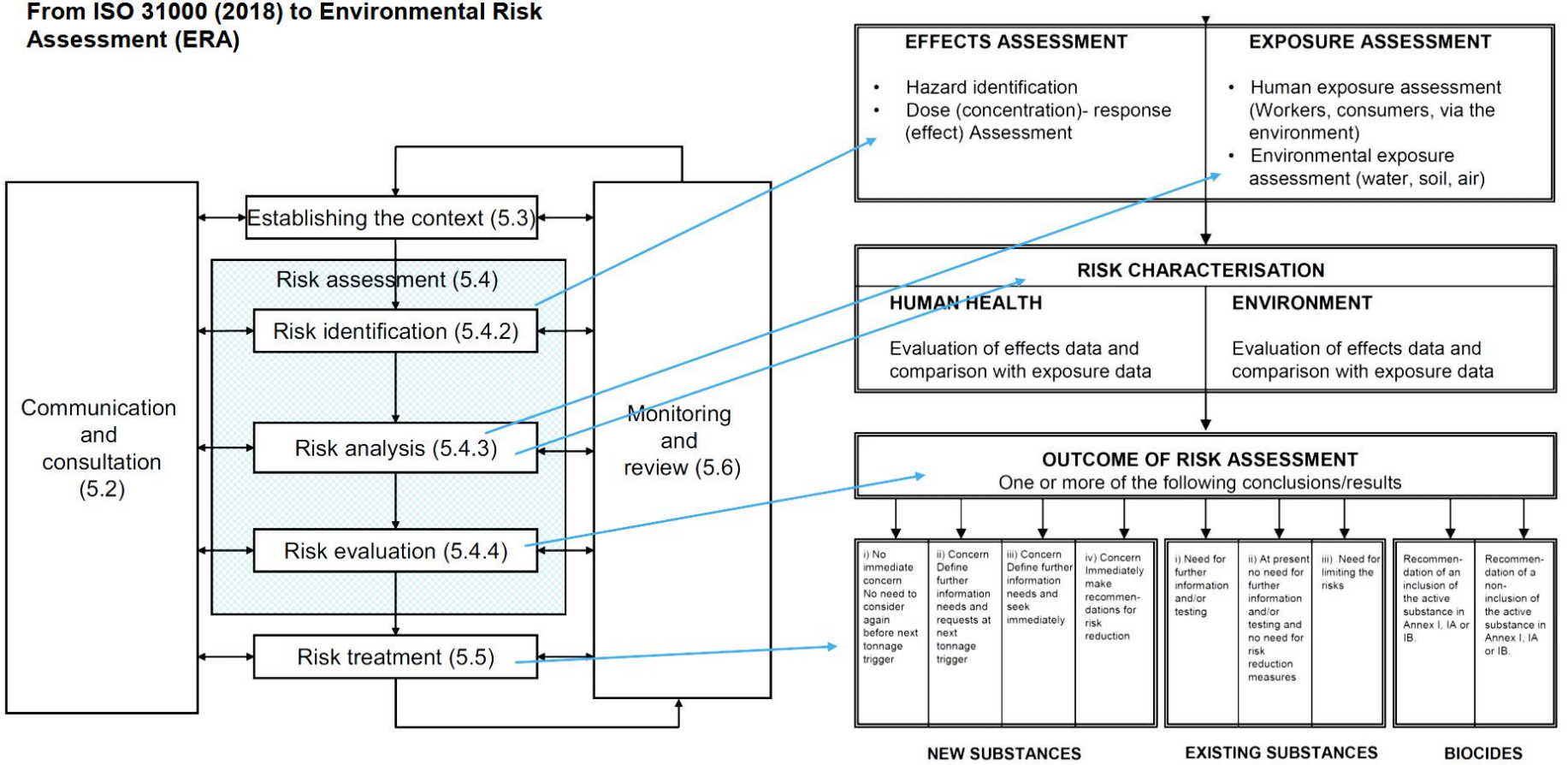

Figure 3 — Risk management process

ISO 31000

European Chemicals Bureau (2003). *Technical guidance document on risk assessment, Part I.*

Figure 8. Comparison between ISO 31000 and the European environmental risk assessment model (e.g., under Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)).

2 FRAMEWORK AND STRUCTURE OF THE SUBJECT

Risk Management is one of the subjects of the Erasmus Mundus Master course in Chemical Innovation and Regulation. It, together with two other two complementary subjects on "Chemical Reactivity Hazards" (2 ECTS) and "Chemical Process Safety" (2 ECTS), constitute a module dedicated to "Chemical Plants Safety" (6 ECTS). Each 2 ECTS subject is taught in one week, in four 3-hour sessions, followed by a period of two days dedicated to tutorial support, if needed. Tutorial support will continue until the assessment, which will take place one month after the end of the subject.

The foreseen contact time is 12 hours, with no predefined subdivision per type (theoretical, practical, or other); and the private study time is planned to be of about 38 hours, completing a total of 50 hours of study time for the subject (i.e., 25 h per ECTS, as established in the Master's regulation, and close to the 26 hours per ECTS set in Regulation 131/2021, dated 10/02, about the application of the system of credits to study courses in the Universidade do Algarve). Consecutive subjects should complement each other, overlaying in part, giving a sense of forward motion, but avoiding unnecessary repetitions.

The limited number of contact time and the modularity is didactically challenging for lecturers (and students), as the subjects should provide theoretical support as well as practical applications with relevance for practitioners.

The option was to build each one of the daily sessions as self-contained topics, but with formal relationship between them, where the theoretical basis is given during the first hour, being followed by a theoretical-practical two-hour period where the learned topics are applied in solving one practical real-world exercises. At the end of the subject the students will have completed four exercises, one of which, at their choice, will serve as the basis for the written report used for the assessment.

The Master's Regulation leaves some freedom as to the assessment method, which may depend in the nature of the subject. Assessment modes may be written assignments, performance of exercises and calculations, report of laboratory activity, report on a literature survey, review of a scientific paper or set of papers, oral presentation. Team work may be required and assessed in some modules when appropriate.

Keeping in mind the need to reproduce professional work conditions, the written reports can be made in groups of up to two students. During the tutorial sessions the lecturer can guide both elements of the group to contribute equally to the report.

Any added work and the writing of the report is not expected to take place in the same week as the classes. Instead, the deadline for submitting the final is one month after the last day of classes. This gives time for students to assimilate the contents, study the supporting materials, explore the results, and prepare the written report.

3 LEARNING OBJECTIVES

The subject will provide the basic understanding of risk management, with focus on chemical substances and their impact on human health from exposure through the environment and consumer products.

Students will learn:

The concept of risk and the various components of risk, including hazard, exposure, vulnerability, and impact.

The principles of risk management, including risk assessment, risk communication, and risk monitoring.

To apply their knowledge of risk management to real-world scenarios, including the long-term effect of chemical substances on human health.

4 LEARNING COMPETENCES

After completing the subject, the students should be able to:

Understand the risk management framework and risk management processes, including the ISO 3100 in the context of organizations, and environmental risk management, as set up by health and environmental agencies.

Understand how the physic-chemical properties of substances affect their emission, environmental fate, exposure, and effects in human health.

Know where to obtain and how to use hazard assessment data.

Know which parameters are relevant and where to obtain exposure assessment factors.

Know how to estimate the risk using analytical and numerical models (know how to use the simpler, and where to find the more complete).

Know how to interpret the risk estimates in the context of other risks, in support of a better risk communication.

Understand where and when to act to minimize risks.

Understand the difference between deterministic and probabilistic risk assessment, namely for characterizing uncertainty propagation and for sensitivity analysis.

5 SYLABUS

5.1 Subject matters

1. Introduction

1.1 Where does the subject fit in the course structure
The subject is shown in the context of preceding and posterior subjects, pinpointing expected background the students must already have, and where the new competences will be used ahead.
1.2 Subject organization and contents
Explain the teaching methodology, the expected learning competences, bibliography, and evaluation method.
1.3 Justification for risk management
Numbers of mortality and morbidity due to exposure to environmental and consumer products are compared to natural risks, showing their higher relative importance. Risk levels for several occupational and daily life activities are presented to better associate causes to quantitative effects – better perception of the risks. The concept of acceptable level of risk is discussed,
1.4 The concepts and international frameworks for risk management
Introduce the ISO risk management system, the EU risk management framework, including REACH and how they relate. The definitions used in risk management are also discussed.
1.5 The fundamental bibliography and information sources
The main documentation is listed, along with complementary one and international information sources, including databases and computer programs.

2. Concepts and methods

2.1 Risk perspectives
Namely the actuarial, toxicological and epidemiological, engineering, economic, psychological, social and cultural. They are discussed in terms of base unit of measurement, predominant method of assessment, the scope of the risk concept, basic problem area and major applications, and instrumental and social functions.
2.2 Risk frameworks
The ISO 31000 (2018) International Standard's principles and generic guidelines on risk management are related to the European risk management framework, showing how the processes on the latter reflect those of the former.
2.3 The distinction between hazard and risk
Where risk is shown to be a function of the hazard and the consequence; how hazard in inversely related to probability; how consequence is related to exposure and vulnerability (or sensitivity); and that there is no risk if any of these terms is null. This helps to justify the way how risk models conceptualize the different components of the risk assessment (hazard identification, dose-response assessment, exposure assessment, and risk characterization).

3 Origin and structure of the environmental risk assessment methods

The origin of the general environmental risk assessment method is reviewed and explained. The different components are associated with the EU risk assessment framework, and in particular with REACH regulations. The objectives and methods for the different components are discussed. Their association with other subjects in the master are explained (hazard identification and dose-response assessment).

4 Estimation of environmental concentrations

Some illustrative databases of data for environmental concentrations are presented, including for water, soil, air, biota, dietary, and consumer products. The key physical-chemical parameters affecting environmental fate are reviewed and their impact on partition and persistence is discussed. Simple mass balance models are used to exemplify the partition between environmental compartments.

5 Estimation of exposure and risk through consumer products

The quantification of exposure and risk characterization is explained, including the regulation, guidance, analytical models, exposure factors, and databases. The main computer applications for estimating exposure in EU and the United States are introduced. The analytical models and the former are used in the practical component. The quantification of risks is explained for carcinogenic and non-carcinogenic substances.

6 Estimation of exposure and risk through the environment

The quantification of exposure and risk characterization is explained, including the regulation, guidance, analytical models, exposure factors, and databases. The main modelling methods for estimating environmental concentrations are very briefly discussed. The quantification of risks is explained for carcinogenic and non-carcinogenic substances, as it is similar to the one already introduced.

7 Risk analysis

The analysis of management alternatives for risk-reduction is discussed. It takes advantage of the skills learned in other subjects, including green technologies, environmental economics, environmental monitoring, and risk communication. The purpose here is to make students understand how the risk estimates obtained during the risk assessment phase can contribute to support management and what are the main hurdles, in particular in transmitting information to the public and decision-makers.

5.2 Practical exercise on environmental exposure to a substance produced/commercialized in the EU

The exercise exemplifies the estimation of the level of human exposure to benzyl salicylate (BS), a rather trivial substance found in many products used in our daily life. In the case of BS, concerns exist for being an endocrine-disrupting chemical. Its selection, instead of a more hazardous substance, is intended to show that no substance is innocuous, hence the need for characterizing its risks. It is particularly important for professionals who deal with many chemical substances, being responsible for their production and commercialization.

BS is used, e.g., in polishes and waxes, washing and cleaning products, cosmetics and personal care products, perfumes and fragrances, biocides and welding and soldering products. Its production in EU and imports are up to 10 000 metric tonnes per year, regulated under REACH.

The students should use the EUSES - European Union System for the Evaluation of Substances software application to obtain the estimates of exposure through the environment. They are referred to ECHA's website for information on manufactured amounts, uses, toxicity classification, physical and chemical properties, environmental fate and pathways, toxicological information, and guidance on safe use. Students may complement physical-chemical properties and data, and fate parameters using USEPA EpiSuite database. Other equivalent sources of information were indicated in the theoretical part.

Exposure estimation usually follows a stepwise approach, using relatively simple (Tier 1) models, such as the EUSES, as the first step. Such Tier 1 models should provide a simplified description of the product's use and

generally apply worst-case (reasonable) assumptions about the conditions of use and associated exposure to chemicals, and the results yield conservative exposure estimates.

Students are expected to apply the software and obtain the estimated daily exposure, which should be compared to the lowest effective dose, characterizing the risk through the hazard quotient or the margin of safety. The application has its own database on the produced, transported and used amounts of the chemicals, which facilitates and speeds up the calculation.

The discussion of the results should include: the manufactured amounts, uses, toxicity, physical and chemical properties, environmental fate and pathways, exposure assessment, risk characterization, and risk management that may be justifiable based on the obtained results.

5.3 Practical exercise on domestic exposure to a substance present in a consumer good

The second exercise is on human exposure to dichloromethane evaporated from a commercial paint removal. The exercise simulates the exposure of a non-professional male individual when applying a paint removal, on a weekly basis for a prolonged period, while making carpentry works as a hobby at home in Italy.

The exercise is intended to demonstrate the application of the methodology for human exposure to substances present in consumer goods, other than cosmetics or personal care products. The exercise is solved with the web application ConsExpo, one of the recommended higher tier models under REACH. It complements the tier 1 analysis of the previous example.

Dichloromethane did not become an important industrial chemical until the years immediately after World War II, when production increased fivefold. One of its first uses was in paint strippers, and it remained the predominant use for many decades. Dichloromethane paint strippers remove many types of finishes from a variety of surfaces. Concentrations in paint strippers range from 10 to 90%.

Human studies involving oral exposure to dichloromethane are limited to case reports of neurological impairment, liver and kidney effects (as severe as organ failure), and gastrointestinal irritation in individuals who ingested amounts ranging from about 25 to 300 mL. Neurological effects with these individuals consisted of general central nervous system depressive symptoms, such as drowsiness, confusion, headache, and dizziness. Hemoglobinuria has been noted as a kidney effect associated with ingestions. dichloromethane is "likely to be carcinogenic in humans" (USEPA, 2011).

The students are asked to determine the 95th percentile of the exposure level through inhalation using a given exposure scenario (room volume, ventilation rate, amount of product used, release area, duration of the application, molecular weight matrix, exposure duration, and mass transfer coefficient). For chemical properties the EpiSuite database is recommended. For body weight data, the reference data comes from Hall et al. (2011), carried out by the European cosmetics industry to update at the exposure data, which supports assessments in EU (SCCS, 2011). The former publication contains the fundamental exposure factors necessary to solve the exercise. For the concentration of dichloromethane in the paint removal, a worst-case scenario should be used.

All the data for which statistical information is available, it should be introduced with the appropriate statistical distribution in ConsExpo to allow the probabilistic assessment of exposure levels (air concentrations).

The discussion of the results should include: Manufactured amounts, uses, toxicity, physical and chemical properties, environmental fate and pathways, exposure assessment, risk characterization. The comparison of the estimated air concentrations against reference values (published by USEPA, 2011 and endorsed by the European Commission (SCCS, 2021), and if superior, propose use conditions for reducing the exposure conditions to appropriate concentrations – which could constitute use recommendations and warnings in product's labelling.

5.4 Practical exercise on exposure to a hazardous substance present in a cosmetic product

The third exercise is about exposure to cadmium present in lipstick as production residue. The exercise demonstrates the calculation of exposure levels for consumers exposed to this metal when using lipstick brands which are currently on the market in several countries. The data used on the exercise has the same statistics as a real dataset from a study I am currently involved in.

Cadmium is a heavy metal that occurs as an environmental pollutant in nature as well as from industrial and agricultural sources. For the non-smoker general population, food is the main source of cadmium exposure. It is primarily nephrotoxic and can cause kidney failure. Can also cause bone demineralization. Is classified as a human carcinogen (group 1) based on occupational studies, being responsible for increased risk of cancer, particularly in the lungs, endometrium, bladder, and breast (EFSA, 2012).

Students should consult the reference documentation for the necessary exposure factors and population body weight, namely in SCCS (2021), RIVM (2006), and Hall et al. (2011).

The exercise is to be done using ConsExpo and repeated using the analytical expressions given in the theoretical part, implementing the models in Excel and running Monte Carlo simulations. The latter are explained as I show how to use the Argo add-in (https://boozallen.github.io/argo/) for Excel. The type of statistical distribution and their statistics can be determined easily using software or online tools (e.g., www.statskingdom.com).

The discussion of the results should include: Exposure factors, metal toxicity, exposure assessment, risk characterization using the two methods. The comparison of the estimated exposure values against reference values (USEPA, 1989; EFSA, 2012), propose use conditions for reducing the exposure conditions to appropriate concentrations, if needed. Compare exposure and risk in different countries using the hazard quotient or the margin of safety.

5.5 Practical exercise on environmental exposure and risk due to the presence of PAH in the environment

The fourth exercise is on risk assessment due to the presence of polycyclic aromatic hydrocarbons (PAH) in the environment, including in food items. The exercise demonstrates the use of chemical partition methods (Parnis and Mackay, 2021) to estimate the concentrations in the different environmental compartments (air, water, sediment, soil, biota, and suspended matter) in the Ria Formosa costal lagoon. The exercise uses real data, obtained from published scientific documents (thesis and journal articles), reproducing a real-world condition.

The students do not need to do the modelling, as that would take too long and is outside the objective of the discipline. Instead, they are asked use the raw data and modelled estimates to assess the exposure through the different routes (ingestion of food, inhalation, absorption through the skin), and based on that compute the individual increased lifetime cancer risk (ILTC) per route and per PAH individual compound, and finally the total risk computed using benzo(a)pyrene equivalents for cancer evaluations of polycyclic aromatic hydrocarbons (Nisbet and LaGoy, 1992; ATSDR, 2022) and the respective cancer slope factor (https://oehha.ca.gov/chemicals/benzoapyrene)

The exercise is intended to be solved using a spreadsheet or hand calculator.

The discussion of the results should include: PAH toxicity, exposure routes, exposure assessment, risk characterization for carcinogenic substances, discuss the value of the estimated ILTC in the context of other risks.

6 TEACHING METHODOLOGY

Teaching is divided in four 1-hour theoretical lessons, followed 2-hour theoretical-practical lessons. In the former the theoretical concepts are introduced and discussed. Teaching here is expositive. In the latter component, students will be guided through the solving of practical examples, as indicated above. Supporting texts, software, and databases are available on a dedicated web page as well as through the e-learning tool used by the institution (Moodle).

Students are invited to fuel the discussion of the taught topics, bringing in their own experiences, problems found and the solutions, as well as their aspirations for the future, including what they expect to learn in the subject and in the Master.

Teaching materials and all recommended bibliography are made available before the beginning of the subject via the Moodle and my personal website: https://sitesforprojects.wixsite.com/luismiguelnunes/riskmanagement

The total workload to complete the subject is expected not to surpass the 50h on average.

The attendance to the lessons is compulsory, following Erasmus program rules.

7 ASSESSMENT

The assessment is made through a single technical report, no longer than 25 pages, excluding appendices. Groups of up to two people are allowed. The theme of the report can be any of the practical exercise and is started while in the classroom, when going through the practical exercise, being completed within the month following the end of the lessons. During this period, I follow the evolution of the work in tutorial sessions, which are arranged with the students as their work progresses. They can be in presence, by video conference, or through chat or email. They are helpful also in identifying the division of workload between group members and to call their attention to the need to have an equal division. When asked, I review drafts of the report and make the necessary remarks, indicating what may be incorrect, incomplete, or non-compliant with the formatting criteria. The students are informed of this possibility when I explain the teaching and assessment methods.

They are also informed of the basic formatting of the report and what I expect to find on each section of the report as shown below (e.g.):

Cover /
Back cover /
Table of contents /
Table of figures /
Table of tables /
(this last section is number in roman numerals, I, ii, iii, ...)
(the following section is numbered an Arab numerals (1, 2, 3, ...)

1. Objective /
2. Introduction
    a. Hazards
    b. Exposure (what are the routes)
    c. Risk characterization (what do we already know about the risks of cosmetic products) /
3. Methods
    a. Hazard identification (what are the hazards associated with the heavy metal; what databases were consulted)
    b. Exposure (what were the studied routes of exposure – e.g., inhalation, dermal, oral -; describe the equations; identify the method of solution – e.g., PACEweb or Excel + Argo; mention that the method is probabilistic and solved with Monte Carlo simulations)
    c. Risk characterization (i.e., say that it was made by comparing the estimate of exposure with the Reference Dose: Margin of Safety; or Hazard Quotient) /
4. Case-study (describe the population; and the exposure factors – refer where the data came from) /
5. Results and Discussion (show the results – use tables and graphs -, and compare the estimate with the Reference Dose) /
6. Conclusions (take the conclusion – one or two paragraphs)

References (include a complete list of well-formatted references – only the authors cited in the text)

[Note: the symbol "/" indicates page break.]

In complement to this, students are informed of the assessment criteria I use when grading the reports, namely regarding the organization of the document, the completeness and correctness, and fulfilment of report objectives (Table 3).

All information provided here is made available to the students through both the Moodle and my web page, at: https://sitesforprojects.wixsite.com/luismiguelnunes/riskmanagement

Table 3. Evaluation criteria

Report organization (30%)			Contents: : completeness and correctness (30%)				
Structure	Tables and Figs	List of refs.	Objective	Case-study	Methods	Results and Discussion	Conclusions
Follow the template; follow the formatting rules. Reports that do not comply will not attain a positive grade (>9.5).			State clearly at the beginning.	Include only the necessary and sufficient details to support the discussion. Indicate clearly where the data came from, how it was collected and by whom, and what kind of processing it has already been through (e.g., correction of outliers).	Explain the workflow, indicating the sequence of methods used in the analysis; indicate uncertainties. Report all the pre-processing steps, namely, unit conversions. Report the origin of constants and the consulted databases.	Put in the body of the text the results that are relevant for the analysis and discussion; the other that you may have obtained can be put in the Appendix (explaining what they were used for, and how they compared to the ones you ended up using in the analysis). Report the results of the computations. Discuss the results with the objective in mind. Use your own knowledge and bibliography to support it.	The conclusion must show that the objective was attained: use the main results to show it.

Fulfillment of report objectives (40%)			
Coherence of methods with objectives	Coherence of workflow	Coherence of discussion & conclusions	Final grade (0-20)
Choose the methods that best helped to go from data to conclusions. Even if you used others, do not include them if they did not contribute to the solution - may be added as appendix, if they are any relevant.	The workflow must be logic and technically defendable, e.g., exposure assessment must precede the risk characterization.	The discussion is where you make use of the methods, exposure data and hazard information to characterize the risk; and discuss risk management. Do not focus the discussion on the methods. What I want to understand is whether you can make use of the methods to support the analysis of the subject under study.	Weighted average of the individual grades

REFERENCES

Apostolakis, G. E. (2004). How useful is quantitative risk assessment?. *Risk Analysis*, **24**(3), 515-520.

ATSDR (2022). *Guidance for calculating benzo(a)pyrene equivalents for cancer evaluations of polycyclic aromatic hydrocarbons*. Agency for Toxic Substances and Disease Registry, Atlanta, GA.

Calow, P. (1998). *Handbook of environmental risk assessment and management*. Blackwell Science, Oxford (U.K.).

CCME (2006). *A protocol for the derivation of environmental and human health soil quality guidelines*. Canadian Council of Ministers of the Environment, Winnipeg, Manitoba.

DEFRA/UKEA (2000). *Guidelines for environmental risk assessment and management*. Department for Environment, Food and Rural Affairs (DEFRA) and the United Kingdom Environment Agency, Rotherham.

ECB (2003a). *Technical guidance document on risk assessment, Part III*. European Chemical Bureau, European Commission, Ispra.

ECB (2003b). *Technical guidance document on risk assessment, Part I*. European Chemical Bureau, European Commission, Ispra.

ECB (2003c). *Technical guidance document on risk assessment, Part II*. European Chemical Bureau, European Commission, Ispra.

EEA (1999). *Environmental risk assessment - approaches, experiences, and information sources. Environmental Issues Series No. 4*. European Environment Agency, Copenhagen.

EFSA (2012). *Scientific report of EFSA. Cadmium dietary exposure in the European population*. European Food Safety Authority, Parma, Italy

IOMC (2006). *Conduct effective quantitative risk assessment (QRA) studies*. IOMosaic Corporation, Salem (USA).

ISO (2018). *ISO 31000. Risk management — Principles and guidelines*. International Standardization Organization, Geneva.

Kaplan, S. & Garrick, B. J. (1981). On the quantitative definition of risk. *Risk Analysis*, **1**, 11-28.

Kirchsteiger, C. (2005). Review of industrial safety management by international agreements and institutions. *Journal of Risk Research*, **8**(1), 31-51.

Nisbet, I. C. T., LaGoy, P. K. (1992). Toxic equivalency factors (TEFs) for polycyclic aromatic hydrocarbons (PAHs). Regulatory Toxicology and Pharmacology,16(3), 290–300.

NAS (1983). *Risk assessment in the Federal government: managing the process*. National Academy of Sciences, Washington, DC.

OECD (2003). *Descriptions of selected key generic terms used in chemical hazard/risk assessment. OECD series on testing and assessment. Number 44. ENV/JM/MONO(2003)15*. Organisation for Economic Co-operation and Development, Environment Directorate Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, Paris.

Parnis, J. M., Mackay, D. (2021). *Multimedia environmental models, the fugacity approach* (3nd ed.). CRC Press, Boca Raton, FL.

Paustenbach, D. J. (2002). *Human and ecological risk assessment - theory and practice*. Paustenbach DJ, editor. John Wiley & Sons, Inc., New York.

Pleil, JD; Sheldon, LS. (2011). Adapting Concepts from Systems Biology to Develop Systems Exposure Event Networks for Exposure Science Research. *Biomarkers*, **16**, 99-105.

RIVM (2006). *RIVM report 320104001/2006. Cosmetics fact sheet to assess the risks for the consumer. Updated version for ConsExpo 4*. National Institute for Public Health and the Environment, Bilthoven, the Netherlands

SAIC (1992). *Risk prioritization - National trends, forecasts, and options for the Army*. Army Environmental Policy Institute, Illinois.

SCCS (2021). *The SCCS notes of guidance for the testing of cosmetic ingredients and their safety evaluation 11th revision, 30-31 March 2021, SCCS/1628/21*. Scientific Committee on Consumer Safety, European Commission, Luxembourg.

SCCS (2012). *SCCS opinion on dichloromethane. 17th plenary meeting of 11 December 2012*. Scientific Committee on Consumer Safety, European Commission, Luxembourg.

Starr, C. (1969). Social benefits versus technological risk. *Science*, **165**(3899), 1232-1238.

Starr, C. (1985). Risk management, assessment, and acceptability. *Risk Analysis*, **5**(2), 97-102.

UKEA (2005). *Environment agency guidance on requirements for land contamination reports - Version 1 July 2005*. United Kingdom Environment Agency, Rotherham.

UKRS (1992). *Risk analysis, perception and management*. The Royal Society, London.

USEPA (1992). *Guidelines for Exposure Assessment. EPA/600/Z-92/001*. United States Environmental Protection Agency, Washington, DC.

USEPA (2019). *Guidelines for Human Exposure Assessment*. United States Environmental Protection Agency. Washington, D. C.

USEPA (2011). *Chemical Assessment Summary: dichloromethane; CASRN 75-09-2*. Integrated Risk Information System (IRIS). United States Environmental Protection Agency. Washington, D. C.

USEPA (1989). *Chemical Assessment Summary:* cadmium; CASRN 7440-43-9. Integrated Risk Information System (IRIS). United States Environmental Protection Agency. Washington, D. C.

WHO (2004). *IPCS Risk Assessment Terminology. Part 1: IPCS/OECD key generic terms used in chemical hazard/risk assessment; Part 2: IPCS glossary of key exposure assessment terminology*. World Health Organization, Geneva.

WHO (2020). *WHO methods and data sources for global burden of disease estimates 2000-2019. Global Health Estimates Technical Paper WHO/ DDI/DNA/GHE/2020.3*. World Health Organization, Geneva.