A revision of current models for environmental and human health impact and risk assessment for application to emerging chemicals

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ABSTRACT

Nowadays, we are living in the global circular economy, where products are produced, used and finally disposal in different parts of the world. These products have a huge amount of additives, that in many cases can be hazardous if there are not treated properly. The risk assessment of human health and the environment due to exposure to chemical additives is necessary.

In this chapter the risk assessment is briefly introduced. Risk assessment is divided in four steps: hazard identification, hazard characterisation, exposure assessment, and risk characterisation. This chapter also highlights five risk and life cycle impact assessment models (EUSES, USEtox, GLOBOX, SADA, and MAFRAM) that allows for assessment of risks to human health and the environment. In addition other 12 models were appointed. Finally, in the last section of this chapter, there is a compilation of useful data sources for risk assessment. The data source selection is essential to obtain high quality data. This source selection is divided in two parts. First, 6 frequently databases used for physicochemical and/or toxicological properties (TOXNET, eChemPortal, ATDSR, CPDB, IUCLID and ECOTOX) are presented. Second, 6 estimation data tools are pointed. The estimation tools are useful when it is not possible to find data parameters to assess the risk, for example, in the case of emerging pollutants or new substances.

In conclusion, there is no risk assessment model better than another. All models have their strengths and weaknesses. Many of them are focused on one particular aspect such as a single environmental compartment or in a kind of pollutant. It is important to remark that the selection of the data source is essential to obtain a quality results.

Introduction

Currently, in the global economy, products are manufactured in one part of the world, used in another part and there is little knowledge about where these products will be disposed of. Most consumer products contain a large variety of chemical additives, in many cases, new substances, since they are poor studied. This together with the lack of knowledge about the additives used, cause concern about the impact of these additives on human health and the environment.

These additives may come into contact with humans and the environment not only during the use of the product but throughout their life cycle: during the production of the additive, during the manufacture of consumer product where the additives are used and during the product's end of life treatment. As discussed in the previous chapter (See chapter (x) Suciu et al.) the emissions of the additives in a given environmental compartment are distributed to others. Therefore, the human population is not only exposed directly to these additives by the use of products but also indirectly through the

environment. Moreover, these substances can also enter into the food chain and accumulate in fish, animals, crops, fruits and vegetables where they could later be ingested by humans.

Due to this,, it is necessary to assess the risk to human health and the environment due the exposure to these chemical additives. In this chapter the impacts that a substance can cause to a certain receptor (humans and the environment) and the harms to the receptor at different exposure levels are identified in hazard identification and hazard characterisation steps, respectively. Exposure assessment takes into account the amount, frequency and duration of the exposure to the substance. Finally, risk characterisation evaluates the increased risk caused by such exposure to the exposed population.

This chapter also highlights a selected number of models that allows for assessment of risks to human health and the environment. Finally, in the last section of this chapter, there is a compilation of useful data sources for risk assessment.

1 Risk assessment

Risk analysis is defined as a process for controlling situations where a target could be exposed to a hazard [1]. It consists of three parts: risk assessment, risk management and risk communication (Fig. 1). Risk communication is the exchange of information about risks between risk assessors, public managers, policy makers, interested groups and the general population. Risk management is related to decision-making processes involving considerations of political, social, economic, and technical factors with relevant risk assessment information.

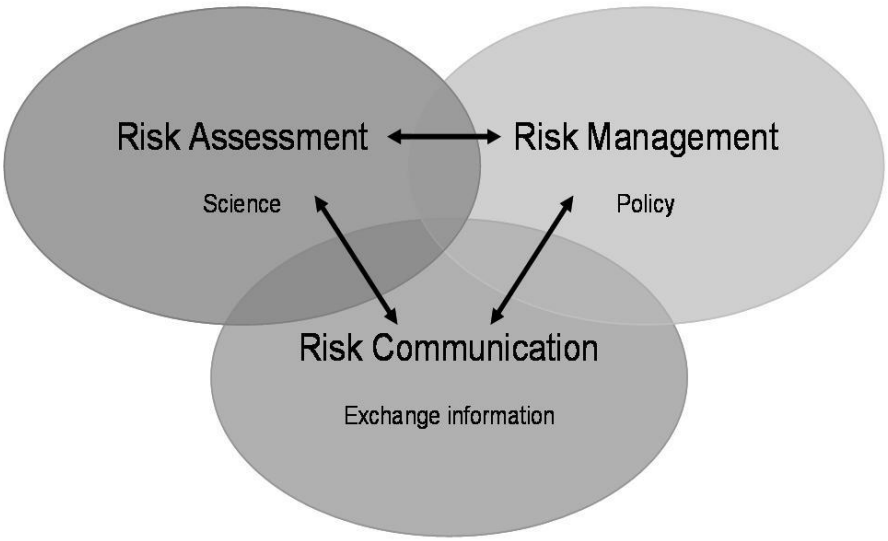

Fig. 1. Risk analysis structure (Adapted from FAO[2]).

The organisation for economic co-operation and development (OECD) define risk assessment as the process intended to calculate or estimate the probability, including the identification of attendant uncertainties, of an adverse effect in an organism, system or (sub) population caused under specified circumstances by exposure to an agent, taking into account the inherent characteristics of the agent of concern as well as the characteristics of the specific target system [1]. According with this definition the risk assessment process consists of four steps:

1. Hazard identification consists in identifying the type and nature of adverse effects caused by the agent in the receptor (target organism, system or (sub) population).

2. Hazard characterization (or dose-response assessment) is the qualitative and, as far as possible, quantitative description of the inherent properties of an agent or situation having the potential to cause adverse effects. This step should include a dose-response assessment that describes the severity of adverse effects (the responses) related to the amount and condition of exposure to an agent (the dose).
3. Exposure assessment is the process of predicting or estimating the concentration or amount of an agent, the frequency and the duration that reaches the receptor.
4. Risk characterization is the determination, qualitative and as far as possible quantitative, of the probability of occurrence of adverse effects in a given target, under the predicted or estimated exposure conditions.

In the following two sections, a deeper explanation of human health and environmental risk assessment is given.

2 Human Health risk assessment

2.1. Hazard identification.

The goal of the hazard identification is to identify the effects of substance to environment or human health.

A substance can cause one or more effects. Common effects are: acute and long-term toxicity, skin irritation, corrosiveness, sensitisation, mutagenicity, carcinogenicity, reproductive effects, and developmental toxicity.

2.2. Hazard characterisation.

Hazard characterization is the estimation of the relationship between the dose of a substance and the effects observed. To evaluate this relationship, the following studies can be performed: (in order of reliability):

- Human studies including case reports, epidemiological studies, and, in some cases, direct human studies (with volunteers). The advantages of these studies are that toxic effects are evaluated in humans and no interspecies extrapolation is needed. However the subjects of these studies are exposed to an uncontrolled environment that may interfere with the results.
- Animal toxicological and in vitro studies. In animal or in vitro studies the system is more controlled than in human studies, the external influences are minimized (more in in vitro than in animal tests). However, in both cases, an extrapolation is required: interspecies in the case of animal studies and at least from system to organism extrapolation in the case of in vitro test.
- Qualitative structure-activity relationship (QSAR) methods. (See section 5.2)

For the two aforementioned steps, hazard identification and hazard characterisation, data adequacy is of high importance. The data adequacy is defined by the reliability and the relevance of the data for human risk assessment [3].

2.3. Exposure assessment.

Exposure assessment is one of the most important steps in risk assessment. It is the process that predicts or estimates the amount of the substance under study that reaches the human body. To assess the exposure, it is necessary to define in detail the exposure pathway, the route of exposure, the concentration of the pollutant in the particular media, the contact

rate, the frequency of exposure, and the population exposed (age, gender, and vulnerable population, among others). A general equation (Eq.1) to determine the exposure dose is:

$$Dose \equiv \frac{Concentration \times Contact\_Rate \times Frequency}{Body\_weight} \quad \text{(Eq. 1)}$$

2.3.1 Exposure routes

Exposure pathway describes how the substances enter into the human body. All possible pathways are not considered for all substances and emission scenarios, only the ones that are relevant for a specific substance and emission scenario are included. For example in the case of substances that are not present in the air, the inhalation route is not taken into account.

The most common routes of exposure are:

- Inhalation, of air and particles.
- Ingestion, of soil, dust, food and drinking water.
- Dermal contact: absorption trough the skin.
- Others common routes of exposition could be percutaneous, in the case that the substance enters into the body through a wound in the skin or intravenous in the case of direct injection into the bloodstream.

2.3.2 The need of realistic scenarios for exposure evaluation

For human health risk assessment, it is necessary to elaborate realistic scenarios. Knowledge of real scenarios where the contaminant is emitted to the environment will help to obtain information about the fate and transport of the contaminant once is emitted to the environment and the route of exposure for the human beings living in this scenario of concern. There are different types of exposure i.e. direct, indirect (as is the case of food contaminated by the air, water or soil contaminated by the emission), occupational exposure, and consumer goods coming form outside the scenario of concern. Depending on the objective of the study it will be necessary to consider in the exposure assessment one or more types of exposure

In each context, it is essential to define suitable parameters of the exposure scenario for a realistic risk assessment.

- Environmental exposure (direct). Exposure through air inhalation, soil and dust ingestion and dermal contact of soil and dust are the principal exposure pathways. Other exposure pathways (e.g. water dermal contact) can be taken into account in some scenarios. Monitoring campaigns or multimedia fate models are used to assess the exposure (See chapter of this book entitled “Environmental Fate Models”).
- Food and water ingestion (dietary exposition). To assess the dietary exposure, ingestion rates of the different food products and water are needed. Multimedia fate models or food sampling campaigns are the main ways to determine the concentration of substances in food products and water at the specific scenario. These models consider cattle, meat, milk, fish, crops, drink water among others.
- Occupational exposure (work place exposure). Exposure may occur as a singular event, a repetition singular event or as continuous exposure during the work time. Exposure can be through inhalation, ingestion or dermal contact. Every workplace has its characteristics, therefore information have to be collected about the substances, duration of exposure and frequencies of exposure, among others.. One aspect to be considered in the exposure assessment at work is weather or not workers are using personal protective equipment. Exposure models and monitoring of contaminants in the workplace are the two most widely used tools for exposure assessment. Biological monitoring

(e.g. blood, hair, breast milk) of the workers can give additional information on the occupational exposure to a substance.

– Consumer goods (non-dietary). The consumer is a member of the general population, who may be exposed to (a new or existing) substance by using consumer products. The examples are almost endless, exposure to solvents used in adhesives, paints and furniture, substances that can be released from a consumer product, the exposure to substances used for cleaning and decoration of houses, exposure to raw materials of cosmetics, etc. The wide range of cases makes it impossible to generalise a scenario. Substance data quality (amount in products, exposure pathway) and the consumer goods (frequency and duration of use, users of that product) are essential to build a realistic exposure scenario.

2.4. Risk characterization

The last step in risk assessment is the risk characterization where the probability and the severity of adverse health effects in the exposed population are assessed.

2.4.1 Non-carcinogenic risk

In the case of non-carcinogenic substances, there exists a threshold; this is an exposure with a dose below which there would not be adverse effect on the population that is exposed. This is the reference dose (RfD), and it is defined as the daily exposure of a human population without appreciable effects during a lifetime. The RfD value is calculated dividing the no observed effect level (NOEL) by uncertainty factors. When NOEL is unknown, the lowest observed effect level (LOEL) is used. NOEL and LOEL are usually obtained in animal studies. The main uncertainty factor, usually 10-fold, used to calculate the RfD are the following: the variations interspecies (from animal test to human), presence of sensitive individuals (child and old people), extrapolation from sub-chronic to chronic, the use of LOEL instead of NOEL. Non-cancer risk is assessed through the comparison of the dose exposed calculated in the exposure assessment and the RfD. The quotient between both, called in some studies as hazard quotient, is commonly calculated (Eq. 2). According with this equation, population with quotient > 1 will be at risk to develop some specific effect related to the contaminant of concern.

$$Risk_{non-cancer} = \frac{Dose}{RfD} \quad \text{(Eq 2)}$$

2.4.2 Carcinogenic risk

There is some controversy regarding the carcinogenic effects [4]. There exist two main points of view that define the carcinogenic risk characterisation. The first one considers that there is not a threshold dose in the carcinogenic substances due to exposure at any level of the substance that may have a probability to cause adverse effects (tumoral cell)[4]. The second point of view suggests that the human body can detoxify a carcinogenic substance in low doses and in consequence, a threshold exists for that carcinogenic substance. To protect the human health, the no-threshold approach is commonly chosen. Different mathematical models are used (linear in low dose model, nonlinear models, and multi extrapolation models). In the low-dose region, the equation (Eq. 3) is used to assess the risk, where SF is the slope factor, a toxicity value for evaluating the probability of an individual developing cancer from exposure to contaminant levels over a lifetime.

$$Risk_{cancer} = Dose \times SF \quad \text{(Eq. 3)}$$

3 Environmental risk assessment

The hazard identification and hazard characterisation steps that some methodologies define as a single step as "Effect assessment", estimate the predicted no effect concentration (PNEC) in each environmental compartment. PNEC, that means the concentration below which an adverse effect will most likely not occur, is usually calculated on the basis of results of laboratory monospecies test. The PNEC is calculated dividing the lowest value of toxicity test (L(E)C50 (short term) or no observed effect concentration (NOEC) (long term) by an assessment factor. The assessment factor represents the uncertainty in: the variability intra and interspecies, the short to long toxicity extrapolation, and the extrapolation of the laboratory toxicity test for a limited number of species to a real environment. The assessment factor depends on the number of spices tested and the trophic levels selected, the quality of data and the duration of the test (short or long term). For example, in the European Commission Technical Guidance Document on Risk Assessment [3], an assessment factor of 1000 is used to calculate aquatic PNEC if a minimum of one short term L(E)C50 for each of the three trophic levels is known. On the other hand, an assessment factor of 10 is used if long term NOECs are known for at least three species representing the three trophic levels.

Exposure Assessment using monitoring data or fate and transport models calculate the predicted environmental concentration (PEC) in each environmental compartment. More information can be obtained from chapter of this book "Environmental fate models" by Suciu et al.

Finally, in the risk characterization step, the PEC/PNEC quotient that defines the risk of the substance in the environment is calculated. If the quotient (PEC/PNEC) is less than 1, the substance do not present risk to the environment. More information is available in the European Commission "Technical Guidance Document on Risk Assessment" [3] and in the United States Environmental Protection Agency's "Guidelines for Ecological Risk Assessment" [5].

4 Models

There are many models for assessing risks to human health and/or the environment. Some of them are multimedia models, which assess the exposure and risks in different environmental matrices, such as soil, air, water and food chains with different degrees of complexity within each medium. Conversely, others are more specific with regard to a medium or a system (e.g. river or food chain). Other models assess only human health risks or environmental risks, while some assess both risks. Based on the type of scenario that is studied, an appropriate model will be chosen.

Apart from the risk assessment models, there exist models for assessing impacts to human health and the environment in LCA. Both tools (risk assessment and Life Cycle Impact Assessment) have different purposes and aims that are summarized in Table 1 [6].

Table 1. Differences in the principles of assessing the potential for ecotoxicological and toxicological effects in risk assessment vs. life cycle impact assessment (based on Olsen et al. (2001)[6]).

Risk Assessment (RA)	Life Cycle Impact Assessment (LCIA)
Absolute assessment	Relative assessment due to the use of a functional unit
Chemical-oriented	Product-oriented
For specific circumstances of use or environ-	For products during their entire life cycles

mental recipients	
Typically carried out by or for the authorities	Its use is controlled primarily by the needs of the companies
The result expresses a verifiable risk of effect	The result is a relative environmental impact potential that cannot be verified
Tiered approach; a conservative assessment of, particularly, the exposure can be used in the preliminary steps	A conservative assessment is unwanted; a true measure of the environmental impact is aimed

Despite the fact that there exist some differences between both methodologies, the cooperation between the aforementioned tools seems to be advantageous to use in environmental management [6]. Moreover, there are also steps in Life cycle impact assessment (LCIA) that also exist in the risk assessment, (i.e. exposure assessment). Therefore, models used in LCIA can be used also to assess human or environmental exposure to chemicals. For that reason LCIA models are also included in the review of models of risk assessment.

Following a brief summary of a selected number of models currently used is showed.

4.1. EUSES

The European Union System for the Evaluation of Substances (EUSES) [7] is the software provided by European Chemical Bureau (ECB) to implement the EU Technical Guidance Documents on Risk Assessment for New Notified Substances, Existing Substances and Biocides [3]. The development of EUSES 2.1 was commissioned by the European Commission to the National Institute of Public Health and the Environment (RIVM) of The Netherlands. The work was supervised by an EU working group comprised of representatives of the JRC-European Chemicals Bureau, EU Member States and the European chemical industry.

The EUSES environment is represented as a set of nested scales. The local scale is nested into the regional scale which is nested in the continental scale. The continental scale is nested into the moderate climate zone, which has two adjacent zones, an arctic and a tropic zone respectively. All the scales are divided in boxes (environmental compartments). The boxes of all scales include at least air, soil, water, and sediment compartments.

The human sub-populations and ecological systems and populations considered to be protection goals in EUSES are: human populations (workers, consumers, non-professional users of biocides, and man exposed via the environment) and ecological systems (micro-organisms in sewage treatment systems, aquatic ecosystems, terrestrial ecosystems, sediment ecosystems, and predators). Repeated dose toxicity, fertility toxicity, maternal toxicity, developmental toxicity, carcinogenic risk, and lifetime cancer risk can be calculated for the cases that literature data is available.

The risk characterization procedure will result in a quantitative comparison per substance of the outcome of the exposure assessment and of the effects assessment. This comparison is made through the ratio PEC/PNEC. The generic name for PEC/PNEC in EUSES is Risk Characterization Ratio (RCR). Other ratios are used in EUSES for the risk characterization such as the Margin of Safety (MOS) or the ratio of the estimated no-effect or effect level parameter to the estimated exposure level for human sub-populations and the Acceptable Operator Exposure Level (AOEL).

The exposure assessment in EUSES aims at ‘reasonable worst-case’ i.e. the exposure scenario was the worst scenario without being unrealistic and as much as possible using mean, median or typical parameter values. If the outcome of the ‘reasonable worst case’ risk characterisation indicates that the substance is “not of concern”, the risk assessment for that substance can be stopped with regard to the scenario considered.

4.2. USEtox™

In 2005, a comprehensive comparison of life cycle impact assessment toxicity characterisation models was initiated by the United Nations Environment Program (UNEP) and the Society for Environmental Toxicology and Chemistry (SETAC) in their Life Cycle Initiative. The main objectives of this effort were [8] (1) to identify specific sources of differences between the models' results and structure; (2) to detect the indispensable model components; and (3) to build a scientific consensus model from them, representing recommended practice.

An extensive comparison of the most obvious positive and negative aspects from seven evaluation models (ECOSENSE, EDIP, USES-LCA, CalTOX, BETR, IMPACT 2002+ and WATSON) led to the development of USEtox, a scientific consensus environmental model for characterization of human and ecotoxicological impacts in Life Cycle Impact Assessment that contains only the most influential model elements. USEtox was developed following a set of principles, including [8]:

- Parsimony: as simple as possible, as complex as necessary
- Mimetic: not differing more from the original models than these differ among themselves.
- Evaluated: providing a repository of knowledge through evaluation against a broad set of existing models.
- Transparent: being well-documented, including the reasoning for model choices.

USEtox calculates characterisation factors for human toxicity and freshwater ecotoxicity. Assessing the toxicological effects of a chemical emitted into the environment implies a cause–effect chain that links emissions to impacts through three steps: environmental fate, exposure and effects. Linking these steps, a systematic framework for toxic impacts modelling based on matrix algebra was developed to some extent within the OMNIITOX project [9]. USEtox covers two spatial scales the continental and the global scales.

According to the creators, USEtox provides a parsimonious and transparent tool for human health and ecosystem Characterization Factor (CF) estimates. It has been carefully constructed as well as evaluated via comparison with other models and falls within the range of their results whilst being less complex.

4.3. GLOBOX

GLOBOX [10] is a spatially differentiated multimedia fate, exposure and effect model. It is used for the calculation of spatially differentiated LCA characterisation factors on a global scale. It can also be used for human and environmental risk assessment. The GLOBOX is based on the EUSES 2.0 model. It has primarily been constructed for the calculation of spatially differentiated LCA characterization factors on a global scale. In comparison with the EUSES model, the GLOBOX has a higher level of spatial differentiation, in such a way that the GLOBOX is spatially differentiated with respect to fate and human intake on the level of separated but interconnected countries and oceans/seas. The main goal of the GLOBOX is to construct location-specific characterization factors for any emissions at any locations over the world, considering summed impacts of such emissions in different countries and seas/oceans. The GLOBOX model consists of the following three main modules: an impact-category independent fate module, a human-intake module, an effect module.

Twelve distribution compartments are distinguished: air, rivers, freshwater lakes, freshwater lake sediments, salt lakes, salt lake sediments, natural, agricultural and urban soil, groundwater, sea water, and sea water sediments. In contrast to the EUSES model, where different nested scales (one inside the other) are considered, the GLOBOX is a system of interconnected regions at the same level in the model.

4.4. SADA

Spatial Analysis and Decision Assistance (SADA) [11] is a free software, developed at The Institute for Environmental Modelling at the University of Tennessee. SADA incorporates tools from environmental assessment fields into an effective problem solving software. These tools include integrated modules for human health risk assessment and ecological risk assessment and also geographical information system (GIS), visualization, geospatial analysis, statistical analysis, cost/benefit analysis, sampling design, and decision analysis.

SADA provides a full human health risk assessment module and associated databases. The risk models follow the USEPA's Risk Assessment Guidance for Superfund (RAGS) and can be customized to fit site specific exposure conditions. It calculates risks based on the following exposure pathways: ingestion, inhalation, dermal contact, food consumption and also a combined exposure.

The ecological risk module allows users to perform benchmark screenings for surface water, sediment, soil and biota. Accompanying the ecological risk module is a database of benchmarks and other information that are supported and updated on the SADA web site. Benchmarks are adjusted for site-specific physical parameters as appropriate.

4.5. MAFRAM

Multimedia Agricultural Fate and Risk Assessment Model (MAFRAM) [12] is a comparing and ranking method for new and existing non-volatile organic compounds (NVOCs) used in agricultural activities. MAFRAM was intended to compare and establish the general features of NVOCs behaviour and assess the ecotoxicological risk to the ecosystem.

MAFRAM divides the agricultural environment into two main zones, which are the on- and off-farm zones. Six compartments (air, water, soil, sediment, aboveground plants, and roots) are included in on- and off-farm zones. The MAFRAM output includes the inter-compartmental transport and transfer rates, the primary loss mechanisms, chemical concentration, amount, residence time, and the rank of risk in each compartment.

4.6. Other models

In addition to the models presented above, there are a number of other risk assessment models available. Table 2 briefly presents some of these models that can be used to assess the risk of human health and the environment..

Table 2. Models used in human health and/or environmental risk assessment.

Model	Description	Ref
BREEZE® Risk Analyst	Human health and ecological risk assessment modeling system designed to conduct multi-pathway human health risk assessments and food-web based ecological risk assessment modeling. BREEZE Risk Analyst combines databases, GIS functionality, fate, transport, and exposure modeling equations into one software application	[13]
IRAP-h View™	Interface for conducting a comprehensive multi-pathway human health risk assessment. It simultaneously calculates risk values for multiple chemicals, from multiple sources, at multiple exposure locations. IRAP-h View implements the U.S. EPA - OSW Human Health Risk Assessment Protocol (HHRAP) US EPA [15]	[14]
Eco Risk View™	An advanced ecological risk assessment program for conducting a comprehensive multi-pathway ecological risk assessment by simulta-	[14]

	neously calculating risk values for multiple chemicals, from multiple sources, at multiple exposure locations. EcoRisk View fully implements U.S. EPA guidance for evaluating ecological risks [16]	
EcoFate	EcoFate is a software package for conducting ecosystem based environmental and ecological risk assessments of chemical emissions by point and non-point sources in freshwater and marine aquatic ecosystems, including lakes, rivers and marine inlets.	[17]
RISC5	RISC5 is a software package for performing fate and transport modeling, human health risk assessments and ecological risk assessments for contaminated sites. Fate and transport models are available in RISC5 to estimate receptor point concentrations in groundwater and indoor and outdoor air. It can be used to estimate the potential for adverse human health impacts (both carcinogenic and non-carcinogenic) from up to nine exposure pathways.	[18]
Ecolego	Ecolego is a powerful and flexible software tool for creating dynamic models and performing deterministic or probabilistic simulations. Ecolego can be used for conducting risk assessments of complex dynamic systems evolving over time with any number of species. Ecolego has specialized databases and other add-ons designed for the field of radiological risk assessment.	[19]
@RISK	@RISK performs risk analysis using Monte Carlo simulation to conduct sensitivity and uncertainty analyses	[20]
API-DSS	Exposure and Risk Assessment Decision Support System Software. Estimates human exposure and risk from sites contaminated with petroleum products.	[21]
XtraFood	Xenobiotics transfer in the primary FOOD Chain model calculates transfer of contaminants in the primary food chain. This model describes the whole chain from immission of contaminants at the farm level over concentrations in food to human exposure. The model focuses on the terrestrial food chain.	[22]
RISKAT	RISKAT assesses the risks to populations in the vicinity of plants processing and storing toxic and flammable materials.	[23]
CHARM	CHARM is used to carry out environmental risk assessments of discharges of exploration and production of chemicals, from platforms into the marine environment.	[24]
Impact 2002	This model provides close to 1000 characterization factors for the midpoint categories human toxicity, aquatic ecotoxicity and terrestrial ecotoxicity according to the LCIA methodology. The model is parameterised in a non-spatial and a spatial European model nested in a non-spatial world model, as well as a complete world model.	[25]

5 Data sources

In order to run these models is necessary to have input data, mainly physicochemical properties and toxicological data (for both human and ecosystems), which can be extracted from different information sources. The source selection is essential to obtain data of high quality. In some cases (e.g. emerging pollutants) there is a lack of physicochemical and toxicological data which makes it necessary to use tools such as QSARs (Quantitative structure–activity relationship) .

5.1. Data bases.

Currently, there are many databases where the physicochemical, toxicological parameters required to perform a risk assessment can be obtained. It must be borne in mind that the existence of a quality control parameters included in the databases is of great importance. This quality control can be accomplished through periodic updating of the database, the inclusion of bibliographical references of the origin of each parameter, peer reviewed bibliography, etc.

In Table 3, a selection of physicochemical and toxicological databases is shown. These databases are selected according to the existence of quality controls and their free online availability.

Table 3. Physicochemical and toxicological databases.

Database	Description
TOXNET	The Toxicology Data Network is a cluster of databases covering toxicology, hazardous chemicals, environmental health and related areas published by the United States Library of Medicine. The TOXNET includes, among others, toxicological databases such as: Chemical Carcinogenesis Research Information System (CCRIS), Hazardous Substances Data Bank (HSDB), Integrated Risk Information System (IRIS), International Toxicity Estimates for Risk (ITER) and ChemIDplus.
eChemPortal	eChemPortal is a global portal for information regarding chemical substances. It allows simultaneous searching of reports and datasets by chemical name, CAS number or by chemical property. Direct links to collections of chemical hazard and risk information prepared for government chemical review programmes at national, regional and international levels are obtained. Classification results according to national/regional hazard classification schemes or to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) are provided when available.
ATDSR	The Agency for Toxic Substances and Disease Registry produces the “toxic substances profile” for hazardous substances found in National Priority List (NPL) sites. These hazardous substances are ranked based on frequency of occurrence at NPL sites, toxicity, and potential for human exposure.
CPDB	The Carcinogenic Potency Database contains the results of 6540 chronic, long-term animal cancer tests on 1547 chemicals. The CPDB provides easy access to the bioassay literature, with qualitative and quantitative analyses of both positive and negative experiments that have been published over the past 50 years in the general literature through 2001 and by the National Cancer Institute/National Toxicology Program through 2004.
IUCLID	The international uniform chemical information database is a software application to capture, store, maintain and exchange data on intrinsic and hazard properties of chemical substances.
ECOTOX	The ECOTOX is a database of single chemical toxicity data for aquatic life, terrestrial plants and wildlife.

5.2. Estimation Data Tools.

Despite the existence of several databases for certain substances, it is not possible to find physicochemical and/or toxicological parameters to assess the risk for all substances. The lack of data is one of the main problems in risk assessment. This is especially true for emerging pollutants. One solution to solve this problem is the use of QSAR or estimation tools. QSAR models correlate the structure of the substance with their activities (physicochemical properties, environmental fate and/or toxicological properties).

A selection of the most relevant physicochemical and toxicological estimation tools, which are freely available, are presented below in Table 4.

Table 4. Most relevant QSAR tools to estimate physicochemical and toxicological properties.

Tool	Description	Ref
EPI Siute v4.0	EPIsuite estimate among other Kow, Koc, Koa, Henry's Law constant, melting and boiling points, aerobic and anaerobic biodegradability of organic chemicals, biodegradation half-life of hydrocarbons and bioconcentration factors.	[26]
Danish (Q)SAR Database	The Danish (Q)SAR database is a repository of estimates from over 70 (Q)SAR models for 166,072 chemicals. The (Q)SAR models encompass endpoints for physicochemical properties, fate, eco-toxicity, absorption, metabolism and toxicity.	[27]
TEST	TEST allows for estimates of the value for several toxicity endpoints: 96 hour fathead minnow LC50, 48 hour Daphnia magna LC50, 48 hour Tetrahymena pyriformis IGC50, Oral rat LD50, bioaccumulation factor, developmental toxicity, and Ames mutagenicity. TEST also estimates several physical properties.	[28]
CAESAR	Five endpoints with high relevance for REACH have been addressed within CAESAR: bioconcentration factor, skin sensitization, carcinogenicity, mutagenicity and developmental toxicity.	[29]
ECOSAR	Chemical's acute (short-term) toxicity and chronic (long-term or delayed) toxicity to aquatic organisms, aquatic invertebrates, and aquatic plants are estimated	[30]
OECD QSAR Toolbox	It is developed by OECD to make (Q)SAR technology readily accessible, transparent, and less demanding in terms of infrastructure costs. The Toolbox has multiple functionalities allowing the user to perform a number of operations. The Toolbox potentially covers all relevant regulatory endpoints.	[31]

6 Conclusions

In this chapter human health and environmental risk assessment steps were introduced. Five models (EUSES, USEtox, GLOBOX, SADA, and MAFRAM) risk and life cycle impact assessment models were briefly described and also other 12 models were appointed. There is no risk assessment model better than another. All models have their strengths and weaknesses and many of them also are focused on one particular aspect such as a single environmental compartment or focused in a kind of pollutants. Finally, freely and on line available data sources (databases and estimation data tools) were reviewed. The selection of the data source and, in some cases the scarcity of data are an important issue to obtain a quality results.

References

[1] OECD, Organisation for Economic Co-operation and Development (2003), Descriptions of selected key generic terms used in chemical hazard/risk assessment. ENV/JM/MONO(2003)15. OECD Series on Testing and assessment. Number 44.

[2] Fazil AM (2005) A primer on risk assessment modelling: focus on seafood products. Food and Agriculture Organization of United Fisheries technical Paper, Rome.

[3] Institute for Health and Consumer Protection (2003) Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances; Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances; Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market.

[4] United States Environmental Protection Agency (2005). Guidelines for Carcinogen Risk Assessment EPA/630/P-03/001F. Risk Assessment Forum U.S. Environmental Protection Agency Washington DC, US.

[5] United States Environmental Protection Agency (1998). Guidelines for Ecological Risk Assessment EPA/630/R-95/002F. Washington DC, US.

[6] Olsen SI, Christensen FM, Hauschild et al (2001) Life cycle impact assessment and risk assessment of chemicals –a methodological comparison. Environ Impact Assess Rev 21:385-404

[7] EC (2004) European Union System for the Evaluation of Substances 2.0 (EUSES 2.0). Prepared for the European Chemicals Bureau by the National Institute of Public Health and the Environment (RIVM), Bilthoven, The Netherlands (RIVM Report no. 601900005). http://ecb.jrc.it. Accessed 09 March 2012

[8] Rosenbaum R, Bachmann, TM Gold L.S,, Huijbregts MAJ,, Jolliet O,, Juraske R,, Koehler A, Larsen HF, MacLeod M, Margni M, McKone TE, Payet J, Schuhmacher M, van de Meent D,. Hauschild MZ USEtox: the UNEP-SETAC toxicity model: recommended characterisation factors for human toxicity and freshwater ecotoxicity in life cycle impact assessment International J Life Cycle Assess 13:532-546

[9] Rosenbaum R, Margni M, Jolliet O (2007) A flexible matrix algebra framework for the multimedia multipathway modeling of emission to impacts. Environ Int 33:624–634.

[10] Sleeswijk AW, Heijungs R (2010) GLOBOX: A spatially differentiated global fate, intake and effect model for toxicity assessment in LCA. Sci Total Environ 408: 2817-2832

[11] Stewart RN, Purucker ST (2011) An environmental decision support system for spatial assessment and selective remediation. Environ Model & Softw 26:751-760

[12] Batiha MA, Kadhum AAH, Batiha MM, et al (2010) MAFRAM—A new fate and risk assessment methodology for non-volatile organic chemicals. J Hazard Mater 181:1080-1087

[13] Breeze web. http://www.breeze-software.com/riskanalyst/ Accessed 09 March 2012

[14] Lakes Environmental web. http://www.weblakes.com/index.html Accessed 09 March 2012

[15] United States Environmental Protection Agency (2005) Human Health Risk Assessment Protocol (HHRAP) for Hazardous Waste Combustion Facilities (Final) EPA530-R-05-006 Office of Solid Waste, Washington DC, US

[16] United States Environmental Protection Agency (1999) Screening Level Ecological Risk Assessment Protocol (SLERAP) for Hazardous Waste Combustion Facilities EPA 530-D-99-001A. Office of Solid Waste Washington DC, US

[17] Gobas, FAPC, Pasternak JP, Lien K et al (1998) Development and field validation of a multimedia exposure assessment model for waste load allocation in aquatic ecosystems: Application to 2,3,7,8-tetrachlorodibenzo-p-dioxin and 2,3,7,8-tetrachlorodibenzofuran in the fraser river watershed. Environ. Sci and Technol 32:2442-2449

[18] Groundwater software web. http://www.groundwatersoftware.com/. Accessed 09 March 2012

[19] ECOLEGO web. http://ecolego.facilia.se/ecolego/show/HomePage. Accessed 09 March 2012

[20] Palisade web. More information available at: http://www.palisade.com/risk/. Accessed 09 March 2012

[21] Varshney P (1998) Commentary on API's DSS. J. Soil Contam. 7:275-282

[22] Seuntjens P, Steurbaut W, Vangronsveld J (2006) Chain model for the impact analysis of contaminants in primary food products. Study report of the Belgian Science Policy. Brusels, Belgium.

[23] Health and Safety laboratory (2002) Toxic RISKAT version 3.1 - The Inclusion of the Site Risk Methodology. Report No HSL/2002/Z27. Sheffield, UK.

[24] EOSCA web.http://www.eosca.com/NECCS/Index.htm. Accessed 09 March 2012.

[25]Jolliet O, Margni M, Charles R, Humbert S, Payet J, Rebitzer G, Rosenbaum R (2003) IMPACT 2002+: A New Life Cycle Impact Assessment Methodology. Int J LCA 8:324-330.

[26] United States Environmental Protection Agency (2011) Estimation Programs Interface Suite™ for Microsoft® Windows. http://www.epa.gov/oppt/exposure/pubs/episuite.htm. Accessed 09 March 2012.

[27] Danish Environmental Protection Agency (2005). User Manual for the Internet Version of the Danish (Q)SAR Database. http://130.226.165.14/User_Manual_Danish_Database.pdf. Accessed 09 March 2012.

[28] United States Environmental Protection Agency (2011) User's Guide for T.E.S.T. version 4.0 A Program to Estimate Toxicity from Molecular Structure United States Environmental Protection Agency. http://www.epa.gov/nrmrl/std/cppb/qsar/. Accessed 09 March 2012.

[29] Benfenati E (2010) The CAESAR project for in silico models for the REACH legislation. Chem Cent J. 4:I1.

[30] United States Environmental Protection Agency (2011) Methodology document for the ecological Structure-Activity Relationship Model (ECOSAR) Class Program MS-Windows Version 1.1 Office of Pollution Prevention and Toxics, Washington DC, US. http://www.epa.gov/oppt/newchems/tools/ecosartechfinal.pdf. Accessed 09 March 2012.

[31]OECD QSAR. http://www.qsartoolbox.org/index.html. Accessed 09 March 2012.