Science of the Total Environment 562 (2016) 474–479

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Potential for MERLIN-Expo, an advanced tool for higher tier exposure assessment, within the EU chemical legislative frameworks

Nicoleta Suciu [a,*], Alice Tediosi [b], Philippe Ciffroy [c], Annette Altenpohl [d], Céline Brochot [e], Frederik Verdonck [f], Federico Ferrari [b], Elisa Giubilato [g], Ettore Capri [a], Gabriella Fait [h]

[a] Università Cattolica del Sacro Cuore, 29122 Piacenza, Italy
[b] Aeiforia Srl, 29027 Gariga di Podenzano (PC), Italy
[c] Electricité de France (EDF) R&D, National Hydraulic and Environment Laboratory, 6 quai Watier, 78400 Chatou, France
[d] Österreichisches Normungsinstitut/Austrian Standards Institute, Heinestraße 38, 1020 Wien, Austria
[e] INERIS, Parc ALATA, BP2, 60550 Verneuil en Halatte, France
[f] ARCHE cvba, Liefkensstraat 35d, 9032 Gent-Wondelgem, Belgium
[g] University Ca Foscari Venice, Department of Environmental Sciences, Informatics and Statistics, via Torino 155, 30172 Mestre-Venice, Italy
[h] EFSA, via Carlo Magno 1/a, 43126 Parma, Italy

HIGHLIGHTS

- Exposure and risk evaluation of chemicals
- Coupling environmental exposure and pharmacokinetic models
- MERLIN-expo as a higher tier exposure tool
- MERLIN-expo potential application in EU chemical regulations
- EU legislations and policies related to risk assessment and management of chemicals

GRAPHICAL ABSTRACT

ARTICLE INFO

Article history:
Received 20 February 2016
Received in revised form 10 April 2016
Accepted 10 April 2016
Available online 22 April 2016

Editor: D. Barcelo

Keywords:
Multimedia model
Pharmacokinetic model

ABSTRACT

MERLIN-Expo merges and integrates advanced exposure assessment methodologies, allowing the building of complex scenarios involving several pollution sources and targets. The assessment of exposure and risks to human health from chemicals is of major concern for policy and ultimately benefits all citizens. The development and operational fusion of the advanced exposure assessment methodologies envisaged in the MERLIN-Expo tool will have a significant impact in the long term on several policies dealing with chemical safety management. There are more than 30 agencies in Europe related to exposure and risk evaluation of chemicals, which have an important role in implementing EU policies, having especially tasks of technical, scientific, operational and/or regulatory nature. The main purpose of the present paper is to introduce MERLIN-Expo and to highlight its potential for being effectively integrated within the group of tools available to assess the risk and exposure of chemicals for EU policy. The main results show that the tool is highly suitable for use in site-specific or local

* Corresponding author.
E-mail address: nicoleta.suciu@unicatt.it (N. Suciu).

http://dx.doi.org/10.1016/j.scitotenv.2016.04.072

Exposure assessment
Chemicals
Legislative framework

impact assessment, with minor modifications it can also be used for Plant Protection Products (PPPs), biocides and REACH, while major additions would be required for a comprehensive application in the field of consumer and worker exposure assessment.

1. Introduction

An exposure assessment starts by answering several questions for a particular substance or chemical: Who or what is exposed (e.g.: people, aquatic ecosystem)?; Does the exposure occur through breathing, drinking water, skin contact or any other routes?; How much exposure occurs?; How often and for how long does exposure occur?; etc... Exposure occurs through contact with a chemical. For humans such contact can occur by inhaling air, drinking water, eating food, or touching a variety of products that contain the chemical; however in many cases it occurs trough a complex combination of these routes, and also at different time and spatial scale. The concentration of the chemical and the extent of the contact are important components of exposure assessment (Pocas and Hogg, 2007; Dorne et al., 2009). The results of an exposure assessment are often compared with the results of a hazard assessment of the chemical. Hazard assessment provides an understanding of the potential for the chemical to cause adverse effects to humans and environment. Together, exposure assessment and hazard assessment can be combined into risk assessment in order to reach conclusions on the likelihood of adverse effects in the exposed population (Barlow and Schlatter, 2010). The major flows identified for exposure assessment also apply to hazard assessment: difficulties to predict effects when many stressors are involved, conservative approaches, lack of uncertainty tools.

The 4FUN project funded under the European Union's 7th Framework Programme produced a software, named MERLIN-Expo, containing a library of models for exposure assessment, coupling environmental multimedia and pharmacokinetic models. The aim was to provide decision-makers with a state-of-the-art tool to analyse the current and future trends in environmental conditions and pressures that may lead to health problems. This can be achieved through a range of functionalities able to generate outputs of high concern for health risk assessment: building long-term environmental scenarios, exposure assessment, provision of uncertainty margins, and identification of sensitive pathways and risks. The SWOT analysis (analysis of Strengths, Weaknesses, Opportunities and Threats) carried out for MERLIN-Expo highlighted the possibility to employ it within several European legislative frameworks, as for example for plant protection products (PPPs), Biocidal Product Regulation (BPR) and Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) (de Wilde et al., 2015a, 2015b). Moreover, the CEN (European Committee of Standardization) Workshop Agreement produced a standard documentation of chemical exposure models (CEN, 2015), which can also be used for worker and consumer exposure (Ciffroy et al., in this issue-a, in this issue-b).

In the European Union, each regulatory body uses a risk assessment framework to help the European Commission making regulatory decisions. The Commission defines the mandates of the different regulatory bodies. According to their mandates, the regulatory bodies focus on distinct areas and product categories. For each product category, distinct pieces of legislation regulate product authorisation. There are more than 30 agencies in Europe related to chemical risk evaluation. These agencies have got an important role in implementing EU policies, especially connected to technical, scientific, operational and/or regulatory tasks.

The main objective of the present paper is to give an overview on the applicability of MERLIN-Expo to local impact assessment, and to show how it could be effectively used to assess risk and exposure of chemicals within EU legislations. In order to achieve this aim, the information about the potential of the tool and the existing EU legislation, based on different media (air, soil, water, atmosphere, human body, aquatic food, and terrestrial food) were integrated.

2. Key features of MERLIN-Expo tool

MERLIN-Expo links external and internal exposure for different human populations and integrates environmental and human exposure assessment by including a comprehensive library of environmental multimedia and physiologically based pharmacokinetic (PBPK) models. In MERLIN-Expo these models can be combined in a flexible way in order to build complex scenarios involving a range of chemical substances (metals, organics), and several pollution sources and targets. It allows performing uncertainty and sensitivity analysis (from screening to global variance-based approaches), and deterministic and probabilistic simulations. Furthermore, it offers a full package of on-line training material that support users to learn how the model works. A detailed description of MERLIN-Expo can be found in Ciffroy et al. (in this issue-b).

Three case studies based on actual datasets were performed using MERLIN-Expo. The aims were to demonstrate: the reliability of the modelling predictions through a comparison with actual measurements; the feasibility of building complex realistic exposure scenarios satisfying the needs of stakeholders; and how uncertainty margins can improve risk governance. Furthermore, the case studies allowed to investigate the applicability of MERLIN-Expo to local impact assessment studies.

One case study focused on lead (Pb) and arsenic (As) exposure in preschool children and adults living in the Northern Campine region of Belgium (Fierens et al., 2016; Van Holderbeke et al., in this issue). This region has a long history harbouring polluting smelting industry. The objectives of this case study were to estimate the total internal and external Pb and As exposure and to characterize and rank the different exposure pathways according to their contribution to the measured concentrations in the population.

A second case study aimed at investigating ecological and human exposure to Persistent Organic Pollutants (POPs) in the Venice lagoon and its surrounding areas (Giubilato et al., in this issue; Radomyski et al., in this issue). The Venice lagoon can be defined as a transitional environment, characterized by shallow waters (i.e., the mean water depth is 1.2 meters) (Guerzoni and Tagliapietra, 2006), and influenced by several anthropogenic activities such as industry, tourism, and fishery. These activities caused in the past and still cause the release in environmental media of a wide range of chemical substances, including POPs. The main objective was to estimate ecological exposure and human life time exposure to POPs through the diet, in order to support the characterization of risks to lagoon ecosystems and the assessment of human health risks associated with local fish and seafood consumption.

A third case study focused on perfluorinated compounds (PFCs), and in particular perfluorooctanoic acid (PFOA) and perfluorooctanesulfonate (PFOS), as contaminants of the Ebro River Basin in Spain. The Ebro river is 928 km in length and generates the Ebro Delta, one of the largest wetland areas (320 km²) in the western Mediterranean region. The aims of this case study were to estimate the contamination of the environmental media in the different zones of the Ebro river basin, and the exposure of the human population via food intake (Banjac et al., 2015)

Table 1
PPPs legislation where MERLIN-Expo could be used, based on media.

Legislation	Media considered	Reference
Commission Regulation (EU) No 283/2013 (setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market)	Terrestrial food; aquatic food; atmosphere; river; soil	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396432439926&uri=CELEX:32013R0283
Commission Regulation (EU) No 284/2013 (setting out the data requirements for plant protection products, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market Text with EEA relevance)	Terrestrial food; aquatic food; atmosphere; river; soil	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396432474847&uri=CELEX:32013R0284
Directive 2009/128/EC (establishing a framework for Community action to achieve the sustainable use of pesticides)	Terrestrial food; aquatic food; river; Soil	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396432373985&uri=CELEX:02009L0128-20091125
Regulation (EC) No 1107/2009 (concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC)	Terrestrial food; aquatic food; atmosphere; river; soil	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396432323415&uri=CELEX:32009R1107
Commission Regulation (EU) No 1141/2010 (laying down the procedure for the renewal of the inclusion of a second group of active substances in Annex I to Council Directive 91/414/EEC and establishing the list of those substances)	Aquatic food, atmosphere; river; soil	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396426992262&uri=CELEX:02010R1141-20130516
Commission Regulation (EC) No 33/2008 (laying down detailed rules for the application of Council Directive 91/414/EEC as regards a regular and an accelerated procedure for the assessment of active substances which were part of the programme of work referred to in Article 8(2) of that Directive but have not been included into its Annex I)	Aquatic food; atmosphere; soil	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396427116382&uri=CELEX:02008R0033-20100129
Regulation (EC) No 396/2005 (on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC)	Human exposure	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396601870667&uri=CELEX:02005R0396-20121026

2.1. Reliability of the MERLIN-expo predictions

The case studies helped in assessing the reliability of the predictions obtained using MERLIN-Expo. Good agreement was observed between the model predictions and the actual experimental data shown by a factor less than 3 (Fierens et al., 2016; Van Holderbeke et al., 2016; Giubilato et al., in this issue; Radomyski et al., in this issue; Banjac et al., 2015). Such an agreement between predictions and independent measurement (i.e. the measurement data were not used to calibrate the models) is generally judged acceptable. The models are, in this case, sufficiently generic to be applied to a large number of substances and situations. Although the number of case studies is relatively low to generalize these results, the testing approach gives a reasonable confidence in MERLIN-Expo predictions. Results of the first case study showed that MERLIN-Expo performed best when model parameters are set to values specific to the sites and the populations, allowing to tailor the assessment to local conditions (Fierens et al., 2016; Van Holderbeke et al., 2016).

2.2. Flexibility in building complex exposure scenarios

The three case studies exhibited very different characteristics in order to cover a wide range of substances (e.g.: metals, persistent organic pollutants, emerging pollutants), contamination sources (e.g.: water, wastes, soil, dust, air, food), environmental policy endpoints (e.g.: waste, land management, water quality), spatial/temporal scales (e.g.: close vicinity of industry, lagoon). The case studies offered the opportunity to explore the applicability of the tool at several levels of complexity - ranging from very simple to rather complex scenarios – and a wide spectrum of exposure assessment contexts. The complexity depended on the description of the environment and exposure pathways (number of environmental media selected and their interconnections, default values or site specific values for parameterization), but also on the statistical analyses performed (deterministic or probabilistic). All these different levels of complexity were effectively handled by MERLIN-Expo. Moreover, the case study performed in the Venice lagoon showed that MERLIN-Expo can be used to combine ecological and human exposure assessment, supporting the integrated evaluation of chemical fate and effects, also for long-term scenarios (Giubilato et al., in this issue; Radomyski et al., in this issue). A step by step simulation for the afore mentioned case study is presented in the supplementary information, in order to facilitate the comprehension of the use of MERLIN-Expo for a real case study.

2.3. Incorporating uncertainty in risk assessment

Probabilistic analyses were performed in the case studies in order to study the impact of uncertainty and variability in parameter values of the different modules on the final outputs, such as a biological measure in humans. The probabilistic simulation tools implemented in MERLIN-Expo were used together with the default probability density functions (pre-) defined for model parameters. These analyses produced a mean prediction associated to an interval of confidence for the model outcomes of interest. Sensitivity analyses were also run to identify and rank the key input parameters of the exposure, and also to assess the relative contribution of the different sources, pathways, and routes of exposure on the overall modelled exposure (Fierens et al., 2016; Van Holderbeke et al., 2016).

3. Role within the legislative framework and impact on chemical policy

Information about the potential of the tool, the existing European regulatory bodies, and the existing EU legislation, based on different

Table 2
Biocides legislation where MERLIN-Expo could be used, based on media.

Legislation	Media considered	Reference
Directive 98/8/EC of the European Parliament (concerning the placing of biocidal products on the market)	Terrestrial food; aquatic food; atmosphere; river; soil	http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:31998L0008
Regulation (EU) No **528/2012 (concerning the making available on the market and use of biocidal products)**	Terrestrial food; aquatic food; atmosphere; river; soil	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396432509562&uri=CELEX:02012R0528-20130923

Table 3
Industrial chemical legislation where MERLIN-Expo could be used, based on media.

Legislation	Media considered	Reference
REACH regulation, EC 1907/2006	Terrestrial food; aquatic food; atmosphere; river (aquatic and sediment, freshwater and marine); soil; human exposure	http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32006R190

media (air, soil, water, atmosphere, human exposure, aquatic food, and terrestrial food), were integrated.

In order to identify the legislative framework where MERLIN-Expo can find applicability, a web-based search of all EU authorities/agencies responsible for risk evaluation was made, which allowed to identify relevant EU authorities and agencies. More than 30 EU authorities and agencies responsible for risk evaluation were found, including the European Agency for Safety and Health at Work (EU-OSHA), the European Centre for Disease Prevention and Control (ECDC), the European Chemicals Agency (ECHA), the European Environment Agency (EEA), the European Food Fisheries Control Agency (EFCA), the European Food Safety Authority (EFSA), the European Medicine Agency (EMA), the Consumers, Health and Food Executive Agency (Chafea), the Research Executive Agency (REA). Among these agencies, the following ones were selected as being within the applicability domain of the MERLIN-Expo tool: EU-OSHA, ECHA, EEA, EFSA, and EMA. Their websites were carefully explored in order to identify relevant legislation on exposure and risk assessment of chemicals (a brief summary can be found at: http://4funproject.eu/en/observatory/). Therefore, a classification of MERLIN-Expo use for legislation was made, considering the actual status of the software and possible future modifications.

4. Results and discussion

4.1. MERLIN-Expo for local impact assessment

The three case studies described above demonstrated that MERLIN-Expo is highly suitable for use in site-specific or local impact assessment (Fierens et al., 2016; Van Holderbeke et al., 2016; Giubilato et al., in this issue; Radomyski et al., in this issue; Banjac et al., 2015). Local impact assessments can be subject to national, regional or local requirements, and so environmental compartments and human exposure pathways to be considered can vary. Moreover, local impact assessments are often less standardised or regulated, which allows the use of specific tools or models. These two aspects make MERLIN-Expo highly suitable for site-specific assessment. In fact, the modular format of MERLIN-Expo and its flexibility allow the building of different complex scenarios.

4.2. MERLIN-Expo for PPPs

PPPs are highly regulated at the European level. The European Food Safety Authority (EFSA) is involved in the regulation of these compounds. A SWOT analysis of MERLIN-Expo revealed that the tool would be suitable for PPP regulatory framework with minor modifications (de Wilde et al., 2015a). For the time being the software does not include some specific legislative requirements (e.g.: calculations in groundwater, non-linear sorption, metabolites, spray drift, lateral transfer of chemicals). However, the same analysis highlighted the opportunity and possibility of including easily the PPP requirements in the tool (de Wilde et al., 2015a). Table 1 presents a list of PPP legislations, where MERLIN-Expo could be used for PPPs exposure assessment.

4.3. MERLIN-Expo for biocides

Biocides are non-agricultural chemicals used to suppress organisms that are harmful to human or animal health, or that cause damage to natural or manufactured materials. These compounds were firstly regulated in Europe with the entering into force of the EU Directive 98/8/EC. At European level the agency that is mainly involved in the regulation of these compounds is the European Chemicals Agency (ECHA), which works on implementing the EU chemical legislation for the benefit of human health and environment. The SWOT analysis revealed a low to moderate suitability of the tool for biocides regulatory framework (de Wilde et al., 2015a). However, a benchmarking analysis between MERLIN-Expo and the EUSES model (highly used for biocides regulatory framework) showed a high compatibility between the results of the two models for a specific scenario, and when considering the terrestrial and aquatic compartments. Furthermore, for the other compartments (e.g. food) adaptation or modification of MERLIN-Expo is feasible (de Wilde et al., 2015b). Table 2 presents the biocides legislation where MERLIN-Expo could be considered for exposure assessment.

4.4. MERLIN-Expo for industrial and consumer chemicals

One of the main regulations in the category of industrial and consumer chemicals is the REACH regulation, which aims to improve the protection of human health and environment through the better and earlier identification of the intrinsic properties of chemical substances (Table 3). This is done by the four processes of REACH, namely the registration, evaluation, authorisation and restriction of chemicals. REACH also aims to enhance innovation and competitiveness of the EU chemical industry.

The REACH Regulation places responsibility on industry to manage the risks from chemicals and to provide safety information on the substances. Manufacturers and importers are required to gather information on the properties of their chemical substances, which will allow their safe handling, and to register the information in a central database in the ECHA.

4.4.1. Environmental exposure and human exposure indirect via the environment

Concerning the MERLIN-Expo applicability to REACH regulation, a low to moderate applicability was highlighted by the SWOT analysis even if a high compatibility between the results of MERLIN-Expo and EUSES (for terrestrial and aquatic compartments and for a specific

Table 4
Legislation on indirect exposure of human via the environment where MERLIN-Expo could be used, based on media

Legislation	Media considered	Reference
Directive 2008/50/EC (on ambient air quality and cleaner air for Europe)	Atmosphere	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396432705626&uri=CELEX:32008L0050

Table 5
Consumer legislation where MERLIN-Expo could be used, based on media

Legislation	Media considered	Reference
Directive 2001/95/EC (on general product safety)	Atmosphere	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396434594545&uri=CELEX:02001L0095-20100101
Directive 2002/95/EC (on the restriction of the use of certain hazardous substances in electrical and electronic equipment)	Atmosphere	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396432654942&uri=CELEX:02002L0095-20110910

scenario) were shown by the benchmarking analysis (Table 4). It is considered that a moderate to high applicability could be reached after further tailoring and improving (de Wilde, 2015b). The same study highlighted the high suitability of EUSES and GREAT-ER model for REACH and biocides as the models cover a large amount of the relevance criteria that are important for REACH and biocides (de Wilde et al., 2015b).

4.4.2. Consumer exposure

The consumer, i.e. a member of the general public who may be of any age, either sex, and in any state of health, may be exposed to a substance by using consumer products or articles. A consumer product or article is in general considered to be a product that can be purchased from retail outlets by members of the general public (ECHA, 2012b). Consumer exposure estimation deals with the final step of the supply chain. Considering consumer exposure is important because the possible means of controlling the exposure are very limited and cannot normally be monitored, or enforced beyond the point of sale of the products (ECHA, 2012b). The consumer exposure is also regulated in Europe under REACH Regulation EC 1907/2006, having ECHA as referring EU Agency. Examples of human exposures to substances arising from the use of consumer products and articles include: exposure to solvents from the use of glues/adhesives, exposure to textile finishing chemicals or dyes in clothes and exposure to substances released from articles. Additionally, other exposures are included under "consumer exposure" despite the fact that the exposure does not arise from the use of consumer products or articles but rather as a result of being near where a substance is being used or has been used: exposure to substances at home after use of decorating or cleaning products by professionals; exposure to substances in indoor air (residential air: e.g. household, schools, nurseries) including the fraction adsorbed on dust particles arising from building materials; exposure to substances in public areas (e.g. swimming pools, recreational areas) (CEN, 2015). It is important to note that in REACH guidance, indirect exposure of humans via the environment is not included in consumer exposure, but it is part of the overall risk assessment required by the legislation. Even if the regular exposure assessment of humans with MERLIN-Expo is indirect via the environment by coupling environmental and food models with the PBPK model, a direct use of PBPK model, therefore a direct exposure assessment, is also possible (de Wilde et al., 2015b). Furthermore, another opportunity of MERLIN-Expo for consumer exposure is to include a module for indoor air as exposure route. (See Table 5)

4.4.3. Worker exposure

Substances in the workplace may come into contact with the body and possibly enter the body by inhalation, by contacting and passing through the skin (dermal route), or sometimes by swallowing (ingestion). Exposure to a particular substance should normally be understood as meaning external exposure. This can be defined as the amount of the substance ingested, the amount in contact with the skin, and/or the amount inhaled (which is represented by the airborne concentration of the substance in the breathing zone of a worker). There are four EU agencies that work together to improve and insure workers' safety conditions: (i) European Agency for Safety and Health at Work (EU-OSHA) provides Community bodies, Member States and interested

Table 6
EU legislation for safety at work.

Legislation	Media considered	Reference
Commission Directive 2006/15/EC (establishing a second list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC and amending Directives 91/322/EEC and 2000/39/EC)	Atmosphere	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396434828399&uri=CELEX:32006L0015
Commission Directive 2009/161/EU (establishing a third list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC and amending Commission Directive 2000/39/EC)	Atmosphere	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396434795742&uri=CELEX:32009L0161
Council Directive 98/24/EC (on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC))	Atmosphere	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396434944248&uri=CELEX:01998L0024-20070628
Directive 2000/39/EC (establishing a first list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work)	Atmosphere	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396434901833&uri=CELEX:02000L0039-20100108
Directive 2003/11/EC (amending for the 24th time Council Directive 76/769/EEC relating to restrictions on the marketing and use of certain dangerous substances and preparations (pentabromodiphenyl ether, octabromodiphenyl ether))	Atmosphere	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396432614813&uri=CELEX:02003L0011-20030215
Directive 2004/107/EC (relating to arsenic, cadmium, mercury, nickel and polycyclic aromatic hydrocarbons in ambient air)	Atmosphere	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396432760344&uri=CELEX:02004L0107-20090420
Directive 2004/37/EC (on the protection of workers from the risks related to exposure to carcinogens or mutagens at work (Sixth individual Directive within the meaning of Article 16(1) of Council Directive 89/391/EEC))	Atmosphere	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396434866574&uri=CELEX:32004L0037
Directive 91/322/EEC (on establishing indicative limit values by implementing Council Directive 80/1107/EEC on the protection of workers from the risks related to exposure to chemical, physical and biological agents at work)	Atmosphere	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396434978669&uri=CELEX:01991L0322-
Directive 83/477/EEC (on the protection of workers from the risks related to exposure to asbestos at work (second individual Directive within the meaning of Article 8 of Directive 80/1107/EEC))	Atmosphere	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396435863550&uri=CELEX:01983L0477-20070628
Directive 2009/148/EC (on the protection of workers from the risks related to exposure to asbestos at work)	Atmosphere	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1396435811355&uri=CELEX:32009L0148

parties with technical, scientific and economic information in the field of health and safety at work; (ii) the European Chemicals Agency (ECHA) is responsible for the coordination of REACH related duties; (iii) the European Environment Agency (EEA) has a primary role in maintaining and supplying up-dated, specific and reliable environmental information to, for example, decision makers. Just as other agencies and bodies, the EEA has no regulatory role; (iv) the European Foundation for the Improvement of Living and Working Conditions (EUROFOUND) aims to assist planning and introduction of better living and working conditions in Europe, but does not specifically appear to deal with chemical safety (EC, 2012). Table 6 presents a list of relevant legislations. MERLIN-Expo was not designed for worker exposure as it is for example the case of "Advanced REACH Tool" (ART) (CEN, 2015). However an adaptation of the MERLIN-Expo tool in the long term is also possible by the inclusion of indoor air module and the definition of different air compartment dimensions in order to assess both workers' near-field and far-field exposure. Additional adaptations of the tool for different scenarios required by the in-force legislation should also be considered. Nevertheless, a strong point of MERLIN-Expo that could answer to legislation requirements for worker exposure is the possibility to undertake sensitivity and uncertainty analysis, considering that the majority of available models does not include tools for these purposes (ECHA, 2012a).

5. Conclusions

MERLIN-Expo can be considered an advanced tool for higher tiers in exposure assessment complementary to existing tools used for low tiers.

The potential of MERLIN-Expo to be used in the EU chemical legislative frameworks is high. At present, the tool is very suitable for local impact assessment, as proved by the case studies, where real datasets and realistic scenarios were addressed. Minor modifications would be sufficient to make MERLIN-Expo suitable for its application in the context of PPP, biocides, and REACH regulations. On the contrary, the usage of the tool for consumer and worker exposure would require major additions.

MERLIN-Expo has many advanced functionalities (such as uncertainty analysis, probabilistic simulations, modular approach, dynamic modelling, combination of environmental fate with pharmacokinetics) and models (many fate processes and environmental compartments, different human populations), which are not always required by the current regulatory frameworks. However, these advanced assessment functionalities could be required by the legislation in the future, and then they will become an asset. MERLIN-Expo also takes into account a wide range of chemicals, including emerging chemicals. Therefore, MERLIN-Expo prepares the future in exposure regulation.

The availability of different options for uncertainty and sensitivity analysis in MERLIN-Expo, from simple local methods to more computational expensive non-local methods, is targeted to a wide range of end-users and should facilitate the incorporation of such issues in future decision making. Such analyses then provide valuable information for both risk assessors and decision-makers by supporting decisions to conduct additional analyses or prioritise resource allocations for additional research and/or data collection efforts. This is also in line with the recommendations of international agencies as EFSA, BFR and WHO, and makes MERLIN-Expo an appealing tool for advanced exposure assessment.

Acknowledgements

The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement no. 308440. This publication reflects the views only of the author, and the European Union cannot be held responsible for any use which may be made of the information contained therein.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.scitotenv.2016.04.072.

References

Banjac, Z., Ginebreda, A., Brochot, C., Deliverable D5.3, 2015. Report on Case Study 3. Available at http://4funproject.eu/files/repository/20151130154206_Deliverable5.3_rev.pdf.

Barlow, S., Schlatter, J., 2010. Risk assessment of carcinogens in food. Toxicol. Appl. Pharmacol. 243, 180–190.

CEN, 2015. CEN/WS MERLIN-Expo N38-CWA 16938 Standard Documentation of Chemical Exposure Models.

Ciffroy, P., Altenpohl, A., Fait, G., Fransman, W., Paini, A., Radovnikovic, A., Siciu, N., Simon-Cornu, M., Verdonck, F., 2016a. Development of a standard documentation protocol for communicating exposure models. Sci. Total Environ. (in this issue).

Ciffroy, P., Alfonso, B., Altenpohl, A., Banjac, Z., Bierkens, J., Brochot, C., Critto, A., De Wilde, T., Fait, G., Tediosi, A., Fierens, T., Garratt, J., Giubilato, E., Grange, E., Johansson, E., Radomyski, A., Reschwann, K., Suciu, N., Van Holderbeke, M., Verdonck, F., Vlajic, A., 2016b. Modelling the exposure to chemicals for risk assessment: a comprehensive library of multimedia and PBPK models for integration, prediction, uncertainty and sensitivity analysis — the MERLIN-expo tool. Sci. Total Environ. (in this issue).

De Wilde, T., Verdonck, F., Fait, G., Ciffroy, P., Tanaka, T., Bonnard, R., Banjac, Z., Giubilato, E., Critto, A., Suciu, N., Bierkens, J., Garatt, J., 2015a. Deliverable 2.4: SWOT Analysis of Different Exposure Models. Available at http://4funproject.eu/files/repository/20150925120444_Deliverable2.4.pdf.

De Wilde, T., Verdonck, F., Ciffroy, P., Brochot, C., Alfonso, B., Johansson, E., 2015b. Deliverable D4.3: Report of Benchmarking of the 2-FUN tool. Available at http://4funproject.eu/files/repository/20160220145441_Deliverable4.3.pdf.

Dorne, J.L.C.M., Bordajandi, L.R., Amzal, B., Ferrari, P., Verger, P., 2009. Combining analytical techniques, exposure assessment and biological effects for risk assessment of chemicals in food. Trends Anal. Chem. 28, 695–707.

EC (European Commission), 2012. Minimising Chemical Risk to Workers' Health and Safety Through Substitution. publications office of the european union, luxembourg 978-92-79-25969-2 http://dx.doi.org/10.2767/77360.

ECHA (European Chemicals Agency), 2012a. Guidance on information requirements and chemical safety assessment Chapter R.14: occupational exposure estimation. ECHA-2010-G-09-EN 2012.

ECHA (European Chemicals Agency), 2012b. Guidance on information requirements and chemical safety assessment Chapter R.15: consumer exposure estimation. ECHA-2010-G-09-EN 2012.

Fierens, T., Van Holderbeke, M., Standaert, A., Cornelis, C., Brochot, C., Ciffroy, P., Johansson, E., Bierkens, J., 2016. Multimedia & PBPK modeling with MERLIN-expo versus biomonitoring for assessing Pb exposure of pre-school children in a residential setting. Sci. Total Environ. (in this issue).

Giubilato, E., Radomyski, A., Critto, A., Ciffroy, P., Brochot, C., Pizzol, L., Marcomini, A., 2016. Modelling ecological and human exposure to POPs in Venice lagoon — part I: application of MERLIN-Expo tool for integrated exposure assessment. Sci. Total Environ. (in this issue).

Guerzoni, S., Tagliapietra, D., 2006. Atlante della laguna: Venezia tra terra e mare. Osservatorio Naturalistico del Comune di Venezia. CNR Istituto di Scienze Marine di Venezia, Marsilio Editori, Venezia.

Pocas, M.F., Hogg, T., 2007. Exposure assessment of chemicals from packaging materials in foods: a review. Trends Food Sci. Technol. 18, 219–230.

Radomyski, A., Giubilato, E., Ciffroy, P., Critto, A., Brochot, C., Marcomini, A., 2016. Modelling ecological and human exposure to POPs in Venice lagoon — part II: quantitative uncertainty and sensitivity analysis in coupled exposure models. Sci. Total Environ. (in this issue).

Van Holderbeke, M., Fierens, T., Standaert, A., Cornelis, C., Brochot, C., Ciffroy, P., Johansson, E., Bierkens, J., 2016. Assessing multimedia/multipathway exposures to inorganic arsenic at population and individual level using MERLIN-Expo. Sci. Total Environ. (in this issue).