4FUN

"The FUture of FUlly integrated human exposure assessment of chemicals: Ensuring the long-term viability and technology transfer of the EU-FUNded 2-FUN tools as standardised solution"

Grant agreement No.: 308440 (Collaborative Project)

Deliverable 3.1: Updated 2-FUN library of models

Due date of deliverable: 31 June 2014
Actual submission date: 14 August 2014

Start date of project: 1st October 2012 Duration: 36 months

Coordinator	AEIFORIA
Deliverable Leading Partner	EDF
Contributing Partners	EDF, INERIS
Task	3.1
Revision	

Project co-funded by the European Commission under the Seventh Framework Programme (FP7)		
Dissemination Level		
PU	Public	x
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	

Table of Contents

1 Introduction

The 2-FUN model was developed under the sixth Framework Program of the European Union (contract n° FP6-2005-GLOBAL-4-036976) within the project “Full-chain and uncertainty approaches for assessing health risks in future environmental scenarios”. 2-FUN aimed to provide decision-makers with state of the art tools to analyse the current and future trends in environmental conditions and pressures that may lead to health problems. Its main objective was to support the evaluation and ranking of management options through a range of functionalities able to generate outputs of high concern for health risk assessment: building of long-term environmental and socio-economic scenarios, exposure assessment, provision of uncertainty margins, and identification of sensitive pathways and risks. The 2-FUN multimedia modelling tool allows the user to assemble a model for a specific scenario, to enter input data and parameter values for selected contaminants and finally to run deterministic (best or worst-case estimate) or probabilistic (Monte Carlo) simulations.

This 2-FUN tool was however only a prototype software containing a library of models for exposure assessment, coupling environmental multimedia and pharmacokinetic models. The objective of the 4FUN project is to further improve and standardise the 2-FUN model and guarantee its long-term technical and economic viability. The tool made available at the end of the 4FUN project will be denominated MERLIN-Expo (**M**odelling **E**xposure to chemicals for **R**isk assessment: a comprehensive **L**ibrary of multimedia and PBPK models for **I**ntegration, Prediction, u**N**certainty and Sensitivity analysis).

This report summarizes the models that are/will be developed in the final library of models available in the MERLIN-Expo tool.

2 Models of the MERLIN-Expo library

This section lists all the models that are/will be available in the MERLIN-Expo library, with a short description of the goals, potential decision and regulatory frameworks, and main processes incorporated in the model. A complete documentation of each model will be provided in D4.4.

2.1 The River model

- Goal: to dynamically simulate the distribution of organic contaminants and metals in abiotic media (i.e. water, suspended particulate matter and sediments) of river systems;
- Potential decision and regulatory frameworks:
  - ✓ to provide an estimation of the time-dependent concentration of the targeted contaminant(s) in raw water or filtered water. This/these output(s) can be used for evaluating the risk to exceed a given regulatory threshold for environmental risk (e.g. Predicted Non Effect Concentration (PNECs), Environmental Quality Standards (EQS) for individual pollutants defined by the European Water Framework Directive);
  - ✓ to provide an estimation of the time-dependent concentration of the targeted contaminant(s) in bottom sediments. This output can be used for evaluating the risk to exceed a given regulatory threshold for environmental risk dedicated to benthic organisms (e.g. Predicted Non Effect Concentration (PNECs), Environmental Quality Standards (EQS) for individual pollutants defined by the European Water Framework Directive);
  - ✓ to provide an estimation of the time-dependent concentration of the targeted contaminant(s) in drinking water. This output can be used for evaluating the risk to exceed a given regulatory threshold for human health or to provide an input for PBPK models;
  - ✓ to provide an estimation of contaminant inputs onto soils and plant leaves originating from irrigation practices;
- Main processes:
  - ✓ Simulation of the Suspended Particulate Matter (SPM) concentration by a rating curve relationship relating the flow rate of the river and SPM;
  - ✓ Sorption/desorption between water and SPM;
  - ✓ Deposition of particulate contaminants to bed sediments;
  - ✓ Resuspension of particulate contaminants from bed sediments;
  - ✓ Diffusion between water and sediment pore water;
  - ✓ Diffusion between water and atmosphere;
  - ✓ Degradation.

2.2 The Soil model

- Goal: to dynamically simulate the distribution of organic contaminants and metals in abiotic media (i.e. soil particles, pore water) of soil systems, with a description of their depth profile in the root zone;

- Potential decision and regulatory frameworks:
  - ✓ to provide an estimation of the time-dependent concentration of the targeted contaminant(s) in total soil and/or soil pore water over a given depth. This/these output(s) can be used for evaluating the risk to exceed a given regulatory threshold for environmental risk (e.g. Predicted Non Effect Concentration (PNECs), Environmental Quality Standards (EQS) for individual pollutants defined by the European Soil Directive(s));
  - ✓ to provide an estimation of the time-dependent concentration of the targeted contaminant(s) in the soil profile. This output can be used for evaluating the residence time of contaminant(s) in soil and the risk over time to exceed a given regulatory threshold for environmental risk dedicated to soil organisms (e.g. Predicted Non Effect Concentration (PNECs), Environmental Quality Standards (EQS) for individual pollutants defined by the European Soil Directive(s));
  - ✓ to provide an estimation of contaminant inputs into plant crops originating from root uptake;
  - ✓ to provide an estimation of contaminants emitted from soils to the atmosphere (especially relevant for contaminants directly deposited onto soil and able to reach atmosphere through volatilization);
  - ✓ to provide an estimation of the time-dependent concentration of the targeted contaminant(s) in soil available for e.g. pica children. This output can be used for evaluating the risk to exceed a given regulatory threshold for human health or to provide an input for PBPK models.

  Main processes:
  - ✓ Sorption/desorption between pore water and soil particles;
  - ✓ Evapotranspiration;
  - ✓ Water mass balance in soil and loss by infiltration;
  - ✓ Retardation factor and advection within soil;
  - ✓ Diffusion between water and atmosphere;
  - ✓ Bioturbation;
  - ✓ Diffusion within soil;
  - ✓ Wash-off from soils to river;
  - ✓ Degradation.

2.3 The Fruit model

- Goal: to estimate the time-dependent accumulation (in mass and concentration bases) of organic/metals in the edible part in fruits at harvest;
- Potential decision and regulatory frameworks: Coupled with the information about the ingestion rate of fruit crops (kg fresh weight d^{-1}), the fruit model can estimate the human exposure to organic substances/metals through the ingestion of fruit crops. This output can be used for evaluating the risk to exceed regulatory thresholds for human health or used as an input for PBPK models.
- Main processes:
  - ✓ Sorption/desorption between pore water and soil particles;
  - ✓ Partition between concentrations in roots and in water (xylem water), and concentrations in fruits and in water;
  - ✓ Xylem influx from soil to root driven by plant transpiration;

- ✓ Xylem outflux from root to fruit driven by plant transpiration;
- ✓ Phloem outflux from leaves to fruit driven by fruit growth;
- ✓ Diffusion between fruit and air;
- ✓ Dry and wet deposition from air to fruits;
- ✓ Degradation in roots and fruits;
- ✓ Root uptake (for metals).

2.4 The Root model

- Goal: to estimate the time-dependent accumulation (in mass and concentration bases) of organic/metals in the edible part in root (e.g. carrots) at harvest;
- Potential decision and regulatory frameworks: Coupled with the information about the ingestion rate of root crops (kg fresh weight d^{-1}), the root model can estimate the human exposure to organic substances/metals through the ingestion of root crops. This output can be used for evaluating the risk to exceed regulatory thresholds for human health or used as an input for PBPK models.
- Main processes:
  - ✓ Sorption/desorption between pore water and soil particles;
  - ✓ Partition between concentrations in roots and in water (xylem water);
  - ✓ Xylem influx from soil to root driven by plant transpiration;
  - ✓ Degradation in roots;
  - ✓ Root uptake (for metals).

2.5 The Leaf and Grass models

- Goal: to estimate the time-dependent accumulation (in mass and concentration bases) of organic/metals in the edible part in leafy crops (e.g. salads) at harvest;
- Potential decision and regulatory frameworks: Coupled with the information about the ingestion rate of leafy crops (kg fresh weight d^{-1}), the leafy model can estimate the human exposure to organic substances/metals through the ingestion of leafy crops. This output can be used for evaluating the risk to exceed regulatory thresholds for human health or used as an input for PBPK models.
- Main processes:
  - ✓ Sorption/desorption between pore water and soil particles;
  - ✓ Partition between concentrations in roots and in water (xylem water), and concentrations in leaves and in water;
  - ✓ Xylem influx from soil to root driven by plant transpiration;
  - ✓ Xylem outflux from root to leaves driven by plant transpiration;
  - ✓ Diffusion between leaves and air;
  - ✓ Dry and wet deposition from air to leaves;
  - ✓ Degradation in roots and leaves;
  - ✓ Root uptake (for metals).

2.6 The Grain model

- Goal: to estimate the time-dependent accumulation (in mass and concentration bases) of organic/metals in the edible part in grain (e.g. wheat) at harvest;

- Potential decision and regulatory frameworks: Coupled with the information about the ingestion rate of grain crops (kg fresh weight d^{-1}), the grain model can estimate the human exposure to organic substances/metals through the ingestion of grain crops. This output can be used for evaluating the risk to exceed regulatory thresholds for human health or used as an input for PBPK models.
- Main processes:
  - ✓ Sorption/desorption between pore water and soil particles;
  - ✓ Partition between concentrations in roots and in water (xylem water), and concentrations in grain and in water;
  - ✓ Xylem influx from soil to root driven by plant transpiration;
  - ✓ Xylem outflux from root to grain driven by plant transpiration;
  - ✓ Phloem outflux from leaves to grain driven by fruit growth;
  - ✓ Diffusion between grain and air;
  - ✓ Dry and wet deposition from air to grain;
  - ✓ Degradation in roots and grain;
  - ✓ Root uptake (for metals).

2.7 The Tuber model

- Goal: to estimate the time-dependent accumulation (in mass and concentration bases) of organic/metals in the edible part in tubers (e.g. potatoes) at harvest;
- Potential decision and regulatory frameworks: Coupled with the information about the ingestion rate of tubers crops (kg fresh weight d^{-1}), the tubers model can estimate the human exposure to organic substances/metals through the ingestion of tubers crops. This output can be used for evaluating the risk to exceed regulatory thresholds for human health or used as an input for PBPK models.
- Main processes:
  - ✓ Sorption/desorption between pore water and soil particles;
  - ✓ Partition between concentrations in tubers and in water;
  - ✓ Diffusion from soil to tubers driven by concentration gradient;
  - ✓ Degradation in tubers;
  - ✓ Root uptake (for metals).

2.8 The Fish model

- Goal: to estimate the time-dependent accumulation (in mass and concentration bases) of organic/metals in the edible part in fish at fishing time;
- Potential decision and regulatory frameworks:
  - ✓ to provide an estimation of the time-dependent concentration of the targeted contaminant(s) in fish. This/these output(s) can be used for evaluating the risk to exceed a given regulatory threshold for environmental risk (e.g. Environmental Quality Standards (EQS) in fish for individual pollutants);
  - ✓ to provide an estimation of the time-dependent concentration of the targeted contaminant(s) in fish available for food ingestion. This output can be used for evaluating the risk to exceed a given regulatory threshold for human health (e.g. daily Reference Dose) or to provide an input for PBPK models.
- Main processes:
  - ✓ Respiratory uptake of chemicals;

- ✓ Dietary uptake of chemicals;
- ✓ Respiratory elimination of chemicals;
- ✓ Dietary elimination of chemicals;
- ✓ Elimination of contaminants through biomass production;
- ✓ Metabolic biotransformation.

2.9 The Invertebrates model

- Goal: to estimate the time-dependent accumulation (in mass and concentration bases) of organic/metals in invertebrates living in water ;
- Potential decision and regulatory frameworks: to provide an estimation of the time-dependent concentration of the targeted contaminant(s) in invertebrates. This/these output(s) can be used for evaluating the risk to exceed a given regulatory threshold for environmental risk (e.g. Environmental Quality Standards (EQS) in invertebrates for individual pollutants);
- Main processes:
  - ✓ Respiratory uptake of chemicals;
  - ✓ Dietary uptake of chemicals;
  - ✓ Respiratory elimination of chemicals;
  - ✓ Dietary elimination of chemicals;
  - ✓ Elimination of contaminants through biomass production;
  - ✓ Metabolic biotransformation.

2.10 The Phytoplankton model

- Goal: to estimate the time-dependent accumulation (in mass and concentration bases) of organic/metals in phytoplankton ;
- Potential decision and regulatory frameworks: to provide an estimation of the time-dependent concentration of the targeted contaminant(s) in phytoplankton. This/these output(s) can be used for evaluating the risk to exceed a given regulatory threshold for environmental risk (e.g. Environmental Quality Standards (EQS) in phytoplankton for individual pollutants);
- Main processes:
  - ✓ Respiratory uptake of chemicals;
  - ✓ Respiratory elimination of chemicals;
  - ✓ Elimination of contaminants through biomass production;
  - ✓ Metabolic biotransformation.

2.11 The Beef meat model

- Goal: to estimate the time-dependent accumulation (in mass and concentration bases) of organic/metals in beef meat ;
- Potential decision and regulatory frameworks: to provide an estimation of the time-dependent concentration of the targeted contaminant(s) in beef meat available for food ingestion. This output can be used for evaluating the risk to exceed a given regulatory threshold for human health (e.g. daily Reference Dose) or to provide an input for PBPK models
- Main processes:

- ✓ Dietary uptake/elimination of chemicals;
- ✓ Water uptake/elimination of chemicals;
- ✓ Soil uptake/elimination of chemicals.
- ✓ Metabolic biotransformation.

2.12 The Cow milk model

- Goal: to estimate the time-dependent accumulation (in mass and concentration bases) of organic/metals in cow milk ;
- Potential decision and regulatory frameworks: to provide an estimation of the time-dependent concentration of the targeted contaminant(s) in cow milk available for food ingestion. This output can be used for evaluating the risk to exceed a given regulatory threshold for human health (e.g. daily Reference Dose) or to provide an input for PBPK models.
- Main processes:
  - ✓ Dietary uptake/elimination of chemicals;
  - ✓ Water uptake/elimination of chemicals;
  - ✓ Soil uptake/elimination of chemicals.
  - ✓ Metabolic biotransformation.

2.13 The Human intake model

- Goal: to dynamically simulate the intake of organic contaminants and metals by humans from intentional ingestion of drinking water, crops and animal products, non intentional ingestion of dust and soil particles (for pica children) and inhalation of air contaminants ;
- Potential decision and regulatory frameworks: to estimate the time-dependent intake of the targeted contaminant(s) by humans. This/these output(s) can be used for evaluating the risk to exceed a given regulatory threshold for human health risk (e.g. Reference Dose) or to provide an input for PBPK models;
- Main processes:
  - ✓ Dietary uptake of food by humans of different age classes.

2.14 The PBPK model

- Goal: to simulate the toxicokinetics of contaminants in humans, i.e. the amounts or concentrations in different organs/tissues, under various exposure conditions;
- Potential decision and regulatory frameworks:
  - ✓ Simulation of the internal kinetics of the targeted contaminant(s) in several tissues/organs of the human body;
  - ✓ Computation of toxicokinetic properties in each compartment (e.g. the maximal concentration C_{max}, the time at maximal concentration T_{max});
  - ✓ Prediction of the amount of contaminant that will be excreted or/and metabolised;
  - ✓ Thes outputs can be used for evaluating the risk to exceed a given regulatory threshold for human health (e.g. Equivalent Biomonitoring Reference Doses).
- Main processes:

- ✓ Growth of human individuals influencing anatomy, physiology and metabolism, and thus PBPK parameters;
- ✓ Absorption by inhalation (i.e. route of administration: absorption in the lung tissues);
- ✓ Absorption by ingestion (i.e. route of administration: oral absorption and transport to the gastrointestinal tract);
- ✓ Distribution of chemicals among organs (i.e. partitioning of a compound into the various tissues of the body from the systemic circulation);
- ✓ Metabolism (i.e. irreversible transformation of a parent compound into metabolites by enzymatic reactions);
- ✓ Excretion (i.e. removal of the compound and its metabolites from the body, occuring predominantly via the kidneys in urine).