OpenRiskNet Part I: Development of an open e-infrastructure predictive toxicology and risk assessment

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OpenRiskNet (https://openrisknet.org/) is a 3-year project funded by the EU within Horizon 2020 EINFRA-22-2016 Programme, with the main objective to develop an open e-infrastructure providing data and software resources and services to a variety of industries requiring risk assessment (e.g. chemicals, cosmetic ingredients, pharma or nanotechnologies).

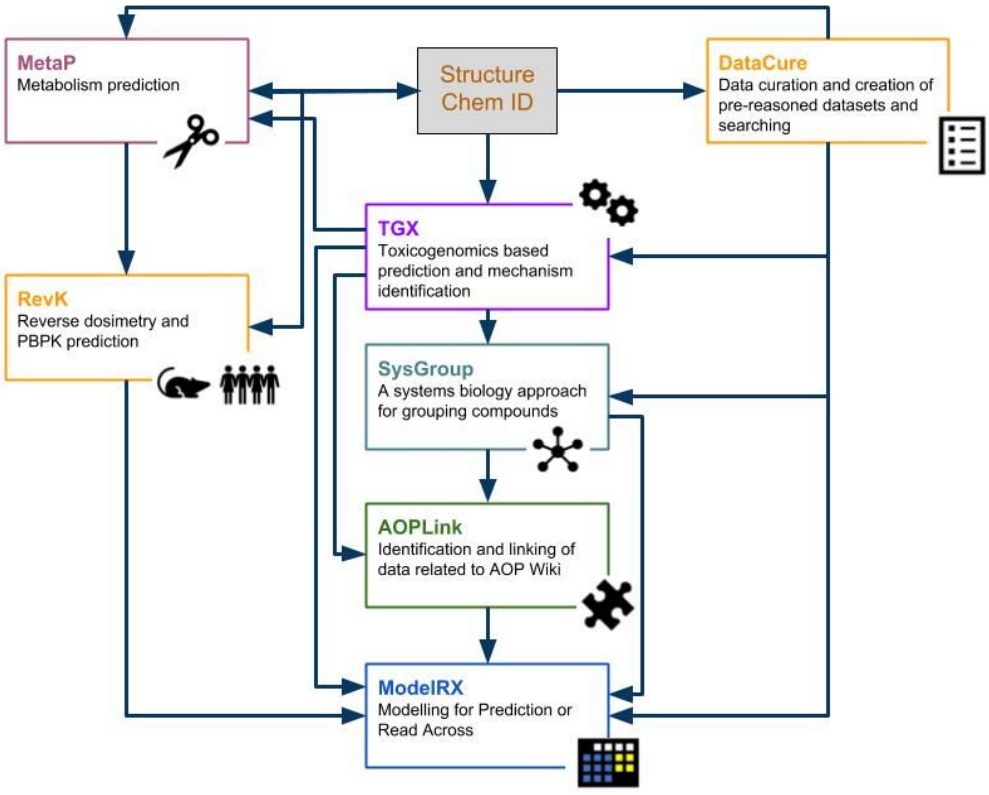

Figure 1: Structure of interlinked case studies targeting different parts of the risk assessment workflow

The infrastructure is built on virtual research environments (VREs), which can be deployed to workstations as well as public and in-house cloud infrastructures. Services providing data, data analysis, modelling and simulation tools for risk assessment are integrated into the e-infrastructure and can be combined into workflows using harmonised and interoperable application programming interfaces (APIs) (https://openrisknet.org/e-infrastructure/services/). For complete risk assessment and safe-by-design studies, OpenRiskNet e-infrastructure functionality is combined via a variety of incorporated services demonstrated within a set of case studies (see figure 1). The case studies present real-world settings such as data curation, systems biology approaches for grouping compounds, read-across applications using chemical and biological similarity, and identification of areas of concern based only on alternative methods (non-animal testing) approaches.

OpenRiskNet is working with a network of partners, organised within an Associated Partners Programme, aiming to strengthen the working ties to other organisations developing relevant solutions or tools.

OpenRiskNet Part II: Predictive Toxicology based on Adverse Outcome Pathways and Biological Pathway Analysis

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Here we present how the concept of Adverse Outcome Pathways (AOPs), which captures mechanistic knowledge from a chemical exposure causing a Molecular Initiating Event (MIE), through Key Events (KEs) towards an Adverse Outcome (AO), can be extended with additional knowledge by using tools and data available through the OpenRiskNet e-Infrastructure. This poster describes how the case study of AOPLink, together with DataCure, TGX, and SysGroup, can utilize the AOP framework for knowledge and data integration to support risk assessments. AOPLink involves the integration of knowledge captured in AOPs with additional data sources and experimental data from DataCure. TGX feeds this integration with prediction models of the MIE of such AOPs using either gene expression data or knowledge about stress response pathways. This is complemented by SysGroup, which is about the grouping of chemical compounds based on structural similarity and mode of action based on omics data. Therefore, the combination of these case studies extends the AOP knowledge and allows biological pathway analysis in the context of AOPs, by combining experimental data and the molecular knowledge that is captured in KEs of AOPs.

OpenRiskNet Part III: Modelling Services in Chemical/Nano-safety, Environmental Science and Pharmacokinetics

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The concept of case studies was followed in order to test and evaluate proposed solutions and is described in https://openrisknet.org/e-infrastructure/development/case-studies/. Two case studies, namely ModelRX and RevK, focus on modelling within risk assessment.

The ModelRX – Modelling for Prediction or Read Across case study provides computational methods for predictive modelling and support of existing data suitability assessment. It supports final risk assessment by providing calculations of theoretical descriptors, gap filling of incomplete datasets. computational modelling (QSAR) and predictions of adverse effects. Services are offered through Jaqpot (UI/API), JGU WEKA (API), Lazar (UI) and Jupyter & Squonk Notebooks.

In the RevK – Reverse dosimetry and PBPK prediction case study, physiologically based pharmacokinetic (PBPK) models are made accessible for the purpose of risk assessment-relevant scenarios. The PKSim software, the httk R package and custom-made PBPK models have been integrated. RevK offers services through Jaqpot (UI/API).

OpenRiskNet Part IV: WEKA Machine Learning Services for the Prediction of Half-Lifes of Chemicals and Nanoparticle Transport

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The OpenRiskNet project (https://openrisknet.org/) is funded by the H2020-EINFRA-22-2016 Programme and its main objective is the development of an open e-infrastructure providing data and software resources and services to a variety of industries requiring risk assessment (e.g. chemicals, cosmetic ingredients, pharma or nanotechnologies).

We will present the WEKA machine learning services within the infrastructure and how they can be used to solve complex prediction tasks: the prediction of (i) half-lifes of chemicals under given environmental conditions and of (ii) nanoparticle transport behavior from physicochemical properties. For that purpose, we will reconstruct previous efforts using complex workflows and architectures and simplify the models while maintaining their prediction performance. In both cases, the overall problem (predicting the fate of a compound depending on its properties and external conditions) is modeled as a cascaded prediction model, where the prediction of one model is, with particular attention to validity and performance, entering another model as input. The approach performs well on the half-life data, while the nanoparticle data are too noisy and incomplete to warrant more than the most basic models. Overall, the reconstruction of the two applications within OpenRiskNet provides more evidence for the power and versatility of the framework.