# Improvements to the information flow of pesticide related metabolism studies

Objectives for the further development

Trusted science for safe food

efsa
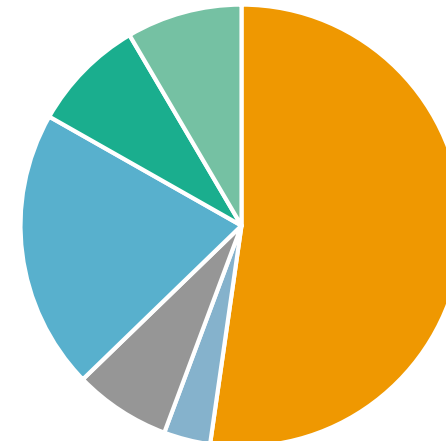European Food Safety Authority

MUG meeting: 10 Nov 2021

- ## EFSA project - Structuring existing data:
  - Based on study summaries after the end of evaluation process
  - **676** validated maps created with MSS composer and validated
  - EFSA public database: https://zenodo.org/record/5525989#.YYP-4mDMLD5

- ## Legacy Database:
  - **792** validated maps (DER and MSS composers)
 - Not (yet) public

Legacy DB contributors
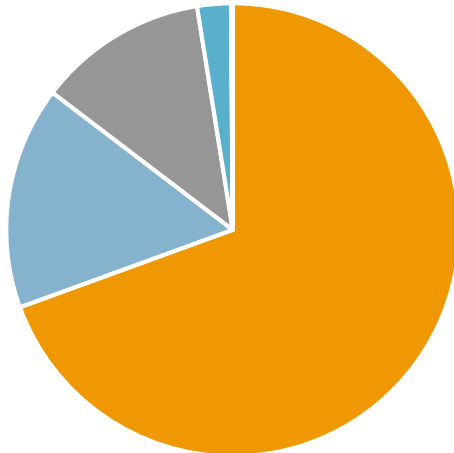
Legacy DB content

- USEPA - ANSES - PMRA - BFR - AGES

- Rat - Other mammals - Fish - livestock - plant - rotational crops

2

Current status: data collection (new)

- Interim workflow (for EU): https://zenodo.org/record/4785179#.YYQA5WDMLD6

- Applicants are requested to enter data in MSS/DER composers and to create validated xml files

- Applicants are requested to submit those data as attachments (xml files) as part of IUCLID dossiers

- For studies already populated in one of the MetaPath databases, new xml files are not requested

- Member States authorities are responsible for the quality check of the submitted xml-files

- Member States authorities and EFSA are responsible for the risk assessment performed with these data

- EFSA is responsible for the sanitization, publication, storage, maintenance and update of the database

- New/future data will feed the EFSA public database

Current status: dataflow

Data: metabolism studies (residues, mam toxicology)

Experimental data
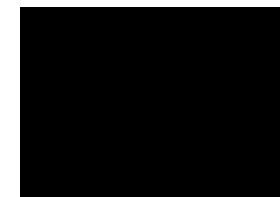
Composers

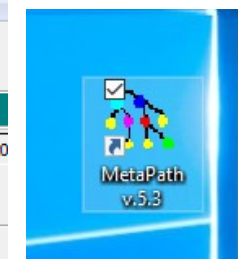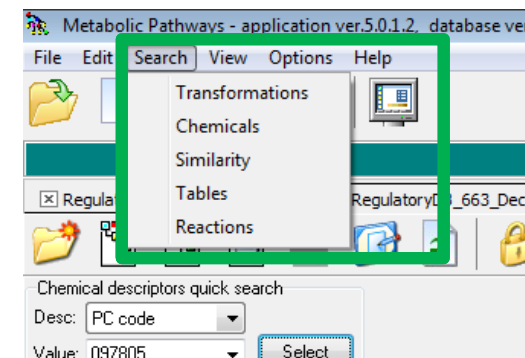Data entry

xml files

Electronic submission (attachment)

MetaPath

Risk assessment

Database

Comparison tools

Prediction?

IUCLID 6

Metabolic Pathways - application ver.5.0.1.2, database ver.3

File   Edit   Search   View   Options   Help

Transformations
Chemicals
Similarity
Tables
Reactions

Regulatory

RegulatoryDB_663_Dec20

Chemical descriptors quick search
Desc: PC code
Value: 097805   Select

MetaPath v.5.3

DER Composer

MSS

- MetaPath software package (https://oasis-lmc.org/products/software/metapath.aspx)
  - MSS composer v.1.9
  - DER composer v.5.2
  - MetaPath v.5.3.1.16

- OECD QSAR toolbox 4.5 (October 2021 Release, https://qsartoolbox.org/download)
  - Included "Extended Data Retrieval and Aggregation (TEDRA)" Plugin that enables enhanced communication between an IUCLID6 server and the OECD Toolbox.

- IUCLID 6.6 (October release)
  - No update for OHT 58 (toxicokinetic)
  - No update for OHT 82-2 (metabolism in livestock)
  - No update for OHT 85-3 (metabolism in crops)
  - Any data entered in IUCLID (OHT 58, 82-2 and 85-3) could not be transferred in MetaPath database
  - Data available in MetaPath database cannot be transferred to IUCLID OHTs

Weaknesses of the current workflow
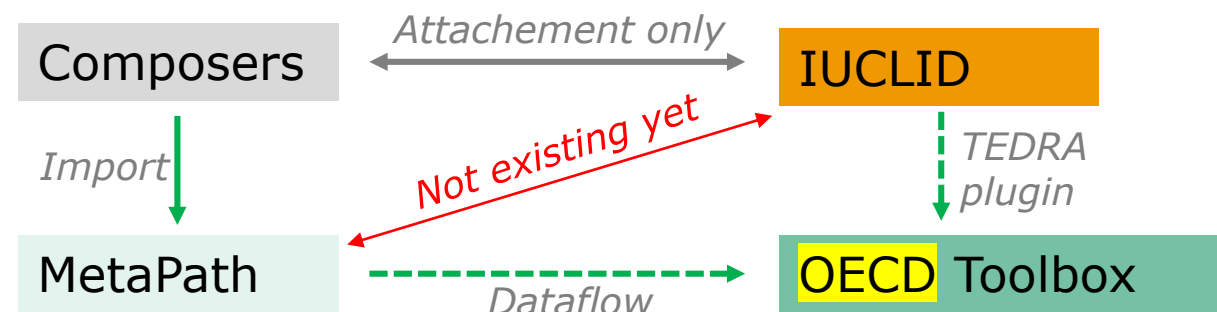
- In 2020, the IUCLID Technical Group identified weaknesses of the current workflow:
  - Duplication of work: composers files, copy/paste in different report formats, manual data management
  - Duplication of information: IUCLID + MetaPath database (e.g. metabolites structures)
  - Lack of data centralization: not all maps are available at the same place for everyone
  - Governance: how to ensure that different software updates go in the same direction
  - Potential of IUCLID not fully used: *e.g.* Validation assistant, confidentiality filter
- EFSA/BfR partnership; BfR was tasked to:
  - Perform analysis of the current workflow
  - Prepare a report: "Improvements to the information flow of pesticide related metabolism studies"
  - Collecting view (survey), report issues encountered, identify area of improvement
  - Propose interoperability solution between IUCLID and MetaPath respecting international data standards
  - Include analysis differences between OHT and MSS Composers schema and possible alignment of formats

- The provided solution should be applicable in the harmonized OECD templates
- The number of needed data interfaces and export/import modules should be minimized
- Focus on the reuse of existing APIs and analysis of the need for additional APIs (Interfaces already developed by LMC under OECD and other projects should be analyzed)
- Evaluators on the applicants and authorities side should use the same set of meta data for risk assessment
- The provided solution should make use of Metapath as it is – but areas for improvement should be identified
- The provided solution should identify manual data transformations steps inside of the evaluation process (For prediction of metabolism pathways, for grouping of metabolites and prediction of toxicological parameters (Q)SAR) and indicate which steps could be automated in a later phase
- User should be able to create an overview (report) of relevant metabolism studies of a specific test substances inside of a local collection of metabolism studies which could be incorporated in an IUCLID flexible summary
- It should be possible to build up an international reference collection of metabolism studies under the Metapath project and user group. A publicly accessible interface should be defined.