Welcome to an international survey of the informational flow of metabolism studies. This survey is organized by the BfR (German Federal Institute for Risk Assessment) and EFSA (European Food Safety Authority). The EPA has promoted the standardized summaries of metabolism studies since 2010. The international scientific community had developed the needed concepts in the MetaPath User Group (MUG). The MSS-Composers and DER Composer were developed to collect study raw data. These templates are available as free software (part of the Metapath Package) and offer the possibility to report study raw data in a structured way and to generate formatted reports. The xml files created with these composers (also named "maps") are compatible with MetaPath. This software was developed for the risk assessment and allows, among other features, comparison of maps, identification of metabolism pathways and common metabolites. An optimal use of Metapath requires a rich collection of studies coded in maps. In March 2021 the transparency Regulation will apply and the use of IUCLID formats for pesticide applications in Europe is an opportunity to improve, streamline and clarify the informational flow of data generated by metabolism studies. As of March 2021, EFSA will require applicants to provide structured data on metabolism studies for pesticide applications submitted at EU level (i.e. active substance approval/renewal, MRL applications). In order to make use of the existing tools, the MSS-Composers (for residue related studies regarding metabolism in/on plants and livestock) and the DER composer (for rat metabolism studies) should be used as the standard formats to report the results of metabolism studies. This will be defined in the updated version of the "Administrative guidance on submission of dossiers and assessment reports for the peer-review of pesticide active substances and MRL application procedure" written by EFSA. The above approach will go live in 2021. But on longer term perspective, the information of data for metabolism studies can be further improved. In a long-term vision, the following questions are still to be addressed:

The above approach will go live in 2021. But on longer term perspective, the information of data for metabolism studies can be further improved. In a long-term vision, the following questions are still to be addressed:

Should we improve the MSS-/DER composer technique for the other metabolism study types (e.g. e-fate…)? How to better integrate the IUCLID data hub with Metapath? How to update the OECD harmonized templates (OECD) to ensure this full integration?

The European context was the initial reason for the publication of this survey, but at the same time it is also aimed at international stakeholders, since this data flow is of international importance. This survey is being issued to relevant groups involved in national, regional and international initiatives in the management of chemicals.

We invite you to take part in this process!

You are invited to choose the most appropriate response for each statement using the

Section A: Your position and your experiences

A1. Which stakeholder group do you feel belonging to?

- ☐ Laboratory which conducts metabolism studies
- ☐ Applicant submitting metabolism studies in dossiers
- ☐ Applicant using metabolism studies of other applicants
- ☐ Authority assessing metabolism studies and using them to perform risk assessment
- ☐ Authority utilizing metabolism studies for risk management decisions
- ☐ Researcher in university
- ☐ Corporate body in supporting the informational flow of metabolism studies
- ☐ NGO
- ☐ General public
- ☐ Other

A2. Responsible for / interested in:

- ☐ Pesticides
- ☐ Biocides
- ☐ Chemicals
- ☐ Other

A3. Belongs to the economic area:

- ☐ European Union
- ☐ Other

A4. How experienced are you in using the following tools regarding metabolism studies?

	1 not experienced at all	2	3	4	5 very experienced
MSS-Composers	☐	☐	☐	☐	☐
MetaPath	☐	☐	☐	☐	☐
OECD QSAR-Toolbox	☐	☐	☐	☐	☐
IUCLID	☐	☐	☐	☐	☐
Other tools to handle data of metabolism studies	☐	☐	☐	☐	☐

Section B: Framework conditions

What are the framework conditions and do we always understand the same thing by the terms?

B1. Which of the following statements do you support regarding the current attitude towards metabolism studies?

	1 disagree at all	2	3	4	5 totally agree	skip this question
All stakeholder have the same understanding regarding the term "metabolism study".	☐	☐	☐	☐	☐	☐
The current data requirements for metabolism studies are a solid basis for the risk assessment.	☐	☐	☐	☐	☐	☐
The current tools for metabolism data storage, handling and dissemination are sufficient.	☐	☐	☐	☐	☐	☐
The summaries of the metabolism studies contain enough detailed information to assess them and to perform the risk assessment (for now and in the future).	☐	☐	☐	☐	☐	☐
The processes of the informational flow on metabolism studies are optimally organized.	☐	☐	☐	☐	☐	☐
There is no duplication of work in the drafting of the metabolism study summaries.	☐	☐	☐	☐	☐	☐
It is easy for the risk assessors to visualize and check the raw results of the metabolism studies.	☐	☐	☐	☐	☐	☐

B2. Do you have any comments regarding the framework conditions (identified concerns / opinions / proposals / ...)?

Section C: MSS-composers

The MSS-Composers and DER Composer were developed to collect study raw data. These templates are available as free software (part of the Metapath Package) and offer the possibility to report study raw data in a structured way and to generate formatted reports. The xml files created with these composers (also named “maps”) are compatible with MetaPath.

C1. Which of the following statements do you support regarding the MSS-Composers?

	1 disagree at all	2	3	4	5 totally agree	skip this question
I trust that creating metabolism pathway maps (xml files) with the MSS-composers is a good investment to improve the quality and the efficiency of risk assessment.	☐	☐	☐	☐	☐	☐
I would welcome an initiative for additional information and tutorials on the MSS-composers.	☐	☐	☐	☐	☐	☐
The current MSS-Composers supports very detailed study descriptions. This level of detail will also be needed in the future.	☐	☐	☐	☐	☐	☐
One MSS-Composers should cover all OHTs relevant for metabolism studies.	☐	☐	☐	☐	☐	☐
During the entry of the study data into the MSS-Composers, confidentiality issues are considered.	☐	☐	☐	☐	☐	☐
It is important to define a transparent governance model for the MSS-Composers.	☐	☐	☐	☐	☐	☐
The MSS-Composers should be able to generate reports corresponding to the format of the Volume 3 of DAR/RAR.	☐	☐	☐	☐	☐	☐

C2. Do you have any comments regarding the MSS-Composers (identified concerns / opinions / proposals / ...)?

Section D: MetaPath

MetaPath is an IT-tool developed to collect, organize and analyze experimental data on metabolism or catabolism, observed biotransformation pathways and crucial supporting metadata. (http://oasis-lmc.org/products/software/metapath.aspx)

The IT-Tool MetaPath is able to work with different collections, the "Metabolic trees databases" (MTB). One of these is the „Regulatory Database“ (created for pesticides since 10 years by EPA). EFSA/ BfR/ Anses are preparing a new data collection with additional pesticide maps, which will be publicly available in 2021.

D1. Which of the following statements do you support regarding MetaPath?

	1 disagree at all	2	3	4	5 totally agree	skip this question
I am aware of all the full package of functionalities offered by MetaPath and how it may be useful for the risk assessment.	☐	☐	☐	☐	☐	☐
I would welcome a training/tutorial on MetaPath.	☐	☐	☐	☐	☐	☐
I need an export function in MetaPath to be able to use data in other IT-Tools.	☐	☐	☐	☐	☐	☐
The IT-Tool MetaPath should be opened to access from other tools.	☐	☐	☐	☐	☐	☐
It is important to define a transparent governance model for IT-Tool MetaPath.	☐	☐	☐	☐	☐	☐
It is important to define a transparent governance model for the public MetaPath "Metabolic trees databases".	☐	☐	☐	☐	☐	☐

D2. Do you have any comments regarding MetaPath (identified concerns / opinions / proposals / ...)?

Section E: OECD Harmonised Templates and IUCLID

The OECD has published the Harmonised Templates (OHTs) which are standard data formats for reporting information on chemicals to determine their properties or effects on human health and the environment (study summaries). IUCLID is the essential tool to record, store, submit, and exchange data on chemical substances in the format of the OECD Harmonised Templates. The IUCLID study summaries can be "re-used" by applicants in different applications.

The 1st question block looks to the life cycle of the study summaries. Which parts of a study summary could only to interpreted in the context of the respective application? Which parts of a study summary are still valid in a renewal procedure?

The overall question of the 2nd block is the transport of raw data with the help of the OHTs.

E1. Which of the following statements do you support regarding the life cycle of study summaries according the OECD harmonized templates (OHT)?

	1 disagree at all	2	3	4	5 totally agree	skip this question
A study is always assessed in the context of a specific application.	☐	☐	☐	☐	☐	☐
The study summary without the administrative data and without the conclusions cannot become out of date.	☐	☐	☐	☐	☐	☐
The administrative data and the conclusions drawn from the study depend on the time point.	☐	☐	☐	☐	☐	☐

E2. Which of the following statements do you support regarding the OECD harmonized templates (OHT) for study summaries of metabolism studies?

	1 disagree at all	2	3	4	5 totally agree	skip this question
The OECD templates and IUCLID should be improved to be the data source for Metapath regarding metabolism studies.	☐	☐	☐	☐	☐	☐
The OECD templates and IUCLID should be improved to be the data source of the QSAR Toolbox regarding metabolism studies.	☐	☐	☐	☐	☐	☐
Although not currently possible, I believe that the OHT should be further developed to be able to submit the raw data of the metabolism studies.	☐	☐	☐	☐	☐	☐
The current OHT for metabolism in residues (85-2 and 85-3) are fit for purpose to report metabolism study results.	☐	☐	☐	☐	☐	☐
The OECD should generalize all OECD templates related to metabolism studies through a generic approach (including plants, livestock, toxicology, environment ...) .	☐	☐	☐	☐	☐	☐
As long as the OHT cannot be used as direct data sources for MetaPath, the results (raw data) of metabolism studies should be attached as MSS-Composer data files in the dossier.	☐	☐	☐	☐	☐	☐
The OHT should mimic the MSS-Composers and replace it on the long term.	☐	☐	☐	☐	☐	☐
IUCLID should be able to import a MSS-Composers output into the corresponding OECD template.	☐	☐	☐	☐	☐	☐
It should be possible to generate all needed reports regarding metabolism studies (eg. Study summaries for the Volume 3 of DAR/RAR, Appendix G) from IUCLID.	☐	☐	☐	☐	☐	☐

E3. Do you have any comments regarding the OECD templates for metabolism studies (identified concerns / opinions / proposals / ...)?

Section F: OECD QSAR-Toolbox

The QSAR-Toolbox is a free software application that supports reproducible and transparent chemical hazard assessment. It offers functionalities for retrieving experimental data, simulating metabolism and profiling properties of chemicals (https://qsartoolbox.org/).

F1. Which of the following statements do you support regarding the OECD QSAR-Toolbox?

	1 disagree at all	2	3	4	5 totally agree	skip this question
I was missing information about the possibility of using QSAR-Toolbox for this topic.	☐	☐	☐	☐	☐	☐
I know the advantages of the QSAR-Toolbox and would like to use this tool in the future.	☐	☐	☐	☐	☐	☐
The pesticide-related QSAR models are of sufficient quality for predicting metabolism pathways.	☐	☐	☐	☐	☐	☐
Collections from MetaPath could be important data sources of the QSAR Toolbox regarding metabolism studies.	☐	☐	☐	☐	☐	☐
The QSAR-Toolbox should be the publicly available reference model for predicting the metabolism of pesticides.	☐	☐	☐	☐	☐	☐
Confidentiality aspects have been clarified for including data of studies into QSAR-Toolbox.	☐	☐	☐	☐	☐	☐
The principles for the reuse of the information (data access) available in the QSAR Toolbox have been clarified.	☐	☐	☐	☐	☐	☐
I would welcome a training/tutorial on QSAR Toolbox.	☐	☐	☐	☐	☐	☐

F2. Do you have any comments regarding the QSAR-Toolbox (identified concerns / opinions / proposals / ...)?

F3. What other QSAR Tools do you use to predict metabolism pathways?

Thank you for participating in this survey.

If you want to have a feedback regarding the results of this survey, please contact this address

stephan.worseck@bfr.bund.de with the subject "Send the results of this survey".

Download complete survey with your answers as PDF!

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