25 May 2021

Reporting structured results of metabolism studies on rats, plants and livestock

Description of process steps of the information flow in EU

1 Background

Applicants submitting an application under Regulation (EC) No 1107/2009 or Regulation (EC) No 396/2005 are requested to provide data on metabolism in the areas of residues and mammalian toxicology as attachments, generated with the MetaPath composer software.

The MetaPath platform is developed to collect, organise and analyse experimental data on metabolism or catabolism, observed biotransformation pathways and crucial supporting metadata. The results from metabolism studies on rats, plants and livestock are compiled and organised into a systematic database.

MetaPath was originally developed by the Laboratory of Mathematical Chemistry, Burgas (LMC, Bulgaria) and the US Environmental Protection Agency (EPA), and it has been integrated with the OECD QSAR toolbox. EFSA identified the MetaPath platform as a suitable tool for powerful searches and information extraction based on chemical structure, biotransformation, experimental metadata as well as for metabolic simulations and predictions. The MetaPath platform allows users to build custom databases and to import and query existing databases such as the Public MetaPath database and the Regulatory Legacy database.

The type of files generated with the MetaPath composer software is .XML. For metabolism data in the area of mammalian toxicology, xml-files are created with the DER composer, and are therefore called „DER-files". For metabolism data in the area of residues (plant and livestock), xml-files are created with the MSS composers, and are therefore called „MSS-files".

How to compile rats, plants and livestock metabolism studies

The MetaPath platform is a tool to structure data from scientific study reports and factually report the results and findings of the respective studies in a structured format, in line with the respective Test guidelines. It should therefore not contain any assessments and opinions by applicants and Regulatory authorities, but entries be restricted to the information reported by the study author as the aim is to use the database in different jurisdictions where different assessment approaches might be applicable.
The MSS composers have been aligned to the OECD Harmonised templates (OHT) in the residue section as much as possible. Due to the existence of several older xml files, backward compatibility had to be ensured by making the format of some tables flexible. However, it is strongly recommended to use the OHT format as guidance when creating new MSS files to ensure harmonised data entry and facilitate the automation of data export for future applications.
Furthermore, fields that are considered mandatory in the EU can differ from other non-EU jurisdictions and vice versa. Therefore, a default warning in Metapath is not issued in case a mandatory field for the EU submission has not been completed.

Applicants submitting data on metabolism in the areas of residues and mammalian toxicology generated with the MetaPath composer software (xml files) as part of a

IUCLID dossier under Regulation (EC) No 1107/2009 or Regulation (EC) No 396/2005 are, therefore, kindly requested to refer to the detailed instructions on the compilation of IUCLID dossiers, available on the dedicated EFSA page. The present document provides further specific information on the process steps and responsibilities of the different actors (Section 3) and clearly defines which fields are mandatory to be completed for metabolism studies to be submitted as part of an EU dossier (Section 4).

In the context of the Transparency Regulation Implementation, a series of Metapath video tutorials (Chapters 1-5, Chapters 6-10) and dedicated webinars on MSS composers for pesticides metabolism studies are available. A calendar of planned activities can be found on the EFSA dedicated webpage.

EFSA's contribution to the database

EFSA has an ongoing procurement project (OC/EFSA/PRES/2019/01 OECD Metapath-Incorporation of Pesticide Residue Data project), for populating MetaPath with the results of peer reviewed and validated metabolism studies in the Residues area. The aim of this project is to reach a complete metabolism database as soon as possible, and therefore priority for populating metabolism studies by the contractor was given to metabolism studies for which the peer review was completed in recent years. The EFSA project does therefore not prioritise substances for which the renewal is upcoming and for which the applicant will be requested to complete the maps and submit these as part of the IUCLID renewal dossier. Exception to this are the substances falling under the EFSA Hypercare programme, as it was agreed to provide additional support to the first submitters. The EFSA procurement project is still ongoing (estimated finalisation date June 2022) and the first batch of sanitised maps has been made publicly available. EFSA will publish new sanitised versions of the mtb file including data on further substances covered by the EFSA project with every new deliverable of the procurement. It is also noted that the EFSA procurement has been set up prior to the implementation of EU e-submissions, i.e. under different conditions and with a different objective, and therefore, the extent of data entered in MSS composer during the EFSA procurement may differ from the field defined as mandatory for submissions by applicants in the remit of a IUCLID dossier.

In this early stage of the implementation of the MetaPath software in the respective pesticide data formats and workflows, EFSA considers it essential to restrict and control the possibility to make changes in maps that have been validated under the aforementioned project, following a strict Standard Operating Procedure ensuring high quality maps. EFSA therefore published the mtb file but will not publish xml files for the time being. This might be reconsidered in the future when all actors gain more experience in using the software and its further implementation in the pesticide risk assessment workflows.

Requirements to applicants

Applicants are requested to provide data on metabolism in the areas of residues and mammalian toxicology as attachments (xml files generated with the DER or MSS composer). However, for those for metabolism studies for which the maps are already available in the Authority database, applicants are not requested to submit the xml-files as part of their IUCLID dossier.
Therefore, prior to starting the completion of metabolism studies in the DER or MSS composer, applicants are requested to check if the respective study has already been populated, consulting the following two lists:

- List 1) Regulatory Legacy collection of maps
- List 2) EFSA public collection of maps (The EFSA public collection of maps is regularly updated with new entries. Users are therefore invited to check the list frequently)

If a metabolism study has already been populated according to the references provided in list 1 or list 2, applicants are requested not to create a new xml file. If the study is already available in either list 1 or 2, applicants are required to report the corresponding individual file number in the IUCLID dossier (in the literature reference of the relevant Endpoint study records).
On the contrary, xml files should be compiled and submitted for new metabolism studies. The individual steps or this process are detailed in Section 3.2 of the present document.

Member States and EFSA's role in the process

Member States Authorities receiving the dossier are responsible of the quality check and validation of the xml-files newly submitted by Applicants, as defined in Section 3.4 and 3.5.

In addition to its direct contribution to the database as define above, EFSA is responsible of the maintenance, the sanitization and the update of the database, as defined in Section 3.7.

2 Used symbols

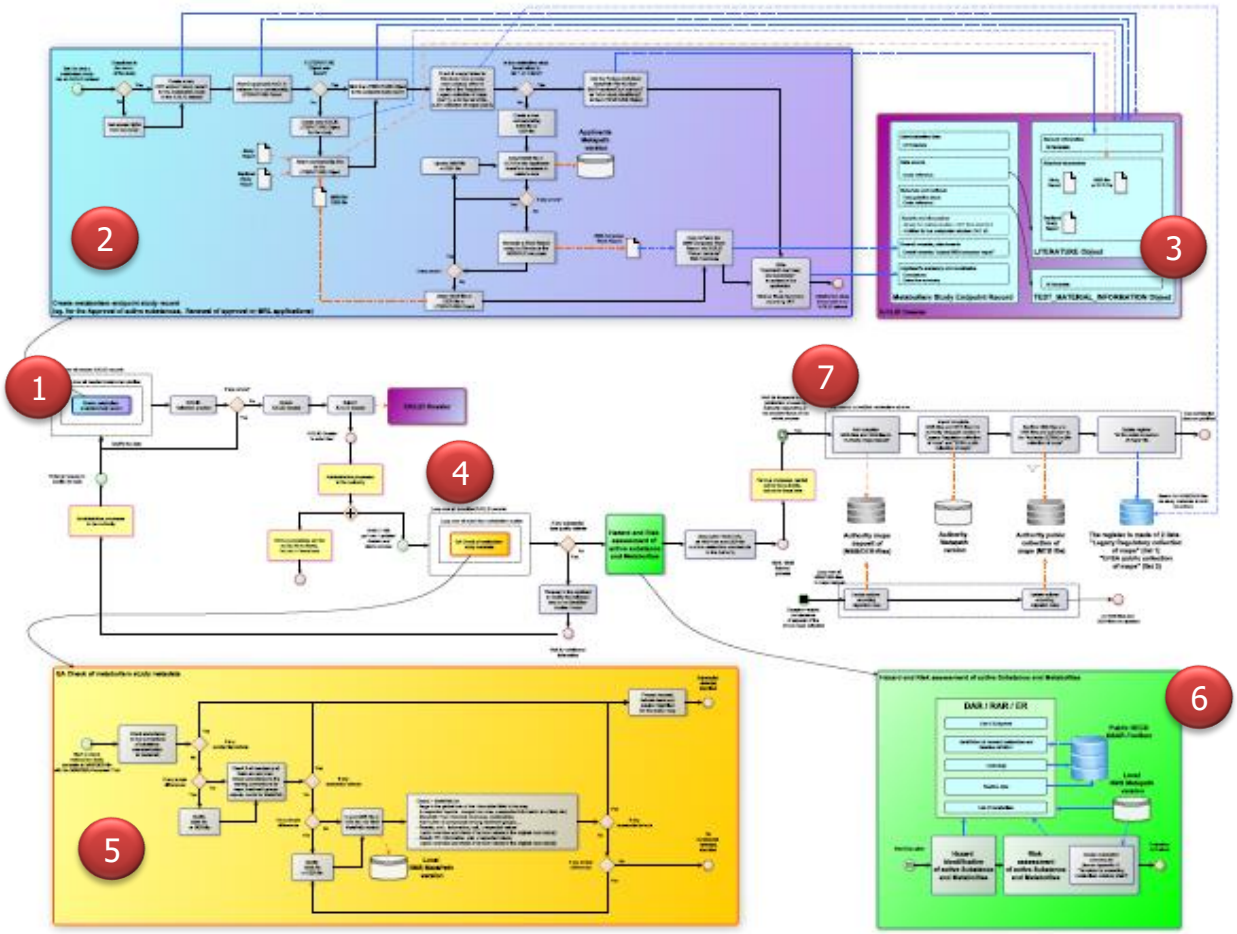
For chapter 3, a form of presentation was chosen that combines a visualisation of

- the sequence of process steps,
- the necessary exchange of information (request / response) and
- the flow of information containers.

For this reason the diagrams combine a mixture of different diagram types. The following symbols were used:

	Task		Tasks of the Authority which are not in focus of this report
	Loop of tasks		Start event
	Physical data stores Different colours and shapes have no meaning		Conditional event
	Physical data object		Time vvv event
	Connection between tasks		Message event
	Connection between tasks, not analysed in deep		Termination
	Task puts information to a data store or makes a request to get information from a data store		Decision Gateway (exclusive)
	Task puts physical data object or gets physical data object		Decision Gateway (parallel)

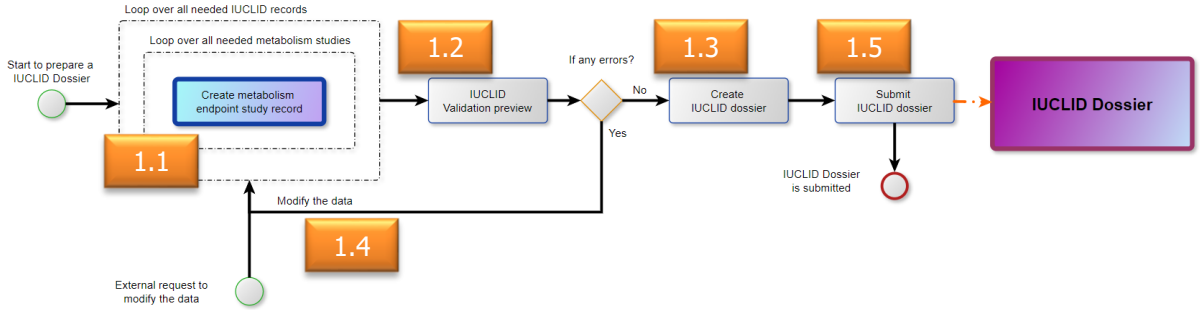
The graphics of this document can only serve for a rough overview and to find the comments in the corresponding table.
The complete scheme is available with a high resolution. See PDF document avaiable under the same page in the Knowledge juction: "Process.model.pdf".



No	Subprocess / Detail	Chapter
1	Applicants process	3
2	Detail of the applicants process for each metabolism study	0
3	Detail of the IUCLID Dossier for one metabolism study endpoint record	0
4	Member states process	3.4
5	Detail for the Quality check	0
6	Detail of the member states process for hazard and risk assessment	3.6
7	Authority processes	3.7

3 Process steps

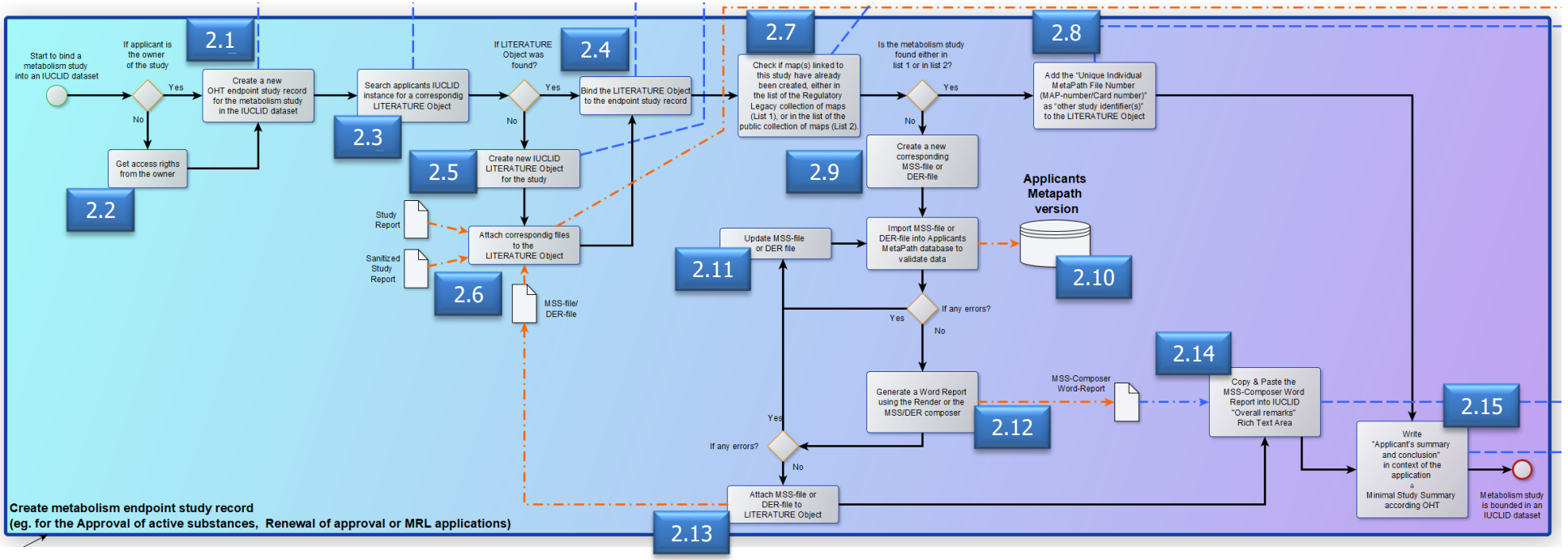
3.1 Applicants process



Process	No	Actions	Role	Comments
Applicants process		*Begin: Loop over all needed IUCLID records*	APPL	
Applicants process		*Begin: Loop over all needed metabolism studies*	APPL	Applicant to report all the available metabolism studies that are considered needed to fulfil the data requirements.
Applicants process	1.1	Create metabolism endpoint study record	APPL	See details in chapter 0
Applicants process		*End: Loop over all needed metabolism studies*	APPL	
Applicants process		*End: Loop over all needed IUCLID records*	APPL	
Applicants process	1.2	IUCLID Validation preview	APPL	If all mandatory fields are duly compiled, the validation assistant of IUCLID should not show any errors.
Applicants process	1.3	Create IUCLID dossier	APPL	

Applicants process	1.4	Modify the data	APPL	Please modiy the data sets until no validation errors are shown.
Applicants process	1.5	Submit IUCLID dossier	APPL	

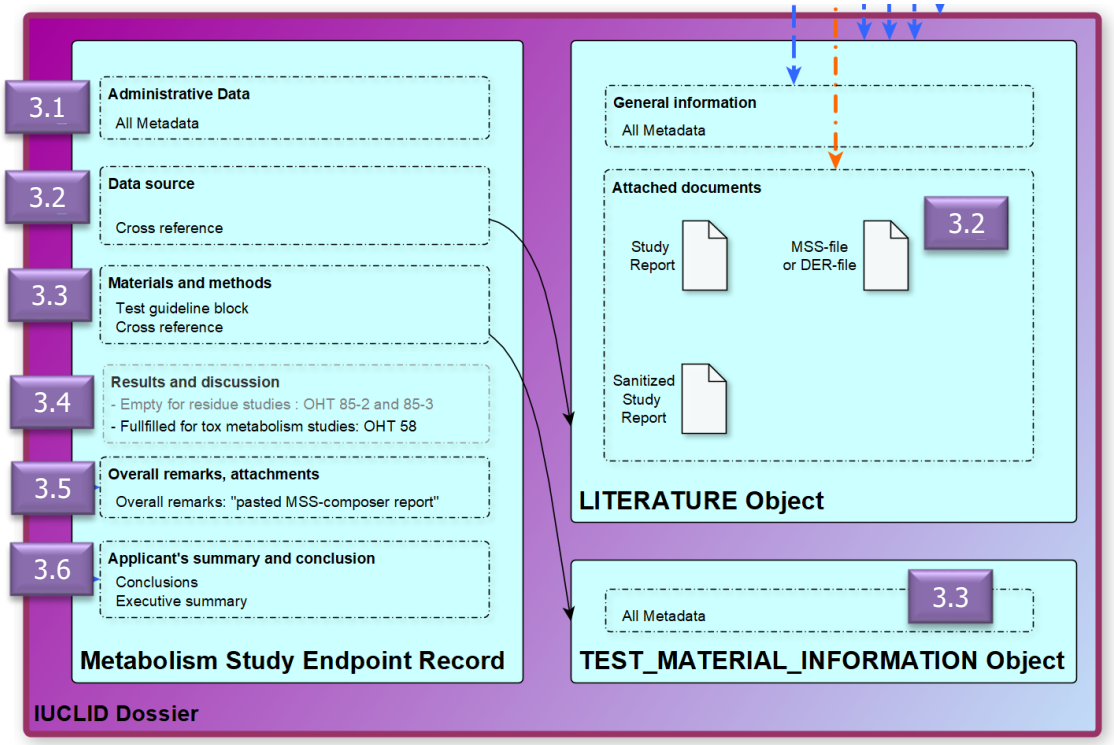
3.2 Detail of the applicants process for each metabolism study



Process	No	Actions	Role	Comments
Metabolism Study	2.1	Create a new OHT endpoint study record for the metabolism study in the IUCLID dataset	APPL	See IUCLID manual.
Metabolism Study	2.2	Get access rights from the owner	APPL	Applicants to check that they have access to the metabolism studies reported the dossier.
Metabolism Study	2.3	Search applicants IUCLID instance for a corresponding LITERATURE Object	APPL	A metabolism study could be used in different legal actions. If applicants had built up an IUCLID instance an existing LITERATURE Object could be "reused".
Metabolism Study	2.4	Bind the LITERATURE Object to the endpoint study record	APPL	See IUCLID manual: common block on "Data source".
Metabolism Study	2.5	Create new IUCLID LITERATURE Object for the study	APPL	See IUCLID manual: "Literature reference".
Metabolism Study	2.6	Attach corresponding file to the LITERATURE Object	APPL	-Full Study Report -Sanitized Study Report
Metabolism Study	2.7	Check if map(s) linked to this study have already been created, either in the list of the Regulatory Legacy collection of maps (List 1), or in the list of the public collection of maps (List 2).	APPL	List 1: Regulatory Legacy collection of maps contains rat studies (mammalian toxicology) and plant and livestock metabolism studies (residues). List 2: Authority public collection of maps contains plant and livestock metabolism studies (residues). This list is constantly growing and updated by EFSA. Both lists can be accessed from the EFSA webpage: https://www.efsa.europa.eu/en/applications/pesticides/tools
Metabolism Study	2.8	Add the "Unique Individual MetaPath File Number (MAP-number/card number)" as "other study identifier(s)" to the LITERATURE Object	APPL	If a MSS-file is found in List 1 or 2, it means that it exists and is available to Regulatory authorities. Therefore, only the reference to the Individual MetaPath File Number (MAP-number) is required. If a DER-file is found in List 1, it means that it exists and is available to Regulatory authorities. Therefore, only the reference to the Individual MetaPath File Number (MAP-number) is required. Currently, applicants will not be provided with the DER/MSS-file (from list 1 or 2) because applicants are requested not to modify the existing DER/MSS-files and do not need to generate reports. The regulatory database is available to Regulatory Authorities.
Metabolism Study	2.9	Create a new corresponding MSS or DER-file	APPL	Please follow the instructions available in the respective manuals:

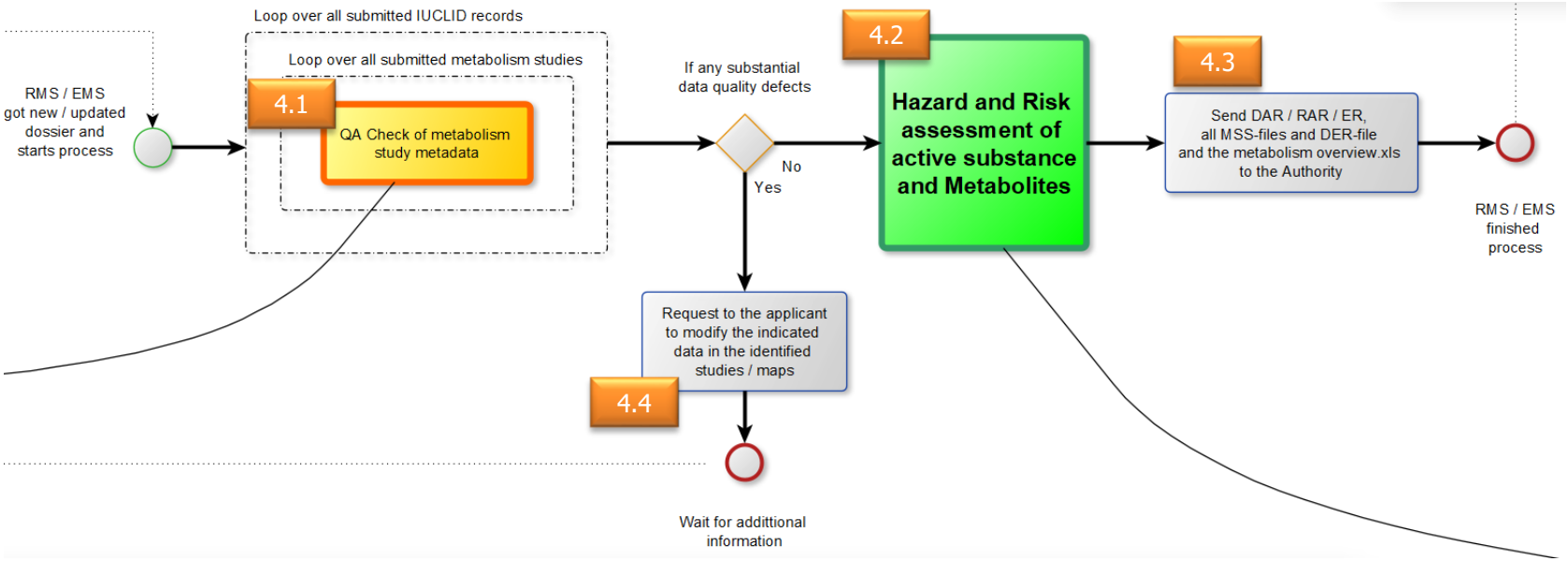
<table>
<tr><td></td><td></td><td></td><td></td><td>For MSS composers:
https://www.efsa.europa.eu/sites/default/files/2021-03/mss-composers-manual.pdf
For DER composers: http://doi.org/10.5281/zenodo.4751078
Please use the appropriate Composer for your experiment.
For MSS and DER composer, please compile all the mandatory fields as defined in Section 4 of the present document.<table><tr><td>MSS Plants Composer</td><td>For residues on plants;</td></tr><tr><td>MSS Crops Composer</td><td>For succeeding crops</td></tr><tr><td>MSS Livestock Composer</td><td>For poultry, lacting Ruminants and other animals</td></tr><tr><td>DER Composer</td><td>For rat or other laboratory animal species (if available)</td></tr></table></td></tr>
<tr><td>Metabolism Study</td><td>2.10</td><td>Import MSS/DER-file into Applicants MetaPath database to validate data</td><td>APPL</td><td>The Applicant MetaPath database version is the "Applicant Knowledge Base on Metabolism Studies". This import step is also necessary for a quality check.</td></tr>
<tr><td>Metabolism Study</td><td>2.11</td><td>Update MSS/DER-file</td><td>APPL</td><td>Please revise the data set until no more import errors occur.</td></tr>
<tr><td>Metabolism Study</td><td>2.12</td><td>Generate a Word Report using the Render of the MSS/DER-composer</td><td>APPL</td><td>The word report is the human-readable version of the data reported in the composers. This report can be generated by the function “Render” available in the MSS and in the DER composer.</td></tr>
<tr><td>Metabolism Study</td><td>2.13</td><td>Attach MSS/DER-file to LITERATURE Object</td><td>APPL</td><td>The error-free MSS/DER file is to be attached in the literature object.</td></tr>
<tr><td>Metabolism Study</td><td>2.14</td><td>Copy& Paste MSS-Composer Word Report into IUCLID “Overall remarks” Rich Text Area</td><td>APPL</td><td>The generated word report made with the MSS-composer can be copied into the IUCLID overall remark field with all its formatting (please avoid merged cells). This is not necessary for the DER report because the material and methods and result fields are also reported in the OHT structure.</td></tr>
<tr><td>Metabolism Study</td><td>2.15</td><td>Write Applicant´s summary and conclusion” in context of the application ≙ Minimal Study Summary encoding OHT</td><td>APPL</td><td>In the context of the application, the "Applicant's summary and conclusion" must now be prepared and reported in the dedicated fields in the IUCLID Study record.</td></tr>
</table>

3.3 Detail of the IUCLID Dossier for one metabolism study endpoint record



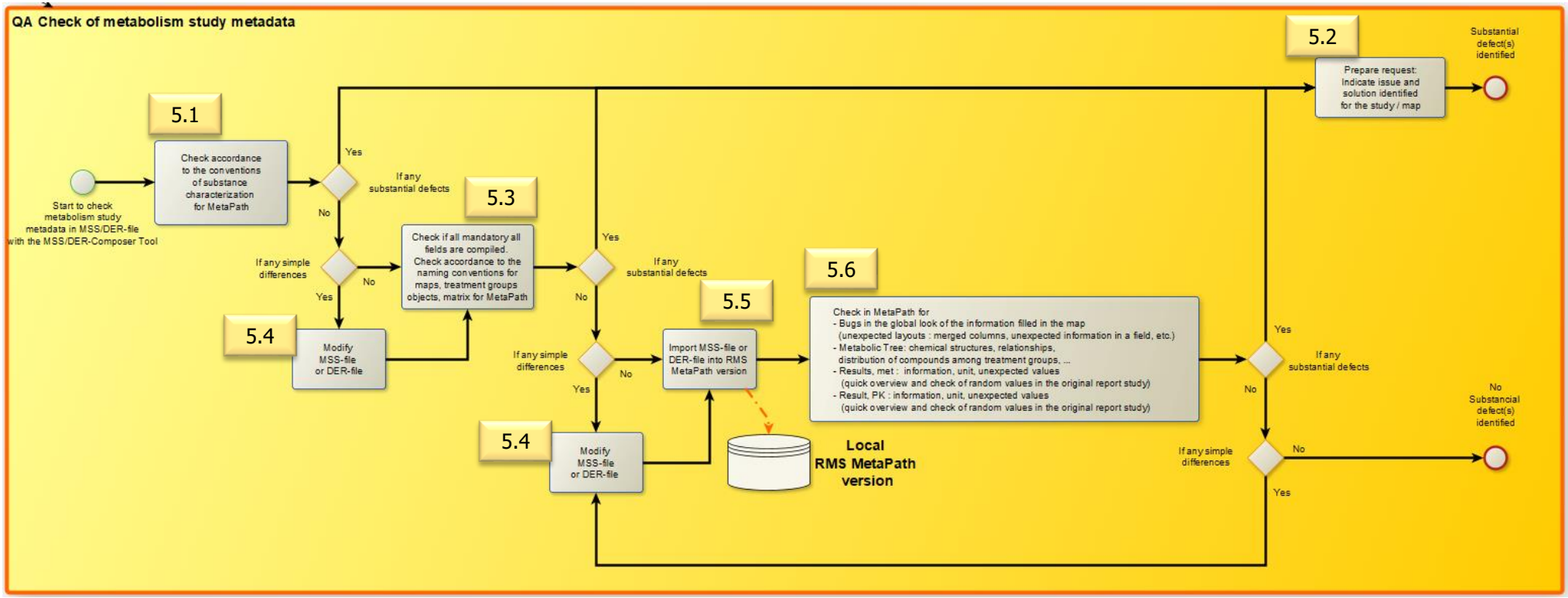
Process	No	Actions	Role	Comments
IUCLID dossier	3.1	Administrative data	APPL	Compile administrative data in the IUCLID study record, as defined in the IUCLID manual.
IUCLID dossier	3.2	Data source and Literature object (attached documents)	APPL	Create a literature doument in IUCLID, as defined in the IUCLID manual and link it to the study record. In the litterature document, attache the full study report, the sanitized study report. If a new xml-file (DER or MSS) was created by the applicant, please also attach this xml-file here.
IUCLID dossier	3.3	Material and methods and Test material	APPL	For both mammalian toxicollogy and residues metabolism studie, please compile the test material in the IUCLID study record, as defined in the IUCLID manual. -For mammalian toxicollogy metabolism studies, the applicants should fill in all the mandatory fields of OHT 58 (see IUCLID manual). -For the residue metabolism studies, applicants are not required to fill all the material and methods fields in OHT 85-2 and 85-3 (see IUCLID manual).
IUCLID dossier	3.4	Results and discussions	APPL	-For mammalian toxicollogy metabolism studies, the applicants should fill in all the mandatory fields of OHT 58 (see also IUCLID manual). -For the residue metabolism studies, applicants are not required to fill the results fields in OHT 85-2 and 85-3 (see also IUCLID manual).
IUCLID dossier	3.5	Overall remarks	APPL	- For the residue metabolism studies, please copy-paste the content of the MSS-composer Word Report in "overvall remarks".
IUCLID dossier	3.6	Applicant's summary and conclusion	APPL	As for any types of studies, please compile the Applicant's summary and conclusion in the IUCLID study record, as defined in the IUCLID manual.

3.4 Member states process



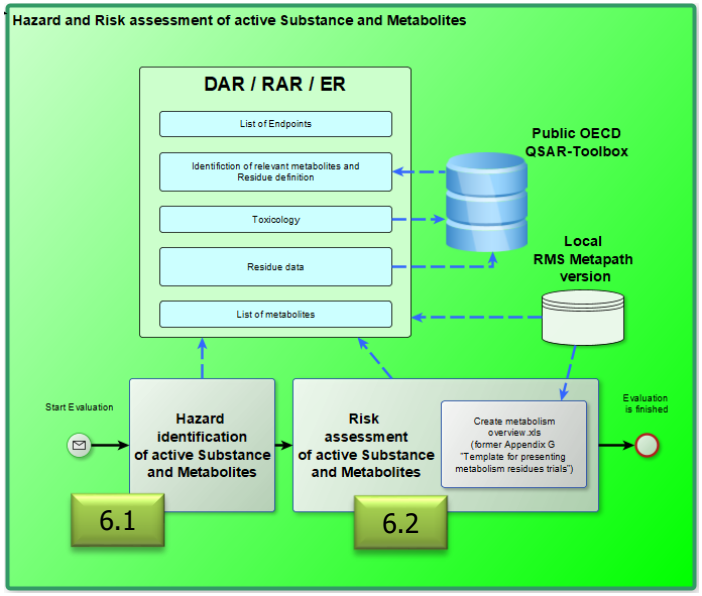
Process	No	Actions	Role	Comments
MS process		*Begin: Loop over all submitted IUCLID records*		
MS process		*Begin: Loop over all submitted metabolism studies*		
MS process	4.1	QA Check of metabolism study metadata	RMS	Check for details in chapter 0
MS process		*End: Loop over all submitted metabolism studies*		
MS process		*End Loop over all submitted IUCLID records*		
MS process	4.2	Hazard and Risk assessment of active substance and Metabolites	RMS	Check for details in chapter 3.6
MS process	4.3	Send DAR / RAR / ER, all MSS/DER-files and the metabolism overview.xls to the Authority	RMS	DAR (Draft Assessment Report): for new active substance approval process. RAR (Reneval Assessment Report): for renewal of active substance process ER (Evaluation Report): for MRL application process There is no change in the preparation of these documents. In addition ot the DAR/RAR/ER, the MS Regulotory Authority also share the MSS/DER-files and the metabolism oveview.xls (formerly reported in Appendix G for residue metabolism studies). The mebolism overview.xls can be prepared via the MetaPath software using the dedicated feature. The MSS/DER-files are shared with the Authority through a specific DMS dedicated folder.
MS process	4.4	Request to the applicant to modify the indicated data in the identified studies / maps	RMS	Message with a list of substantial data quality defects is sent by the MS Authority to applicant. Applicant may be requested to redo the map(s) if substantial quality defects are identified (see also chapter 3.5).

3.5 Detail for the Quality check



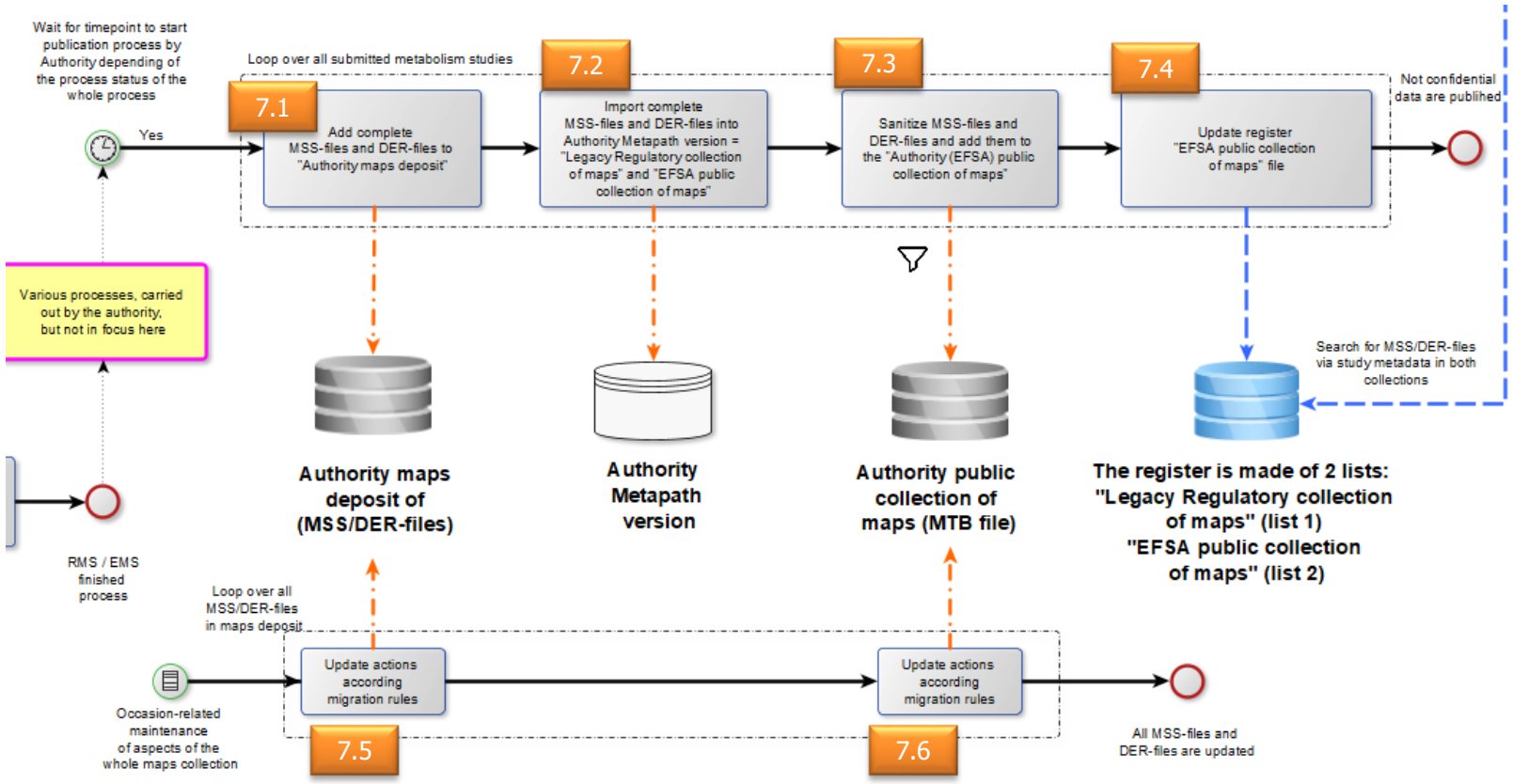
Process	No	Actions	Role	Comments
Quality Check	5.1	Check accordance to the conventions of substance characterization for MetaPath.	RMS	cf. MSS advisory notice: https://www.efsa.europa.eu/sites/default/files/2021-03/mss-composers-manual.pdf cf. DER composer manual http://doi.org/10.5281/zenodo.4751078
Quality Check	5.2	Prepare request: Indicate issue and solution identified for the study/map	RMS	If any substantial defects were found, a request to the applicant is needed.
Quality Check	5.3	Check if all mandatory all fields are compiled. Check accordance to the naming conventions for maps, treatment groups, objects, matrix for MetaPath	RMS	For the mandatory fields: cf **Section 4** of the present document. For naming conventions: cf. MSS advisory notice: https://www.efsa.europa.eu/sites/default/files/2021-03/mss-composers-manual.pdf cf. DER composer manual http://doi.org/10.5281/zenodo.4751078
Quality Check	5.4	Modify MSS/DER-file	RMS	If only simple defects were found, RMS/EMS has to modify the MSS/DER-file..
Quality Check	5.5	Import MSS/DER-file into RMS Metapath version	RMS	Import into a Local RMS MetaPath version, Cf series of MetaPath video tutorials: Chapters 1-5, Chapters 6-10
Quality Check	5.6	Check in MetaPath for • Bugs in the global look of the information filled in the map (unexpected layouts: merged columns, unexpected information in a field, etc.) • Metabolic Tree: chemical structures, relationships, distributions of compounds among treatment groups,… • Results, met: information, unit unexpected values (quick overview and check of random values in the original report study) • Result, PK: information, unit, unexpected values (quick overview and check of random values in the original report study)	RMS	Cf series of MetaPath video tutorials: Chapters 1-5, Chapters 6-10

3.6 Detail of the member states process for hazard and risk assessment



Process	No	Actions	Role	Comments
Hazard and Risk assessment	6.1	Hazard identification of active Substance and Metabolites	RMS	
Hazard and Risk assessment	6.2	Risk assessment of active Substance and Metabolites	RMS	• Use QSAR tools to verify the applicants conclusions. • Use the local RMS MetaPath version, which contain already the metabolism study information, imported in quality check (see 0) • At the end of risk assessment: Create metabolism overview .xls (like former Appendix G "Template for presenting metabolism residues trials") • Write the corresponding chapters in DAR /RAR or ER

3.7 Authority processes



Process	No	Actions	Role	Comments
Authority process 1		*Begin: Loop over all submitted metabolism studies*		The Authority starts the publication process of the data avaialable in MSS/DER-files when the risk assessment phase is finished. In this way, it is ensured that only validated data are made publicly available. It is noted that the data will be published by EFSA as MTB-files rather than individual xml-files.
Authority process 1	7.1	Add complete MSS/DER-files to "Authority maps deposit"	Authority	In the Authority deposit the MSS/DER-files do not need to be sanitized.
Authority process 1	7.2	Import complete MSS/DER-file into Authority Metapath version	Authority	The Authority MetaPath version already contains the "Legacy Regulatory collection of maps" and the "EFSA public collection of maps" and is constantly enriched with new MSS/DER-files created and validated in routine applications.
Authority process 1	7.3	Sanitize MSS/DER-file and add it to "EFSA public collection of maps"	Authority	The Authority remove the confidential fields from the MSS/DER-files (e.g. authors name for vertebrate studies) before sharing them on a public platform. Currently, the MSS/DER-files will not be individually shared but data will be shared through a unique MTB file, which will be regularly updated by EFSA. Cf. Knowledge junction: https://zenodo.org/record/4601174#.YFHUQjqSnIW
Authority process 1	7.4	Update register "EFSA public collection of maps" file	Authority	The Authority regularly update the list of maps available in the Authority public collection of maps (list 2), accessible from this webpage: https://www.efsa.europa.eu/en/applications/pesticides/tools
Authority process 1		*End: Loop over all submitted metabolism studies*		
Authority process 2		*Begin: Loop over all MSS-files in maps deposit*		
Authority process 2	7.5	Update actions according migration rules	Authority	Migration of: Authority maps deposit of (MSS/DER-files)
Authority process 2	7.6	Update actions according migration rules	Authority	Migration of: Authority public collection of MSS/DER-files
Authority process 2		*End: Loop over all MSS-files in maps deposit*		

4 Mandatory fields in the MSS/DER composers

4.1 Plant MSS Composer (primary crops)

I. GENERAL INFORMATION	
References	
Author	**X**
Date	**X**
Study title	**X**
Pages	
Reference type	**X**
Testing laboratory	**X**
Company study number	**X**
Identifiers *[related to the study references]*:	
- MRID Number	
- PMRA Number	
- Other	
Test Material	**X**
Identifiers *[related to the test material]*:	**X**
- PARAM code	**X**
- PC code	
- Other	
Guidelines	**X**
GLP	**X**
Acceptability	**X**
Background information *(free text)*	
Evaluators:	
- Evaluator name	
- Evaluator affiliation	**X**
Product type	
Product use	
Executive summary *(free text)*	
II. MATERIALS AND METHODS	
A. MATERIALS	
1. <u>Test Material</u>	
Common name	**X**
CAS Chemical Name	**X**
CAS no.	**X**
Company experimental name	**X**
Other synonyms (if applicable)	
Molecular Formula	**X**
Analytical Purity	
Impurities:	**X** *(1)*

Physical State	
Stability Under Test Conditions	
Expiration Date	
Lot/Batch #	
Radiolabeled test material	
Radiochemical purity	**X**
Specific activity as received:	
Specific activity of dose:	**X**
Structure	**X**
Physicochemical Properties	
Melting point/range	
pH	
Density	
Water solubility (__°C)	
Solvent solubility (mg/L at __°C)	
Vapour pressure at __°C	
Dissociation constant (pKa)	
Octanol/water partition coefficient Log(Kow)	
UV/visible absorption spectrum	
2. Test Crops	
Crop/Crop Group	**X**
Variety	**X**
Growth Stage at Application	**X**
Growth Stage at Harvest	**X**
Harvested Commodities	**X**
Harvesting Procedure	
Test site type	
3. Soil Type	
Soil Type	**X**
pH	
OM %	
Sand %	
Silt %	
Clay %	
Moisture Holding Capacity (at 1/3 bar)	
CEC mg/100g	
Environmental conditions	
Temperature	**X**
Rainfall	**X**
Lighting	**X**
Potential for degradation of the substance	**X**
B. STUDY DESIGN	
Experimental conditions *(free text)*	

Use pattern information	
Chemical name	
Application method	**X**
Application rate	**X**
Number of applications	**X**
Timing of applications	**X**
PHI	**X**
Sampling *(free text)*	**X**
Extraction and analysis *(flowcharts)*	
Extraction and Analysis *(free text)*	**X**
Identification and Characterization *(free text)*	**X**
III. RESULTS AND DISCUSSION	
A. TOTAL RADIOACTIVE RESIDUES	
Recovered equivalents	**X**
Overall extraction efficiency	**X**
Defined residue	**X**
Defined residue extraction efficiency	**X**
Quantitation *(free text)*	
TRR in matrices	
Matrix	**X**
Timing and application	**X**
Preharvest Interval (days)	**X**
% TRR	**X**
ppm	**X**
B. EXTRACTION, CHARACTERIZATION, AND DISTRIBUTION OF RESIDUES	
Distribution of the parent and Metabolites in Plant Matrices	**X**
C. STORAGE STABILITY OF RESIDUES	
Storage stability of residues *(free text)*	
Summary of storage conditions	
Matrix (RAC or extract)	**X**
Storage temperature (°C)	**X**
Actual storage duration (Days or Months)	**X**
Interval of Demonstrated storage stability (days/months)	**X**
D. IDENTITY OF RESIDUES IN CROP	
Summary of characterization and identification of radioactive residues in plant matrices	**X**
E. PROPOSED METABOLIC PATHWAY	**X**
IV. CONCLUSIONS	
Conclusion *(free text)*	
References *(free text)*	
V. APPENDIX	

Appendix 1	
Test#	**X**
Number	
Application Method	**X**
Number of Applications	**X**
PHI	**X**
Matrix	**X**
Experimental descriptor	
Remarks	
Citation	**X**
RLMT	**X**
Test crop	**X**
Soil type	**X**
Appendix 2	
ID	**X**
Common name/Code	**X**
Chemical name	**X**
SMILES	**X**
Parent(s)	**X**
Expertise	**X**
Appendix 3	**X**
VI. ATTACHMENTS	

(1): If radioactive impurities are at significant levels (i.e., > 5%), then the identity of radiolabelled impurities, if any, derived from the test material should also be reported (OECD GUIDELINE 501).

4.2 Crops MSS composer (rotational crops)

I. GENERAL INFORMATION	
References	
Author	**X**
Date	**X**
Study title	**X**
Pages	
Reference type	**X**
Testing laboratory	**X**
Company study number	**X**
Identifiers *[related to the study references]*:	
- MRID Number	
- PMRA Number	
- Other	
Test Material	**X**
Identifiers *[related to the test material]*:	**X**
- PARAM code	**X**
- PC code	
- Other	
Guidelines	**X**
GLP	**X**
Acceptability	**X**
Background information *(free text)*	
Evaluators:	
- Evaluator name	
- Evaluator affiliation	**X**
Product type	
Product use	
Executive summary *(free text)*	
II. MATERIALS AND METHODS	
A. MATERIALS	
1. <u>Test Material</u>	
Common name	**X**
CAS Chemical Name	**X**
CAS no.	**X**
Company experimental name	**X**
Other synonyms (if applicable)	
Molecular Formula	**X**
Analytical Purity	
Impurities	**X**(1)
Physical State	
Stability Under Test Conditions	
Expiration Date	

Lot/Batch #	
Radiolabeled test material	
Radiochemical purity	**X**
Specific activity as received:	
Specific activity of dose:	**X**
Structure	**X**
Physicochemical Properties	
Melting point/range	
pH	
Density	
Water solubility (__°C)	
Solvent solubility (mg/L at __°C)	
Vapour pressure at __°C	
Dissociation constant (pKa)	
Octanol/water partition coefficient Log(Kow)	
UV/visible absorption spectrum	
2. Test Crops	
Crop/Crop Group	**X**
Variety	**X**
Growth Stage at Application	**X**
Growth Stage at Harvest	**X**
Harvested Commodities	**X**
Harvesting Procedure	
Test site type	
3. Soil Type	
Soil Type	**X**
pH	**X**
OM %	**X**
Sand %	**X**
Silt %	**X**
Clay %	**X**
Moisture Holding Capacity (at 1/3 bar)	**X**
CEC mg/100g	**X**
Environmental conditions	
Temperature	**X**
Rainfall	**X**
Lighting	**X**
Potential for degradation of the substance	**X**
B. STUDY DESIGN	
Experimental conditions *(free text)*	
Use pattern information	
Chemical name	
Application method	**X**

Application rate	**X**
Number of applications	**X**
Timing of applications	**X**
PBI (plant back interval)	**X**
Sampling *(free text)*	**X**
Extraction and analysis *(flowcharts)*	
Extraction and Analysis *(free text)*	**X**
Identification and Characterization *(free text)*	**X**
III. RESULTS AND DISCUSSION	
A. TOTAL RADIOACTIVE RESIDUES	
Recovered equivalents	**X**
Overall extraction efficiency	**X**
Defined residue	**X**
Defined residue extraction efficiency	**X**
Quantitation *(free text)*	
TRR in matrices	
Matrix	**X**
Timing and application	**X**
Preharvest Interval (days)	**X**
PBI (Plant back interval) (days)	**X**
% TRR	**X**
ppm	**X**
B. EXTRACTION, CHARACTERIZATION, AND DISTRIBUTION OF RESIDUES	
Distribution of the parent and Metabolites in Plant Matrices	**X**
C. STORAGE STABILITY OF RESIDUES	
Storage stability of residues *(free text)*	
Summary of storage conditions	
Matrix (RAC or extract)	**X**
Storage temperature (°C)	**X**
Actual storage duration (Days or Months)	**X**
Interval of Demonstrated storage stability (days/months)	**X**
D. IDENTITY OF RESIDUES IN CROP	
Summary of characterization and identification of radioactive residues in plant matrices	**X**
E. PROPOSED METABOLIC PATHWAY	**X**
IV. CONCLUSIONS	
Conclusion *(free text)*	
References *(free text)*	
V. APPENDIX	
Appendix 1	
Test#	**X**

Number	
Application Method	**X**
Number of Applications	**X**
PHI	**X**
Matrix	**X**
Experimental descriptor	
Remarks	
Citation	**X**
RLMT	**X**
Test crop	**X**
Soil type	**X**
Appendix 2	
ID	**X**
Common name/Code	**X**
Chemical name	**X**
SMILES	**X**
Parent(s)	**X**
Expertise	**X**
Appendix 3	**X**
VI. ATTACHMENTS	

(1): If radioactive impurities are at significant levels (i.e., > 5%), then the identity of radiolabelled impurities, if any, derived from the test material should also be reported (OECD GUIDELINE 502).

4.3 Livestock MSS composer

I. GENERAL INFORMATION	
Reference	
Author	**X**
Date	**X**
Study title	**X**
Pages	
Reference type	**X**
Testing laboratory	**X**
Company study number	**X**
Identifiers *[related to the study reference]*:	
- MRID Number	
- PMRA Number	
- Other	
Test Material	**X**
Identifiers *[related to the test material]*:	**X**
- PARAM code	**X**
- PC code	
- Other	
Guidelines	**X**
GLP	**X**
Acceptability	**X**
Evaluators:	
- Evaluator name	
- Evaluator affiliation	**X**
Background information *(free text)*	
Executive summary *(free text)*	
II. MATERIALS AND METHODS	
A. MATERIALS	
1. Test Material	
Common name	**X**
CAS Chemical Name	**X**
CAS no.	**X**
Company experimental name	**X**
Other synonyms (if applicable)	
Molecular Formula	**X**
Analytical Purity	
Impurities	**X**(1)
Physical State	
Stability Under Test Conditions	
Expiration Date	
Lot/Batch #	
Radiolabeled test material	

Radiochemical purity	**X**
Specific activity as received:	
Specific activity of dose:	**X**
Structure	**X**
Physicochemical Properties	
Melting point/range	
pH	
Density	
Water solubility (__°C)	
Solvent solubility (mg/L at __°C)	
Vapour pressure at __°C	
Dissociation constant (pKa)	
Octanol/water partition coefficient Log(Kow)	
UV/visible absorption spectrum	
2. Animals	
Species	**X**
Breed	**X**
Age	**X**
Weight at Study Initiation (kg)	**X**
Health Status	**X**
Description of Housing/Holding Area	**X**
B. STUDY DESIGN	
Dose regime	
Number of animals per dose group	**X**
Rationale for slection of dose group	
Analysis of feed and water	
Test animal dietary regime	
Composition of Diet	**X**
Feed consumption (kg/day)	**X**
Water	
Acclimation period	**X**
Predosing	
Test animal dosing regime	
Treatment type	**X**
Treatment level	**X**
Vehicle	
Parameters	
Dosage Rate	**X**
Timing/duration	**X**
Timing from final dose to sacrifice	**X**
Sampling	
[Milk/eggs] collected	**X**
[Amount of milk/number of eggs] produced during normal production	
Urine, feces and cage wash collected	

Interval from last dose to sacrifice	
Tissues, harvested and analysed	**X**
Extraction and Analysis *(free text)*	**X**
Extraction and Analysis *(flowcharts)*	
Identification and Characterization *(free text)*	**X**
III. RESULTS AND DISCUSSION	
A. TOTAL RADIOACTIVE RESIDUES	
Recovered equivalents	**X**
Overall extraction efficiency	**X**
Defined residue	**X**
Defined residue extraction efficiency	**X**
Quantitation *(free text)*	
TRR in [milk/eggs], tissue and excreta	
Matrix	**X**
% aministered zone	**X**
Ppm	**X**
TRR in [milk/eggs] as function of time	
Interval	**X**
ppb	**X**
% of dose	**X**
Plateauing	**X**
General Health of animals	
B. EXTRACTION, CHARACTERIZATION, AND DISTRIBUTION OF RESIDUES	
Distribution of the parent and Metabolites in Ruminant Matrices	**X**
C. STORAGE STABILITY OF RESIDUES	
Storage stability of residues *(free text)*	
Summary of storage conditions	
Matrix (RAC or extract)	**X**
Storage temperature (°C)	**X**
Actual storage duration (Days or Months)	**X**
Interval of Demonstrated storage stability (days/months)	**X**
D. IDENTITY OF RESIDUES IN POULTRY/LACTATING RUMINANTS/ OTHER ANIMALS	
Summary of characterization and identification of radioactive residues animal matrices	**X**
E. PROPOSED METABOLIC PATHWAY	**X**
IV. CONCLUSIONS	
Conclusion *(free text)*	
References *(free text)*	
V. APPENDIX	
Appendix 1	

Test#	**X**
Sex	**X**
Number	**X**
Dose Route	**X**
Dose (nominal)	
Dose (measured)	**X**
Dose Type	**X**
Test duration	**X**
Matrix	**X**
Experimental descriptor	
Remarks	
Citation	**X**
RLTM	**X**
Species	**X**
Diet	**X**
Dosing	**X**
Samples	**X**
Appendix 2	
ID	**X**
Common name/Code	**X**
Chemical name	**X**
SMILES	**X**
Parent(s)	**X**
Expertise	**X**
Appendix 3	**X**
VI. ATTACHMENTS	

(1): The identity of radiolabeled impurities, if any, derived from the test material should also is reported (OECD GUIDELINE 503).

4.4 Rat DER Composer

I. General Information	
studyClarifications	
studyType	X
compliance	
testmaterial	X
testmaterialpurity	X
executiveSummary	X
citation	X
sponsor	X
iupacname	x
agencyCode	X
agencyCode value	X
casname	
synonyms	X
barcode	
pccode	
submissionNo	
txr	
II. Material and Methods	
A. Materials	
doseSolution/concentration	
testCompound/nonradiolabelled/batch	X
testCompound/nonradiolabelled/contaminants	
testCompound/nonradiolabelled/description	
testCompound/nonradiolabelled/purity	X
testCompound/radiolabelled/activity	X
testCompound/radiolabelled/activity/@units	X
testCompound/radiolabelled/batch	X
testCompound/radiolabelled/purity	X
testAnimals/species	X
testAnimals/strain	
testAnimals/acclimation	
testAnimals/age	
testAnimals/conditions	
testAnimals/diet	
testAnimals/housing	
testAnimals/source	
testAnimals/water	
testAnimals/weight	
doseSolution/vehicle	
vehicle	
dosePreparation	
radiolabelled/testmaterial	X
testCompound/nonradiolabelled/testmaterial	X

testCompound/radiolabelled/testmaterial	X
testCompound/nonradiolabelled/cas	X
radiolabelled/smiles	X
smiles	X
testCompound/nonradiolabelled/smiles	X
testCompound/radiolabelled/smiles	X
B. Methods	
groupArrangements	X
sampleCollection	
statistics	
metaboliteStudies Table 1a	X
pharmacokineticStudies	
III. Results	
preliminaryExperiment	
absorption	
tissueDistribution	
excretion	
HalfLife	
metCharactStudies | Table(s) 8	X
IV. Discussion and Conclusions	
investigators	
reviewer	
studyDeficiencie	
V. Appendix 1 and 2	**X**
VI. Attachments	
filename	
description	