

# **The MetabolAS ecosystem**

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## Prologues

1. This improvement process was started by EFSA as part of the implementation of the European Transparency Regulation.
2. However, the information flow on metabolism studies has an international character. The BfR proposals should therefore be applicable in Europe but also internationally.
3. This presentation could only summarize the proposed ecosystem as a result of the analysis without going into details of the reasons for this proposal.  
This presentation is addressing more general, organizational topics.

# Content

## MetabolAS ecosystem

The process and objects of the information flow

## Why do we need a radical change?

- The age of the “MetaPath” technology used for
  - the database and
  - the front end,
- the number of separate programs of the “DER/MSS-Composer Family” to be adapted,
- the number of different “custom versions” of “MetaPath” and the “DER/MSS-Composer Family” and
- the number of open user requests (see also the list of CropLife Europe) in relation to the user functions that do not require any change

should be arguments for a **radical change**.

## The problem of naming conventions

The used term MetabolAS should be a synonym for:

# **Metabol**ism **A**ssessment **S**ystem

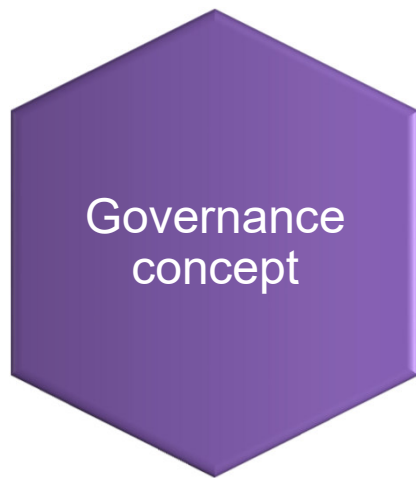
The name could also be **MetaPath II**, because the improvement process should start on basis of the experiences and algorithms of “MetaPath” but on a new technological level.

The radical change could perhaps be better communicated by changing the name.

# The elements of the proposed MetabolAS ecosystem

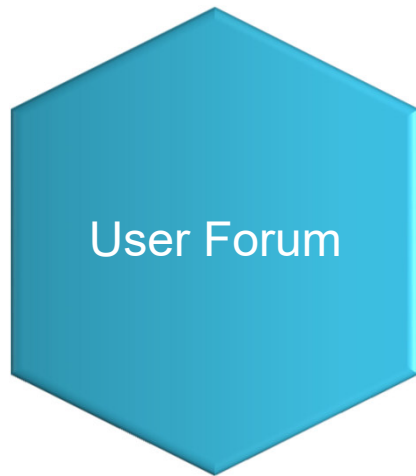


All components of this ecosystem could be used by applicants and authorities because both stakeholders need the same interoperable functionality.



The **preferred solution** would be, that the OECD

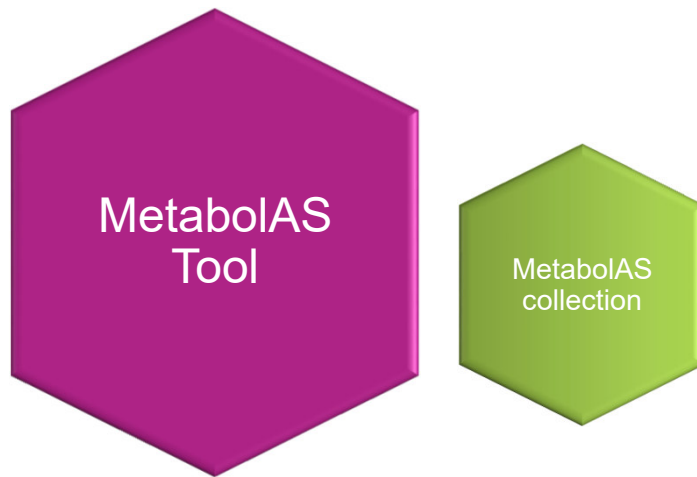
- plays the role of the new “**Governance Body**”,
- will improve its own transport mechanisms for study summaries by the new “**OECD Attachment Type**” and
- has also the responsibility of the needed “**Picklists and Picklist elements**”.



## User Forum

- Inform the “Governance Body” about new identified weaknesses, errors and requirements,
- assists for an adequate prioritization,
- take part in tests,
- communication to the end users

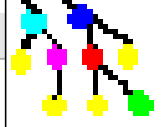




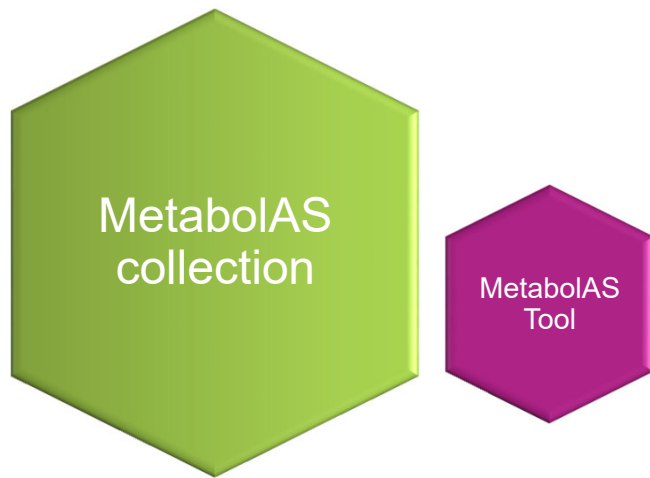
## MetabolAS Tool

- **User interface** of a MetabolAS collection realized with a
- **database management system**,
- optionally created in an **Open Source Project** and
- is able to manage **aggregated raw data** of metabolism studies on study level in a **MetabolAS collection**
- The collection could be organized locally or as a central webservice

# Much more design properties and user functions!

A		B		 <b>A</b>		E <b>B</b>	F <b>C</b>	Metabol AS Tool
1	Function Group	User function, independent of the transport step		Current Metpath environment	Improved Metpath environment	New MetabolAS Tool		
2								
3	Generic approach	Cover all metabolism study types at once		0	0	1		
4	Transparency	Fullfill the requirements		1	1	1		
5	Transparency	Rights of the data donors of a public collection are clear		0	0	1		
6	Chemical structure notation	Downward compatible		0	?	1		
7	Chemical structure notation	Support different notations		0	?	1		
8	Chemical structure notation	Modul to draw structure should satisfy		0	?	1		
9	Chemical structure notation	Markush/generic structures		0	?	?		
10	Chemical structure notation	Search for structure similarities		1	1	1		
11	Chemical structure notation	Search for similarities independent of the used chemical structure notation		?	?	1		
12	Chemical structure notation	The similarity search filter could be combined with additional filter clauses		0	0	1		
13	Substance model	Manage reference substances		0	?	1		
14	Substance model	Assists references from substances to metabolites		1	1	1		
15	Substance model	Option to merge substance duplicates and their references		?	?	1		
16	Assesment process	Usable for "non-guideline experiments "		0	0	1		
17	Assesment process	Manage "tentative results"		0	0	1		
18	Assesment process	Usable for "freestyle" studies		0	0	?		
19	Assesment process	Manage of textual summaries of the interpretation of the results		1	1	1		
20	Assesment process	Flexible reporting by flexible groups (Pivot tables)		0	0	1		
21	Assesment process	Limitation of 7 columns per table was removed		0	?	1		
22	Assesment process	Recalculations of values from one to another substance		0	0	1		
23	Assesment process	Calculation of concentration factors in relation to other matrix		0	0	1		
24	Assesment process	Grouping of metabolites according the OECD Guideline		0	0	1		
25	Assesment process	Manage Q(SAR) responses in a user storable "List of similar substances"		0	0	1		
26	Assesment process	Integrated start into Q(SAR) Tools with SMILES as the parameter		0	0	0		
27	Assesment process	Manage response from the Q(SAR) tools according ECHA guide		0	0	0		
28	Assesment process	Integrated start into predefined external substance databases		0	0	0		
29	Assesment process	Prediction of metabolic pathways		0	?	?		
30	Assesment process	Pooling of identical substances of different names across the studies		?	?	1		

This comparison has in sum 85 rows.



Each MetabolAS collection needs its own MetabolAS Tool.

Local MetabolAS collections could be implemented by applicants and by authorities.

An international curated reference collection of metabolism study metadata is needed. We need the philosophy

**“One study – one evaluated metabolic pathway”**



## Picklists and Picklist elements

### Picklist Management

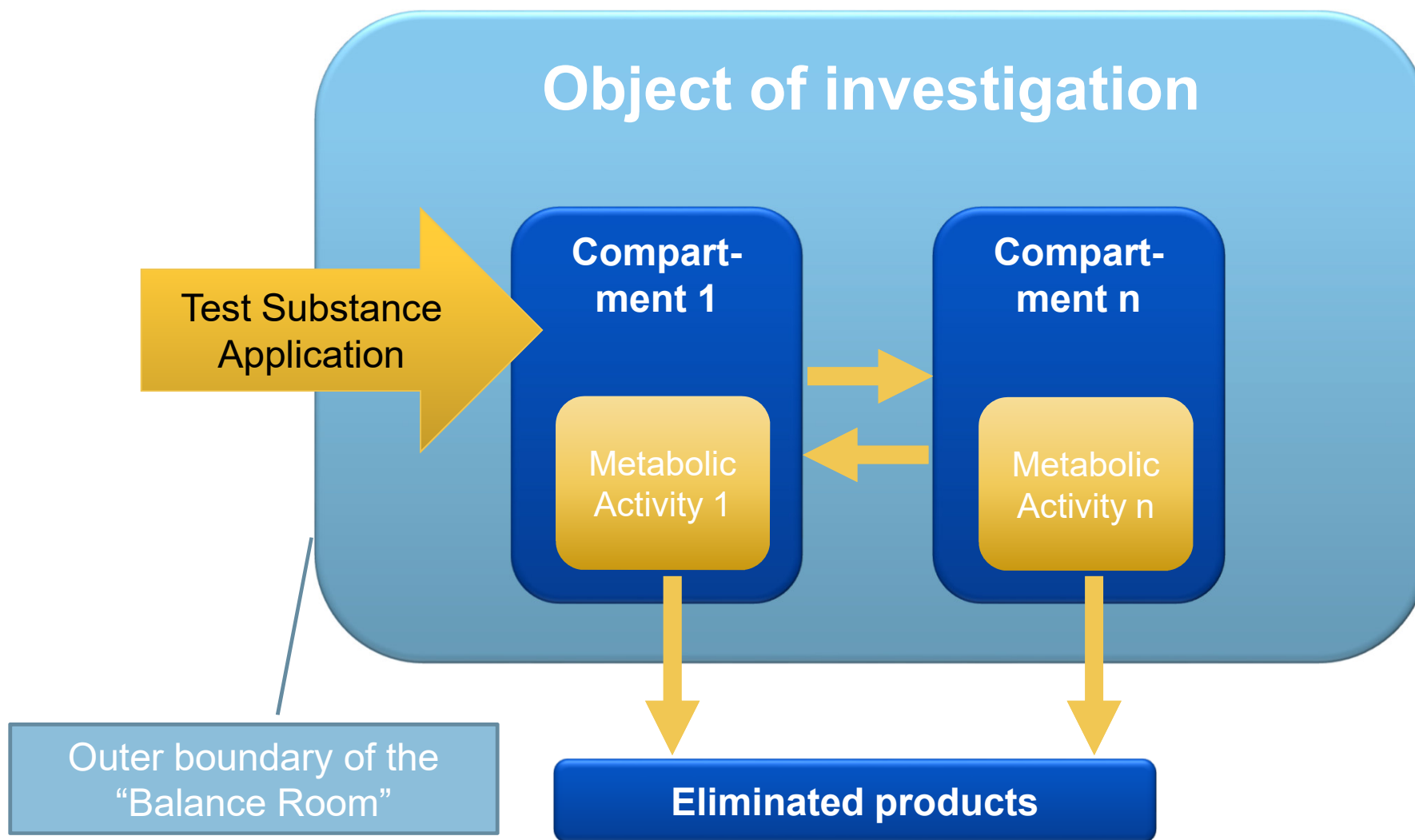
- is needed for
  - a powerful advanced search query and
  - to create faceting groups regarding a full text search in the MetabolAS collection
- Picklists and Picklist elements could be defined by IUCLID mechanisms according to the relevant OHT.  
An independent maintenance would be possible in principle.



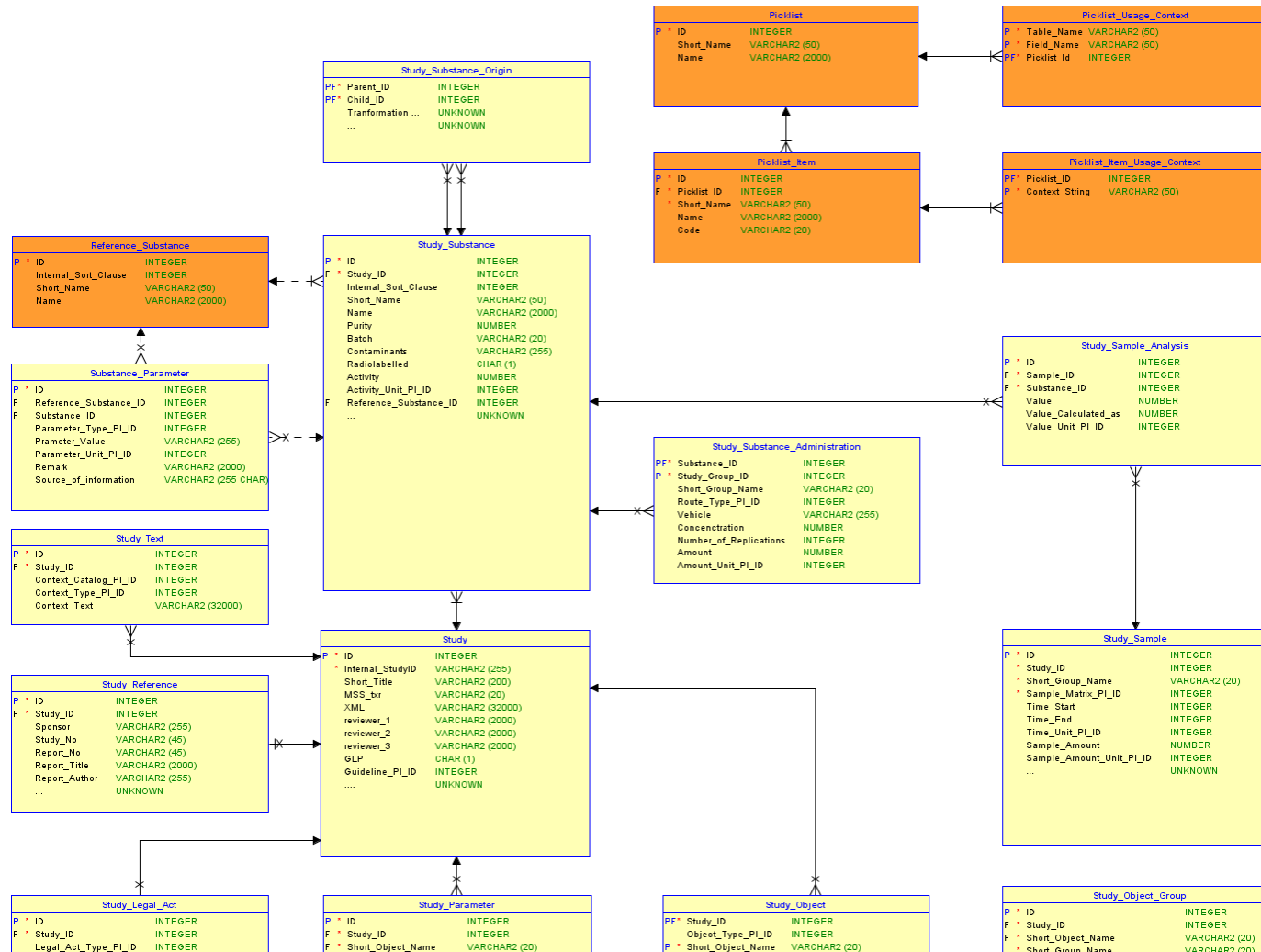
## The scheme definition

- define the **basic interface** to solve interoperability issues,
- **Cover all study types** where radioactive labelled test material is used according to the Test Guidelines
- Flexibility by using different “Picklists and Picklist elements” depending on the type of the metabolism study

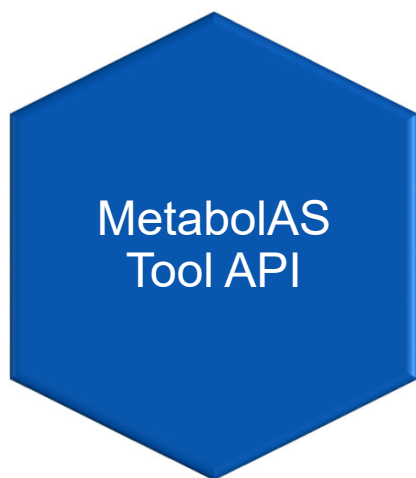
is based on a generalized term of metabolism study



The core structure of the relational database model should be simple



The needed flexibility of the “Scheme Definition” should be possible by using different “Picklists and Picklist elements” depending on the type of the metabolism study.



## The MetabolAS Tool API

- provide functions for reading and writing data in the MetabolAS collection from external tools,
- so (Q)SAR models could “harvest” validated data sets
- External links / tools can open a specific data set of a “MetabolAS collection” via API



## Switch to the voting system now regarding the Governance concept

Are there any questions? Please use the hand raise in the TEAMS environment.

For statements you could use also the TEAMS chat. The chat will be recorded. **So no idea is lost.**

Who should hold the role of the governance body for MetabolAS?

Do you support the implementation of an international curated reference collection?

Should the international curated reference collection of metabolism study metadata be publicly available?

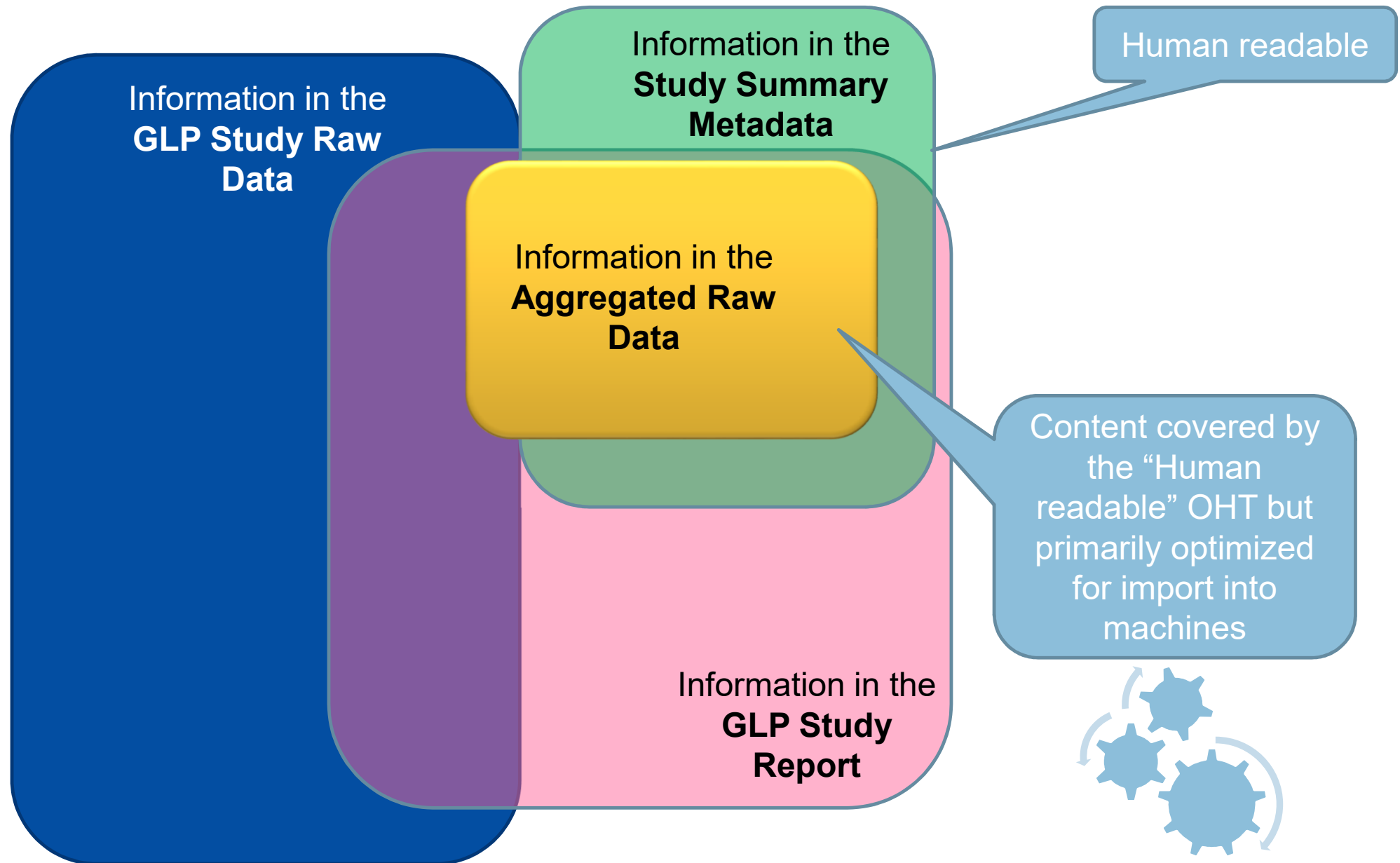


# Content

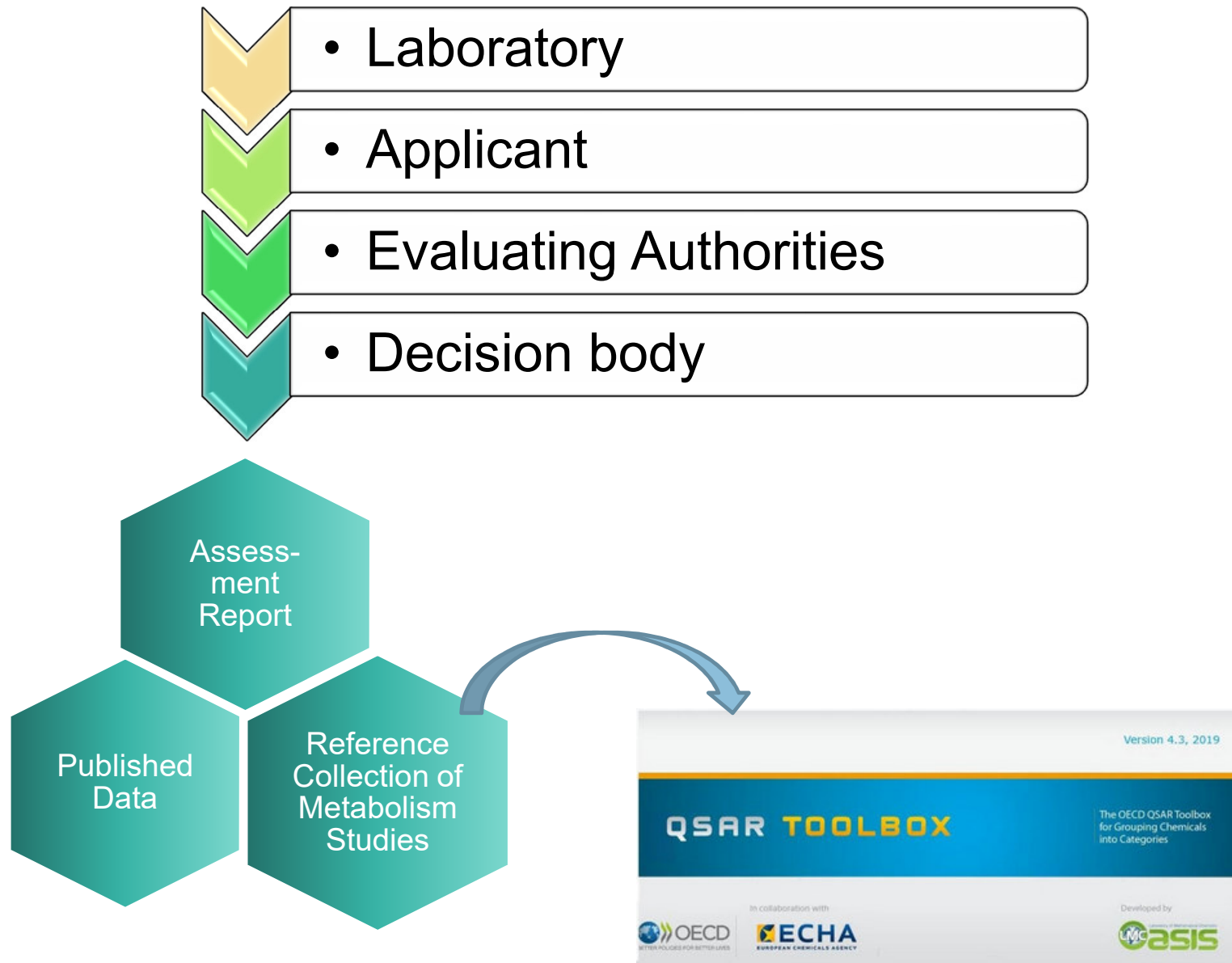
MetabolAS ecosystem

The process and objects of the information flow

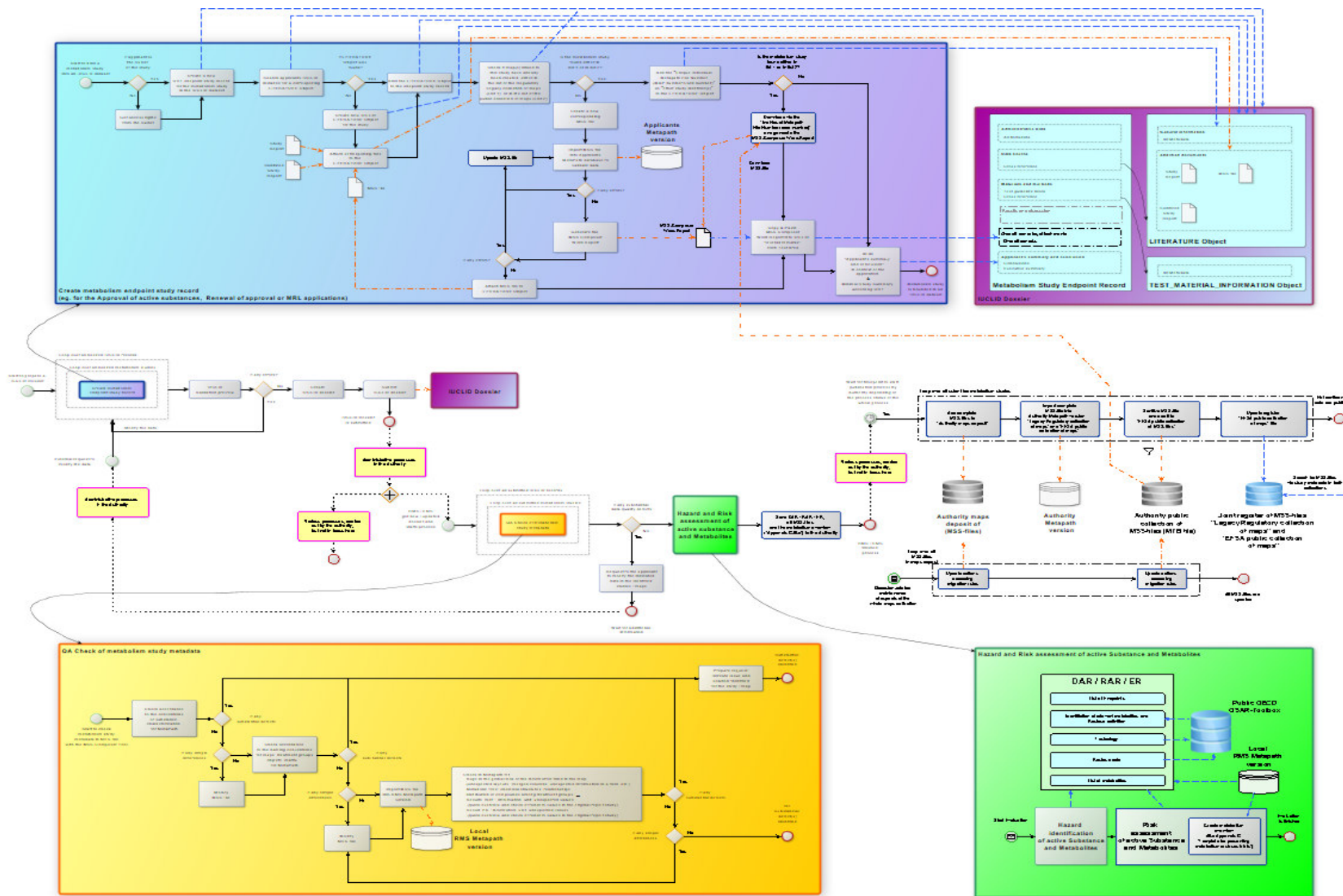
# Relationship of different information sets of a study



## The direct and the indirect “end products” of the process

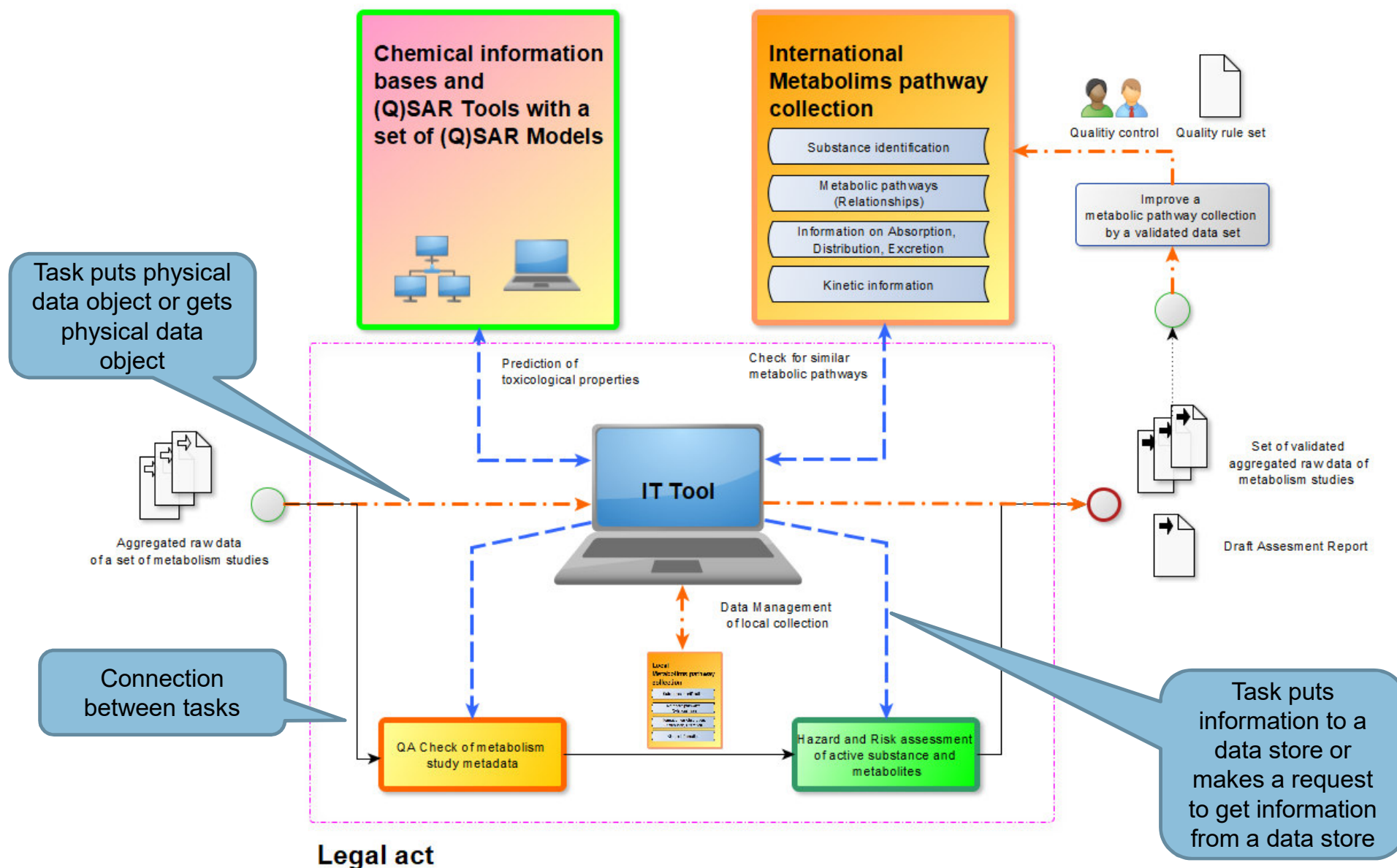


## The current European process



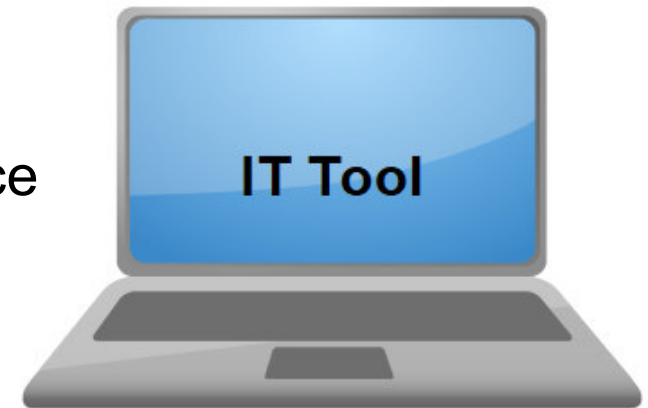
Details in the description on zenodo: [Process Steps for Metabolism Data](#)

# How to read the abstract Authority view on the current European process “Big picture”?



## Some user requirements for the proposed IT-Tool

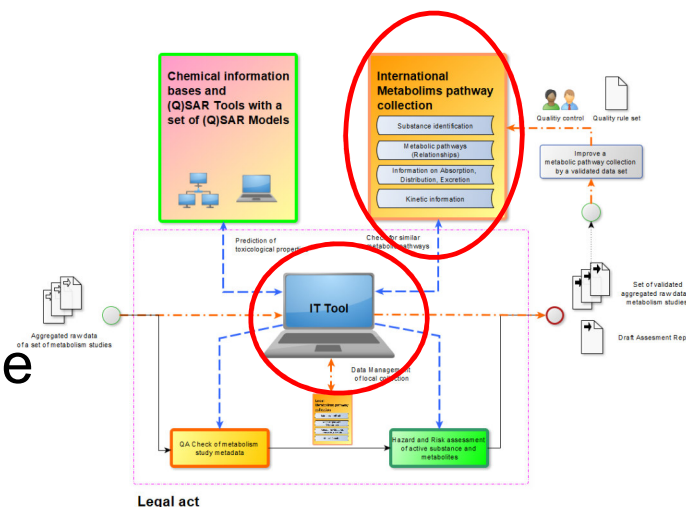
- Program modules with a browser user interface
- Cover all metabolism study types
- No further need for different MSS-Composer
- Tool to import aggregated raw data
- Search for structure similarities quickly
- Visualize and compare metabolic pathways
- Rendering of chemical structures in a sufficient quality
- Manage reference substances
- Flexible reporting by flexible groups (Pivot tables)
- Recalculations of values from one to another substance
- Calculation of concentration factors in relation to other matrix
- Grouping of metabolites according the OECD Guideline
- ...
- Support of an API



# The “Big picture” as an abstract authority view

has to

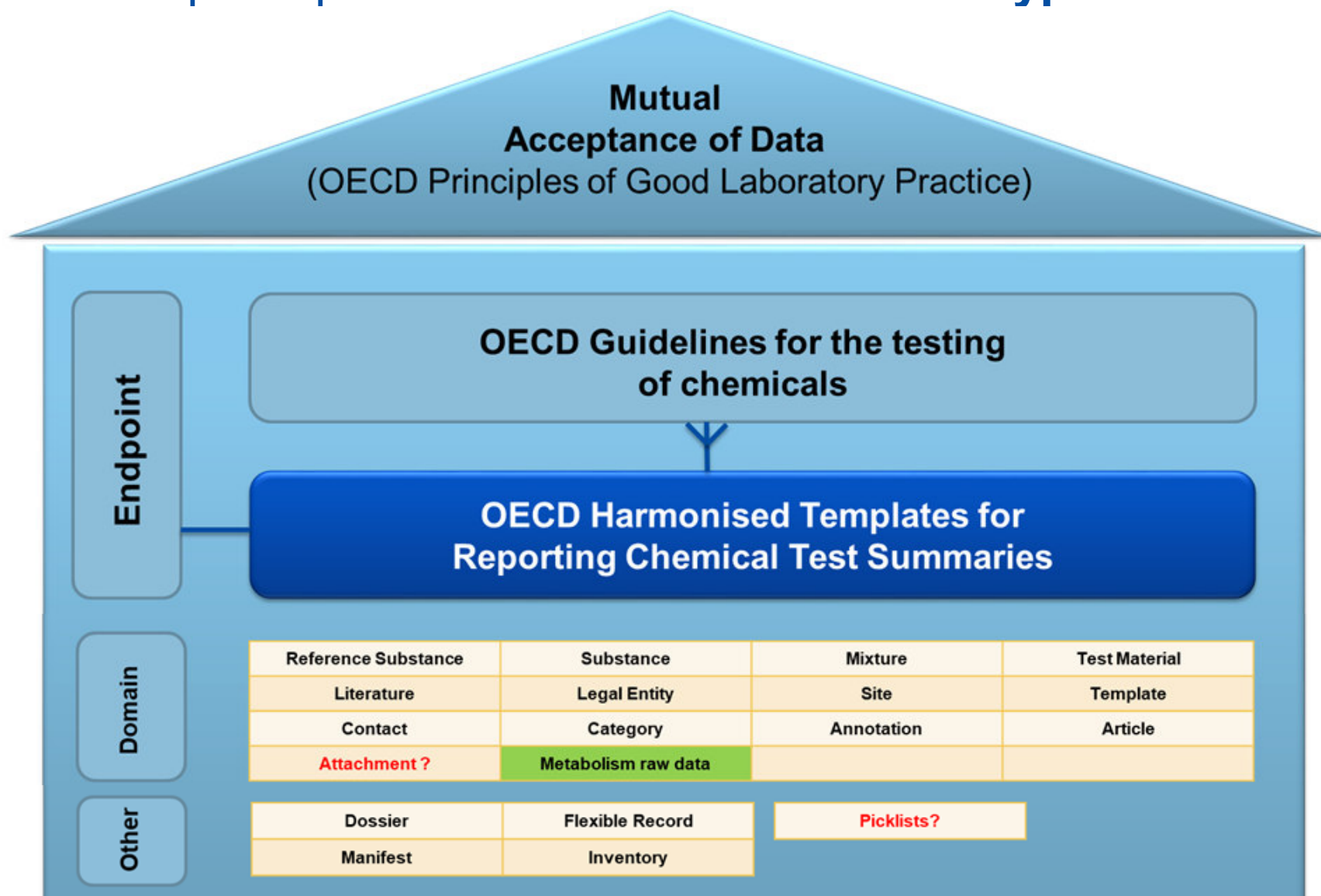
- organize the input and output information according to a legal act,
- provide needed tools to process the data in the evaluation steps,
- provide needed reference information collections and
- organize a process to improve these reference information collections.



- This “Big picture” should be identical after the improvement process, because the “information” and the “end products” of the process are still identical.
- The “transport” step should guarantee that the full information was transported. This could be done in effective or ineffective solutions.
- **The most important points are the IT Tool to process the metabolism raw data and to implement the Authorities MetabolIAS collection**

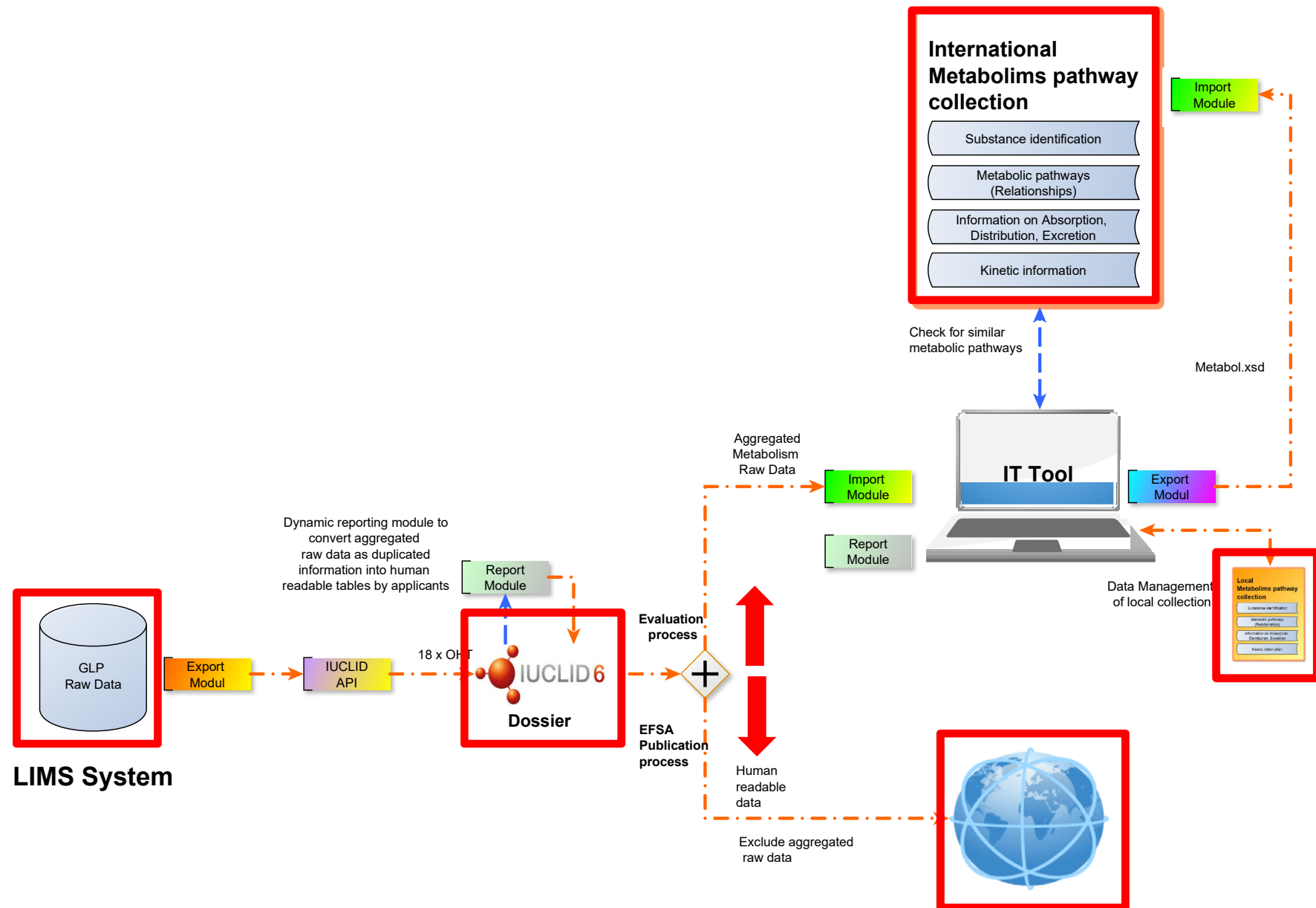


# The transport option of a new **OECD Domain type**



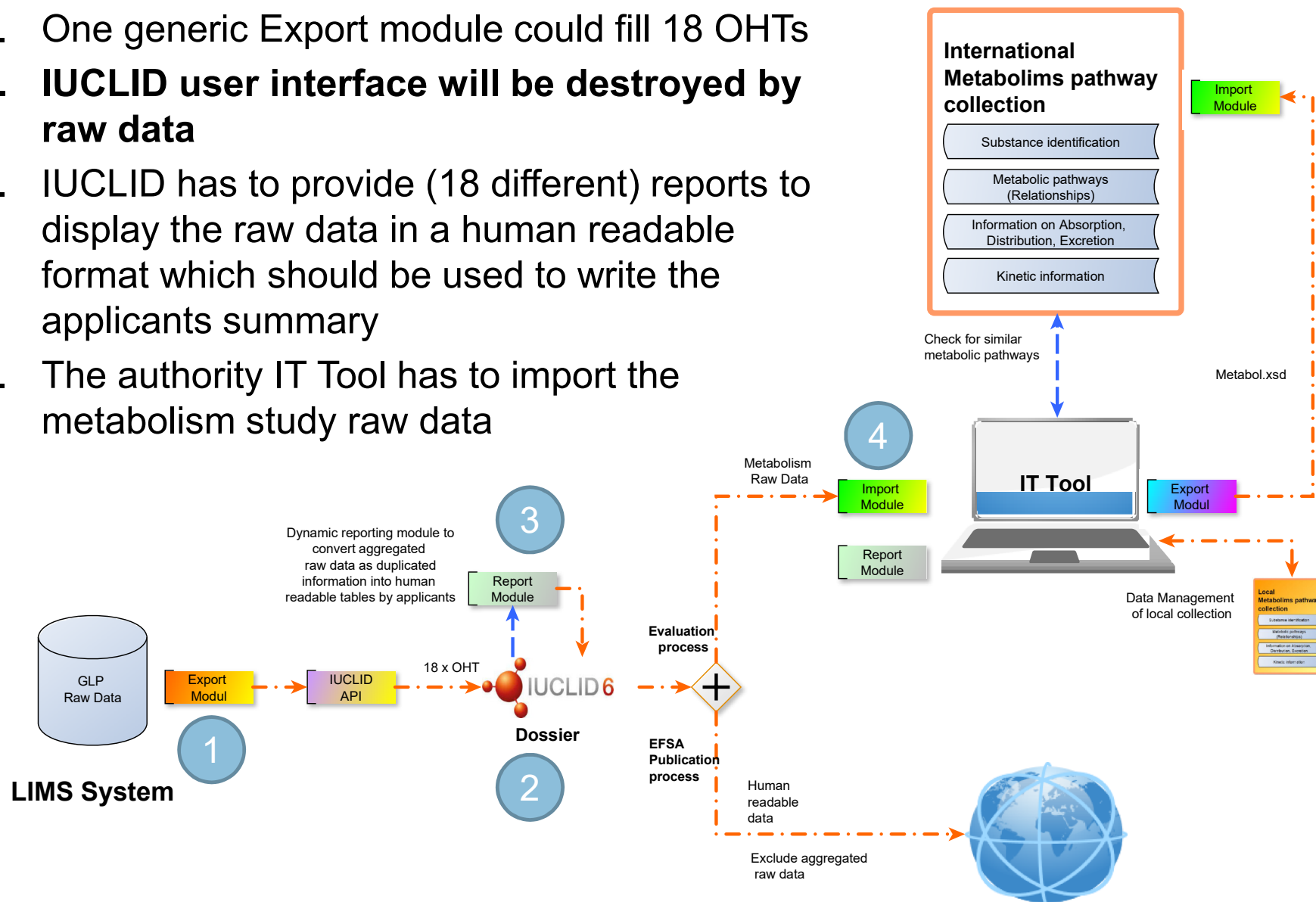
This new Domain type should cover all studies where radioactive labelled test material could be used according the Test Guidelines

# Information instances by using the new OECD Domain type

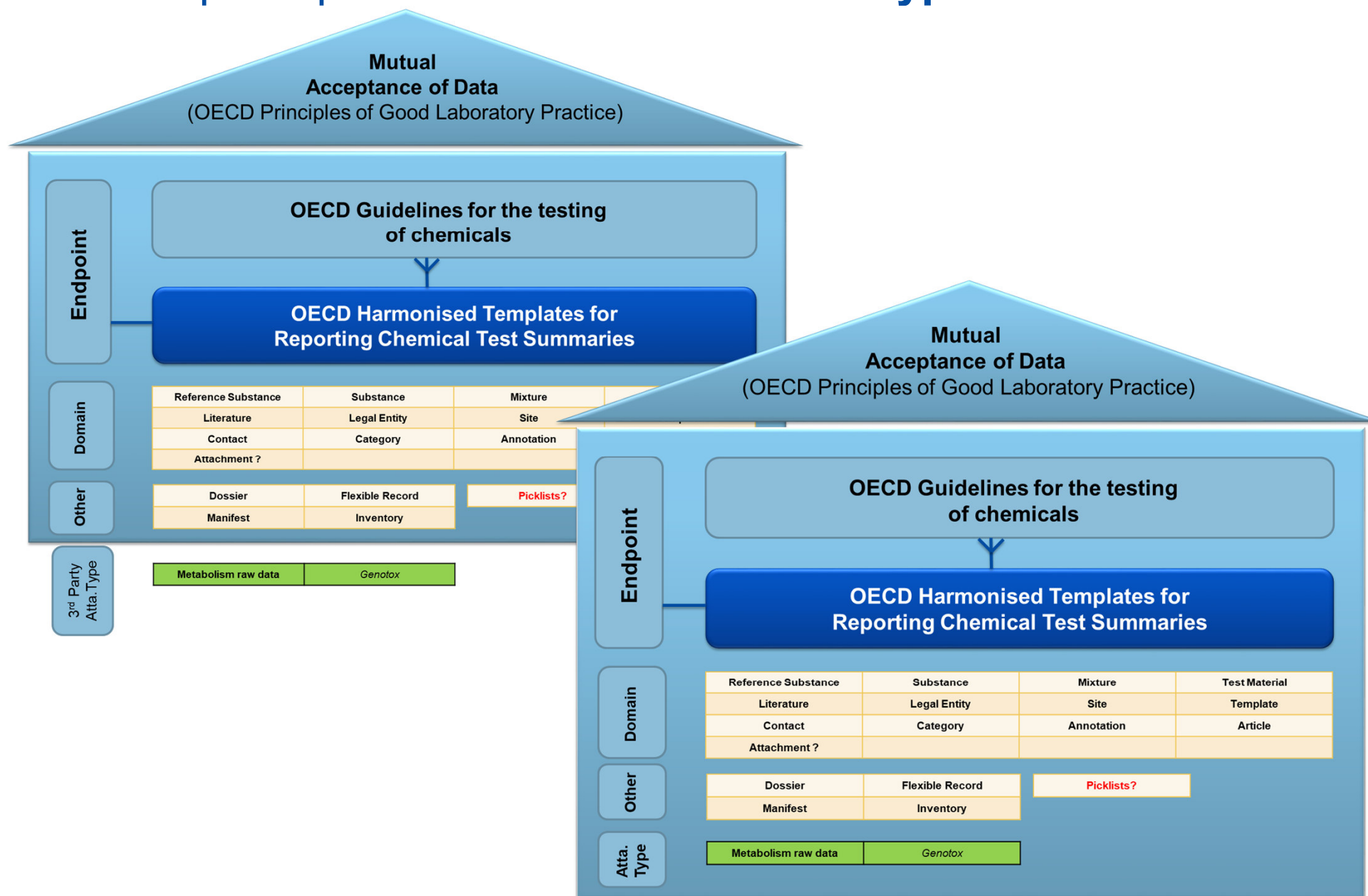


# The transport option of a new OECD Domain type

1. One generic Export module could fill 18 OHTs
2. **IUCLID user interface will be destroyed by raw data**
3. IUCLID has to provide (18 different) reports to display the raw data in a human readable format which should be used to write the applicants summary
4. The authority IT Tool has to import the metabolism study raw data

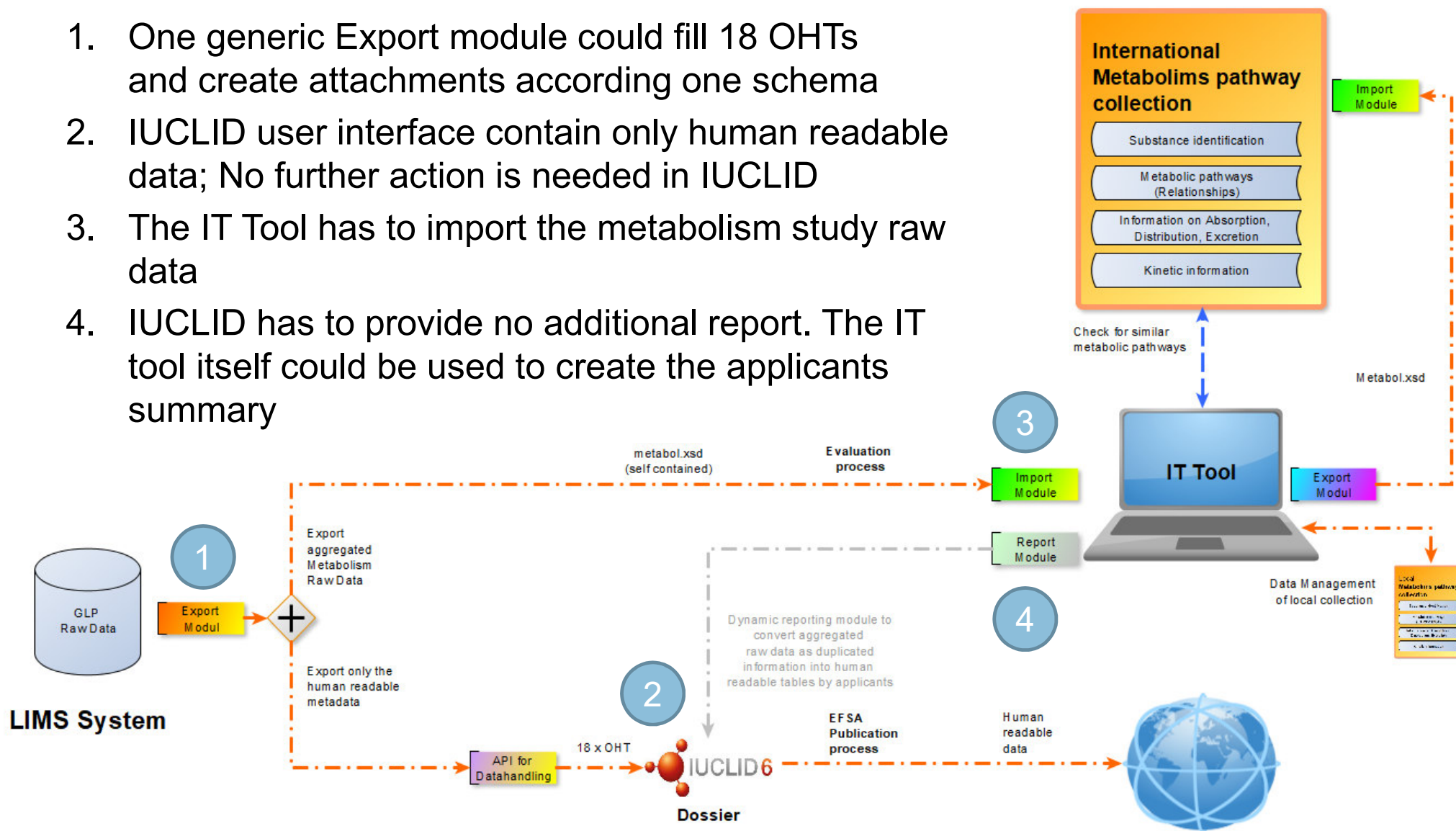


# The transport option of a new Attachment type



## The transport option of a new Attachment type

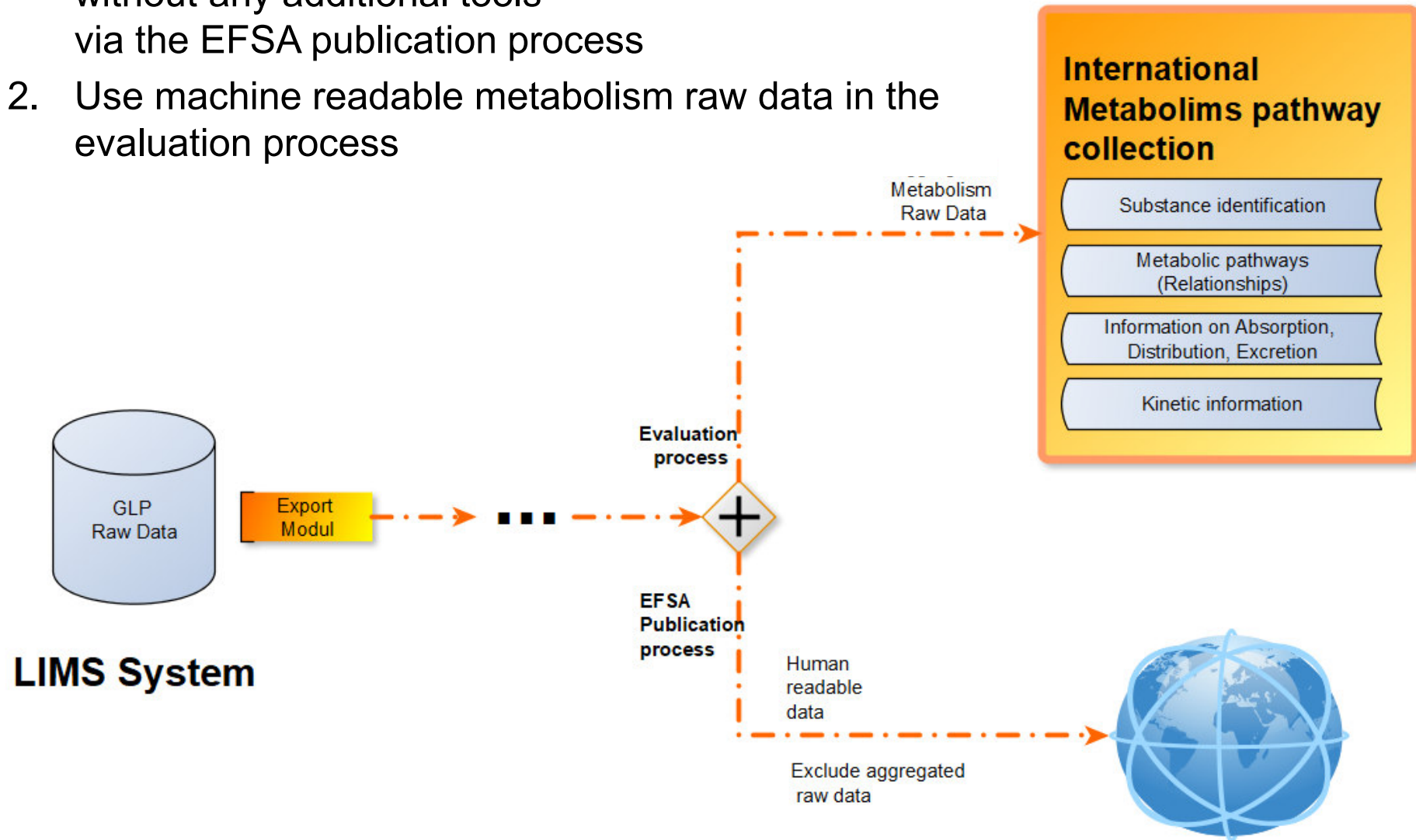
1. One generic Export module could fill 18 OHTs and create attachments according one schema
2. IUCLID user interface contain only human readable data; No further action is needed in IUCLID
3. The IT Tool has to import the metabolism study raw data
4. IUCLID has to provide no additional report. The IT tool itself could be used to create the applicants summary



The BfR preferred option!

## Summary: We need parallel ways for data

1. Publication of data which are human readable without any additional tools via the EFSA publication process
2. Use machine readable metabolism raw data in the evaluation process



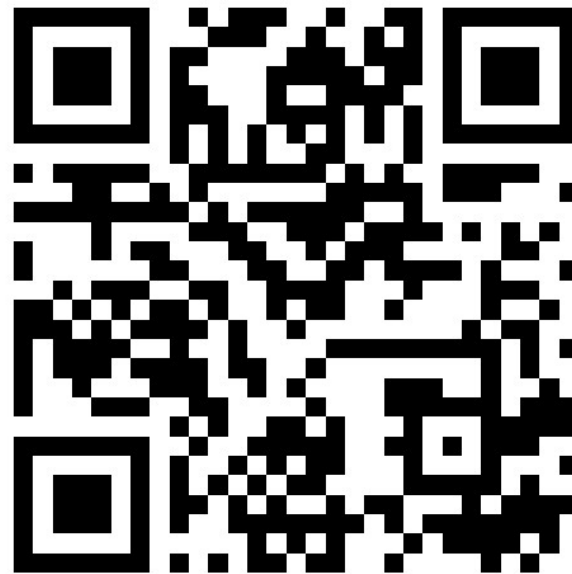


## Switch to the voting system now regarding the transport concept

Are there any questions? Please use the hand raise in the TEAMS environment.

For statements you could use also the TEAMS chat. The chat will be recorded. **So no idea is lost.**

Which transport concept would you recommend regardless of the political hurdles / necessary decisions?



# **Thank you for your attention**

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