Proof of concept pesticides dossier - Conclusions from building 2 dossiers

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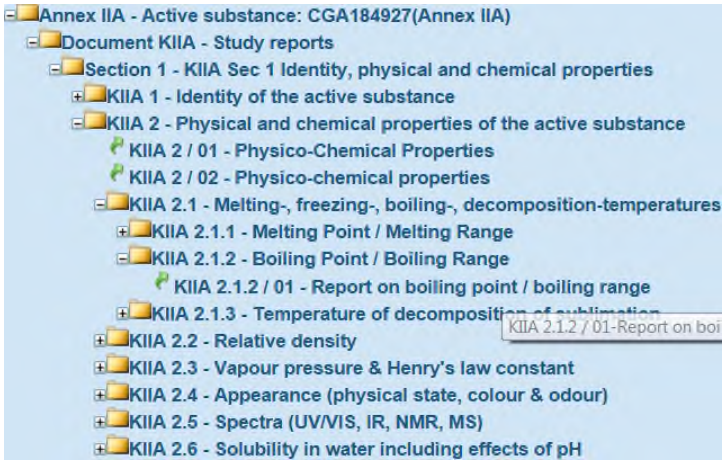
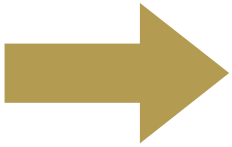
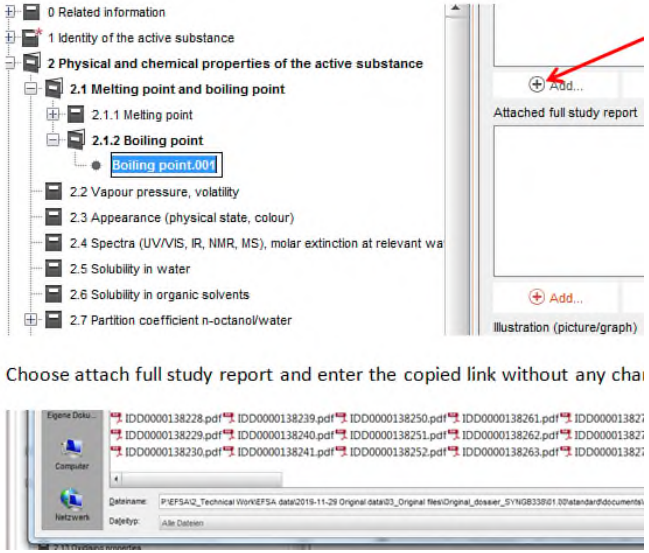
Preparation of 2 dossiers - overview

Preparation of the original dossier

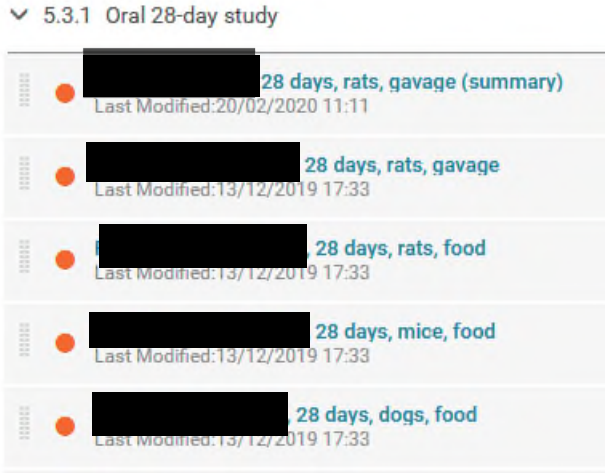
- Data migration: all available study reports were migrated manually from Caddy to IUCLID







- Rule was applied: One study record for one study report



Manual migration of data is time consuming - IT data migration tool from Caddy to IUCLID would be very useful, also for transfer of text from M docs to IUCLID summaries

Preparation of the original dossier

- Preparation of one robust study summary / endpoint – based on documents M-II/M-III (old dossier format)

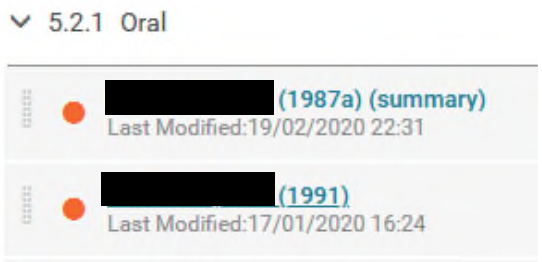
5.2.1 Oral

Report: [redacted]

Guidelines: OECD 401, Deviations from 92/69/EEC m used as highest dose

GLP: Yes (laboratory certified [redacted]

Material and methods: Test material: CGA 184927, Batch: P 612003, Clodinafop-propargyl technical was administered in 0.5% carboxymeth

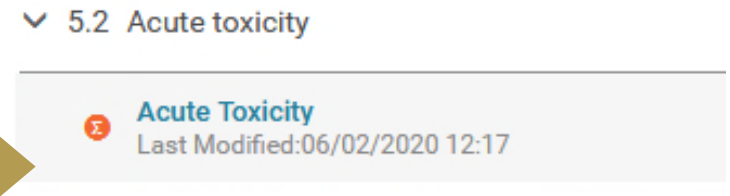


- Preparation of endpoints summaries that include overall conclusions per endpoint – based on documents M-II/M-III and N

5.2 Acute toxicity

Table 5.2-1: Acute toxicity data obtained with clodinafop-propargyl

Study	Species Strain	mg/kg bw, mg/m³, effe
Acute oral LD_{50}	Rat [redacted]	[redacted]
Acute oral LD_{50}	Mouse	> 2000 mg/kg bw



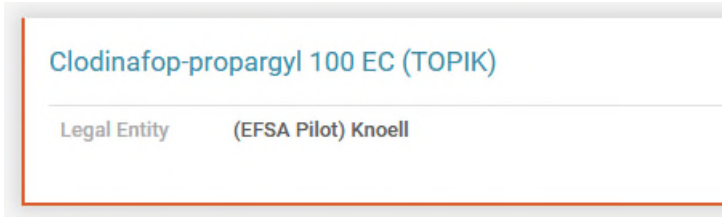
Renewal of clodinafop pesticide dossier - the same a.s. and PPP

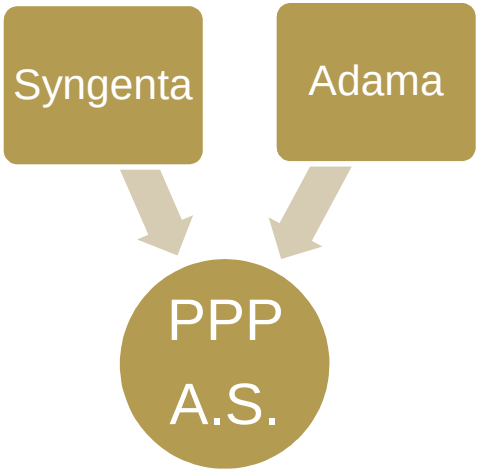
Renewal dossier: 2 dossiers were prepared in IUCLID for this Task Force:

Syngenta: based on original dossier – was updated with new data. It includes both Syngenta and Adama jointly submitted studies and Syngenta confidential data

Dossier size:

~700 MB





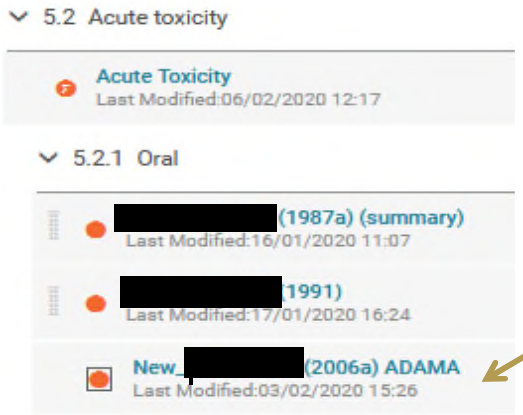
Adama: “small dossier” with only confidential data

Dossier size:

~1 MB

Syngenta dossier:
New study records for new study reports

- **Renewal dossier created** based on the original active substance dossier
- New studies and new study summaries are included in the IUCLID templates
- They can be recognised in the a.s or product dataset by 



NEW STUDY RECORD

- The endpoint summaries are revised in the existing IUCLID data set or newly created (e.g. new section on neurotox)
- Testing of selected administrative templates in accordance to EFSA administrative guidance

Annex point	Document	PPP dossier
1.10 (Cf. 1.9) Identity and content of additives (such as stabilisers)	Appendix J https://efsa.onlinelibrary.wiley.com/doi/10.2903/sp.efsa.2019.EN-1612	New document at section 1.9

Renewal dossiers – old data vs new data

- Within the current project the new studies and study summaries were separated from the data originally submitted by application of the IUCLID templates – new studies were included in the templates

- This is just workaround!

If new study reports/summaries submitted in the renewal should be clearly separated from the originally submitted data, an IT IUCLID solution is needed.

Preparation of 2 IUCLID dossiers in numbers

	Overall budget needed	Data migration	a.s. & metabolites summaries	rep. prod. summaries	Internal meetings, IUCLID handling
Initiation, verification	**~90h**				
Original dossier	**~500h**	~40h	~350h	~70h	~40h
Renewal dossier	**~250h**	~20h	~130h	~50h	~50h
Overall	**~840h**	~60h	~480h	~120h	~90h

*All provided numbers are just approximate values

knoell conclusions / recommendations

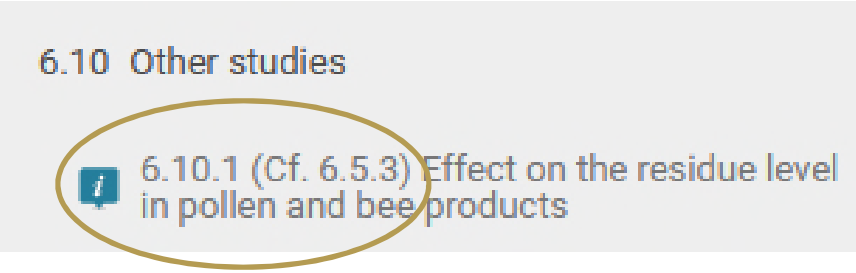
IUCLID for pesticides – it is possible!

- We were able to transfer both dossiers to IUCLID format
- All studies and summaries as well as related documents (e.g. Doc J, etc) were included in IUCLID
- Advantage of IUCLID: data entered in the relevant and define fields, or pick-list are provided in standardize formats. This allows to pull the IUCLID content by the report generator – extraction of data into word or xml format possible. This is the basis for:
  - report generator, e.g. DAR, reference lists, Summary documents e.g. Doc Ns
  - Print file
  - Completeness check/validation assisstant
  - Dissemination preview (sanitized version)
- One dossier is just one file

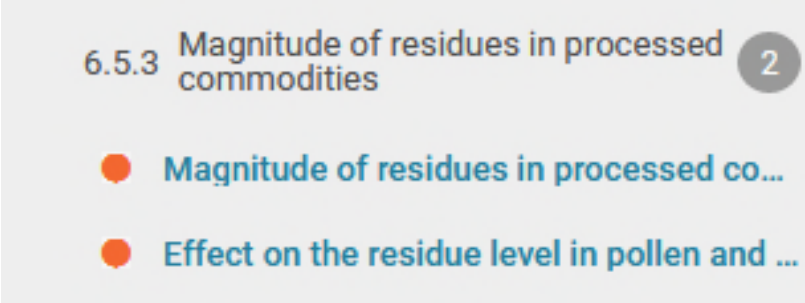
Improvements – cross-references (Cf. …)

Example: Residues / active substance dataset

Entry of study or study summary in section 6.10.1 is not possible – according to IUCLID it should be entered into section 6.5.3:



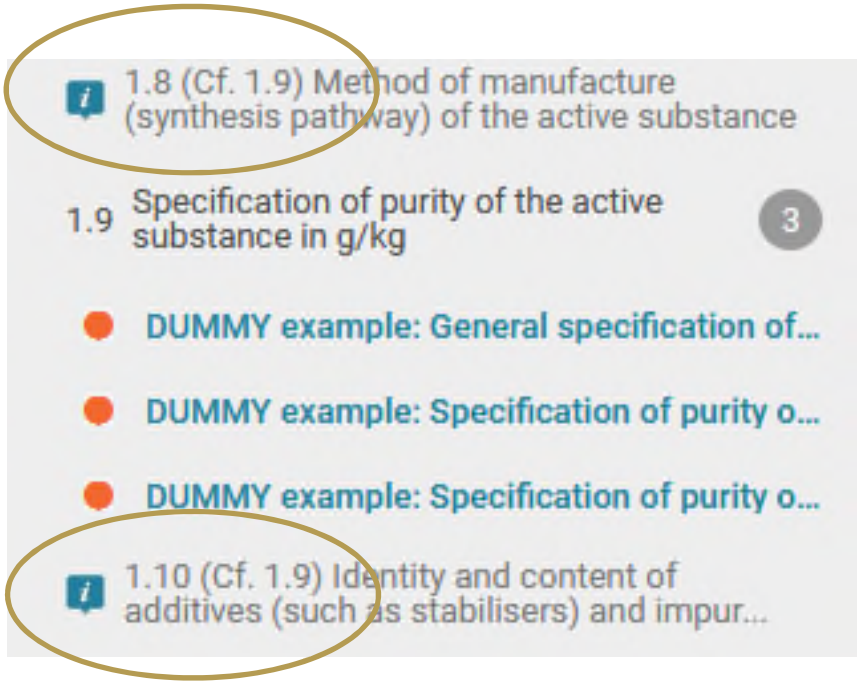
Cross reference from section 6.10.1 to section 6.5.3 does not work: As pollen and bee products are not processed commodities of crops this cross reference makes no sense.



Improvements – cross-references

Example: Identity of active substance / active substance dataset

Section 1 Identity should be developed to meet all requirements of Regulation 1107/2009. There is no possibility to present separately information on method of manufacture (CA 1.8), specification on purity (CA 1.9), information on significant and relevant impurities (1.10) and the analysis of 5 batches. The points 1.8, 1.10, 1.11 are not editable and all summaries have to be done in Point 1.9.



Improvements – IUCLID should include more subchapters according to the SANCO templates

Example: Analytical methods / PPP mixture / product dataset

Section 2, data point 2.8 technical properties: all single technical properties have to be added manually

– here knoell uses transparent record naming rules to indicate the summarized endpoint – one could imagine that every applicant can summarize the data differently if no separate IUCLID summaries are available. Also extraction of data with report generator might be problematic

Recommendation: to add in IUCLID the relevant subpoints 2.8.1 – 2.8.7

Improvements – IUCLID should include more subchapters according to the SANCO templates

Example: Tox / PPP mixture / product dataset

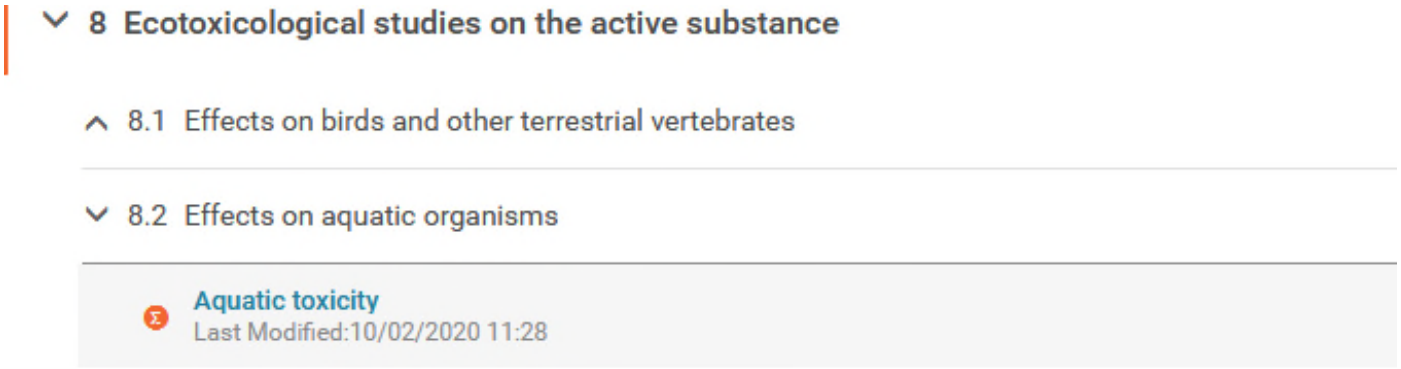
7.2 data on exposure should include subchapters as operator exposure, resident exposure, worker exposure etc.

Recommendation: to add the relevant subpoints in IUCLID

Improvements – no possibility to enter the overall endpoint summaries in some cases

- For several endpoints no overall endpoint summary can be entered.

Example: possible for section 8.2 and not possible for section 8.1 in active substance dataset



Recommendation: to include the possibility to enter the endpoint summary information

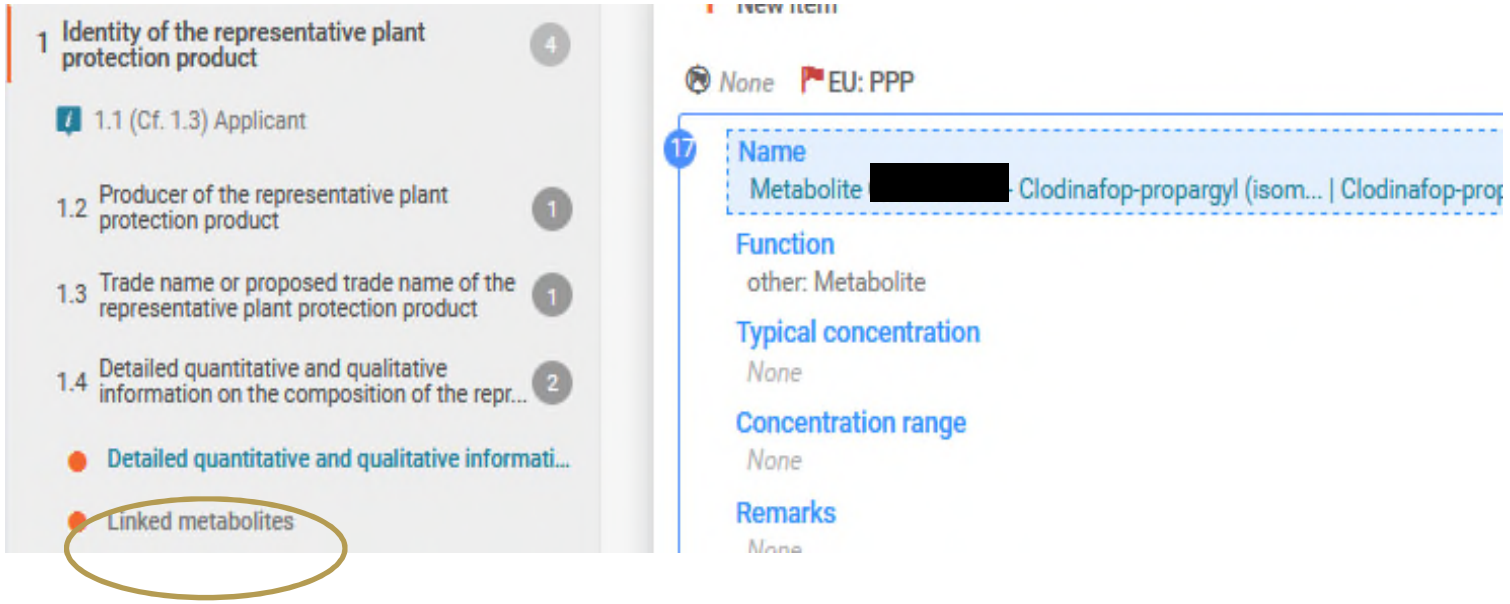
Improvements – missing endpoint summaries or study summaries

- For several endpoints the endpoint summary cannot be entered. e.g. In chapter 5.8.3 the option of a endpoint summaries should be included (potentially in relation to the ED guidance document)

- Also there is no possibility to enter study summaries in specific chapters, e.g. 7.2: If operator exposure studies or DFR studies are available these cannot be included in IUCLID as only a possibility to include an EPS in this chapter is possible

Linking of metabolites

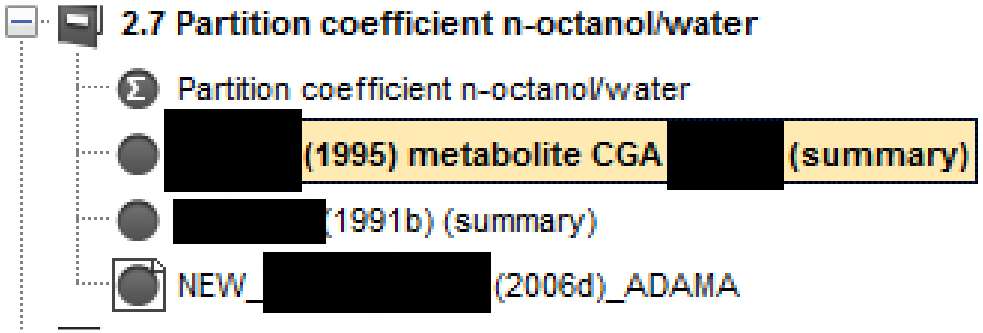
- Current linking of metabolites:



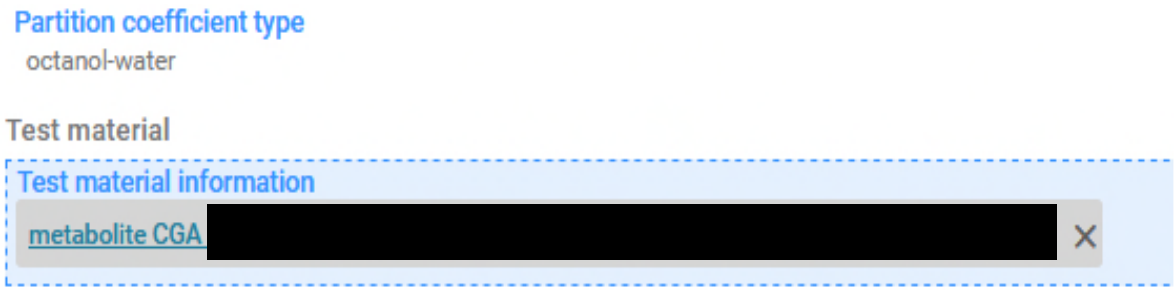
- This is workaround only!

Studies performed on metabolites and impurities - linking

- We propose to rather include this information within the active substance dataset and not in a separate dataset for each metabolite/impurity – also use assessment entities to show relation about a.s. and metabolites



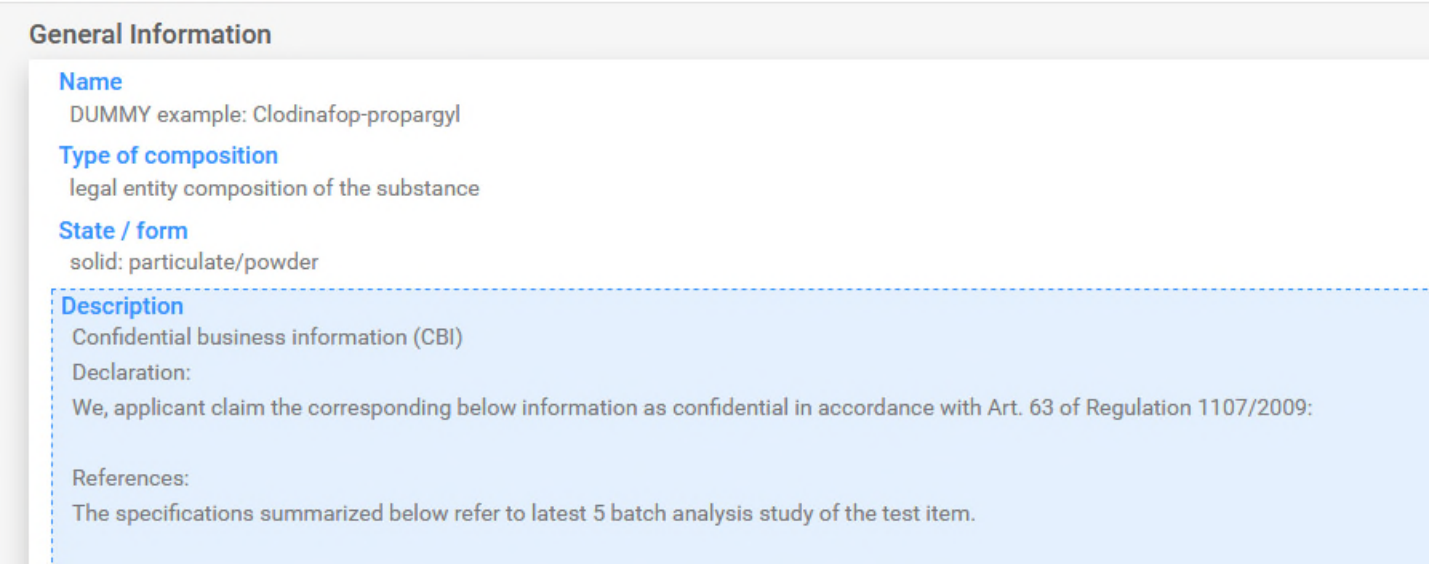
- The test material information filed in study summary informs that the metabolite was tested and not a.s.:



- Report generator could access these data

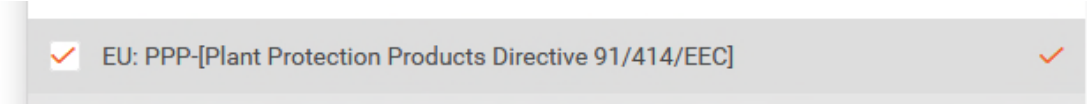
Confidentiality issues

- Clear rules, on what will be disseminated and what always kept confidential in IUCLID, are missing at the moment
- No clear view how to handle confidential data for the Task Force submissions
- In Section 1 / Data point 1.9: there is no possibility to flag all relevant information with the confidentiality flag. We can add the CBI flag separately to each constituent of the technical material and each listed impurity but one cannot flag the manufacturing process description given in the general field „Description”



Some other recommendations & problems

- **Regulatory programme** is wrong- the reference are done to old directive and not to the current regulation



- Set up of IUCLID dossiers and transfer of data to authorities by one applicant: how to handle confidential data within the **task force submission**?

- **Data protection**: the software does not give a possiblity to add the justification, why the data should be treated as protected or why they are not potected anymore.

Some other recommendations & problems

- Template for **GAP table** is not available
- **Risk assessments**: There was no possibility to report the extensive risk assessments properly. A lot of information could only be copied in endpoint summaries
- **Efficacy data**: No data available for testing. Issue that a lot of tables and text are reported.
- **Literature data**: No template was available, Proposal: set up Template in accordance to EFSA guidance (EFSA Journal 2011;9(2):2092. 49 pp.)

General conclusions

- Migration of data to IUCLID – IT solution needed – this is very time consuming

- Allow to enter 1:1 the crop dossier from SANCO templates to IUCLID summaries and endpoint summaries named in the same consistent way. If some sub-endpoints are still missing – we recommend to add them

- Organised content in IUCLID can be perfectly well used by the report generator and other plug-ins in IUCLID
  - Good example is how it is used for REACh applications – for all the registration types all plug-ins function well. CSR is automatically created and final formatting of CSR takes only approx. 4h
  - Still many improvements are needed under BPR

- **Recommendation:** Perform second test phase, after implementation of comments. If IUCLID will not include all improvements, we recommend to support applicants with more detailed IUCLID guide on how to present the data in IUCLID. One could expect that no clear rules will result in chaos of data entry.

knoell
worldwide registration

Thank you for your attention!

QUESTIONS?