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Proof of concept pesticides dossier in IUCLID format

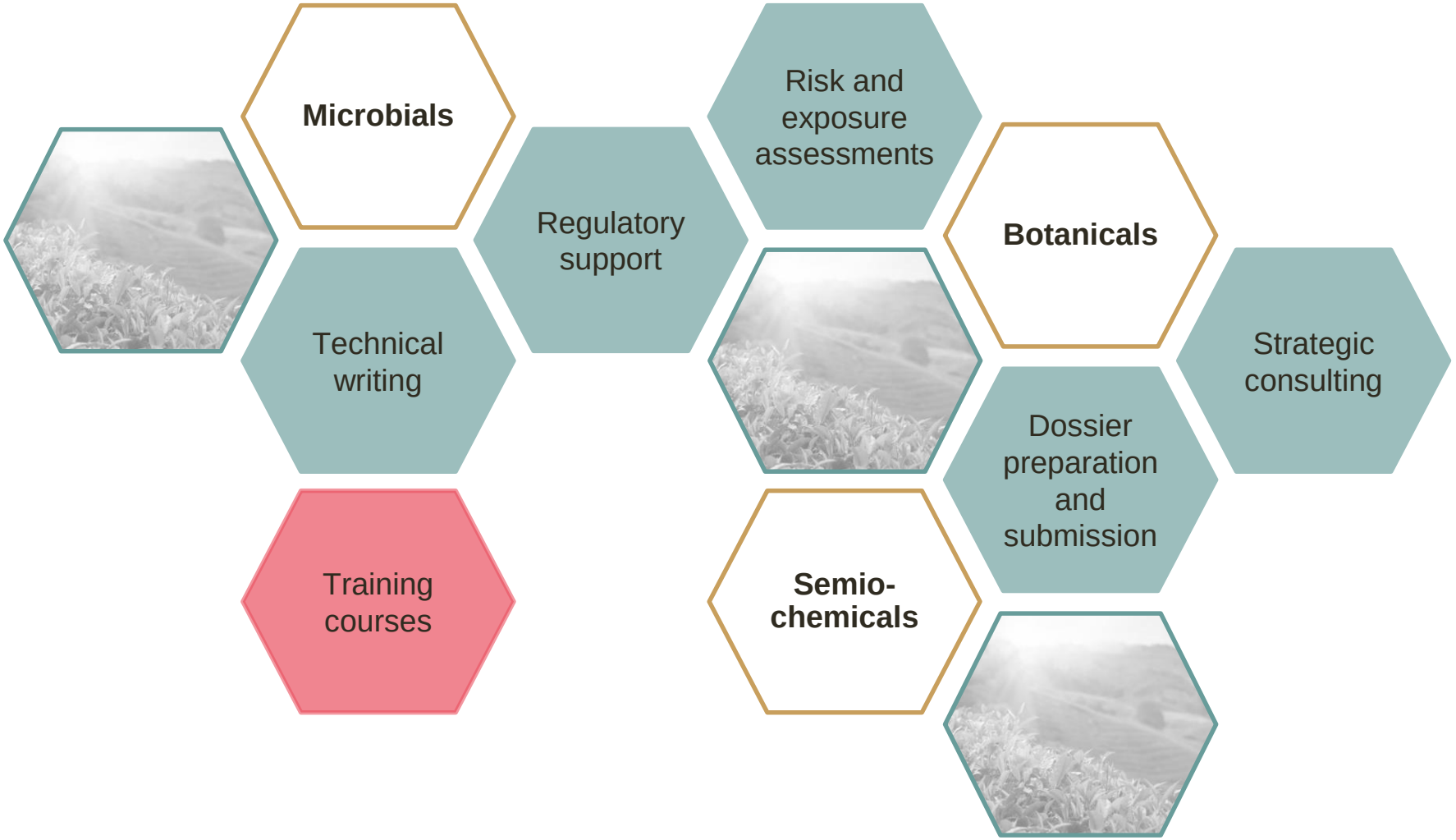
20th October 2020, ABIM conference, Katarzyna Bucior, Christin Cramm

About knoell

- Independent service provider for regulatory sciences and risk assessments for more than 20 years;
- Operating in different regulatory areas (crop protection & nutrition, import tolerance/MRLs, biocides, chemicals/REACH, cosmetics, food contact materials, medical devices, veterinary medicines);
- Privately owned company and no intentions to go public;
- Global services via our own companies (> 550 employees) and an extensive network of cooperation partners.
- Workshops & seminars (knoell academy) https://www.knoellacademy.de/en

Crop Protection - Biocontrol

From pre-submission to post-submission support…and every individual step in-between.



Aim of the EFSA project

Proof of concept pesticides dossier in IUCLID format

…to explore and examine the feasibility of preparing a pesticide dossier in IUCLID format with the aim to improve transparency and maximise access to data on chemicals and their use

- knoell's task was to test the creation and use of an active substance (renewal) dossier in IUCLID format, based on an available dossier, and provide feedback of the overall process, issues, time taken and make future recommendations for the application;

- 2 case studies: for an active substance **clodinafop** and micro-organism **Beauveria bassiana 147**;

- Further tasks included the critical assessment of the feasibility, intuitiveness, effort and benefit to all stakeholders for pesticide dossier creation using IUCLID.

Overall aim: The use of IUCLID should ease the submission and evaluation process for applicants and the relevant authorities.

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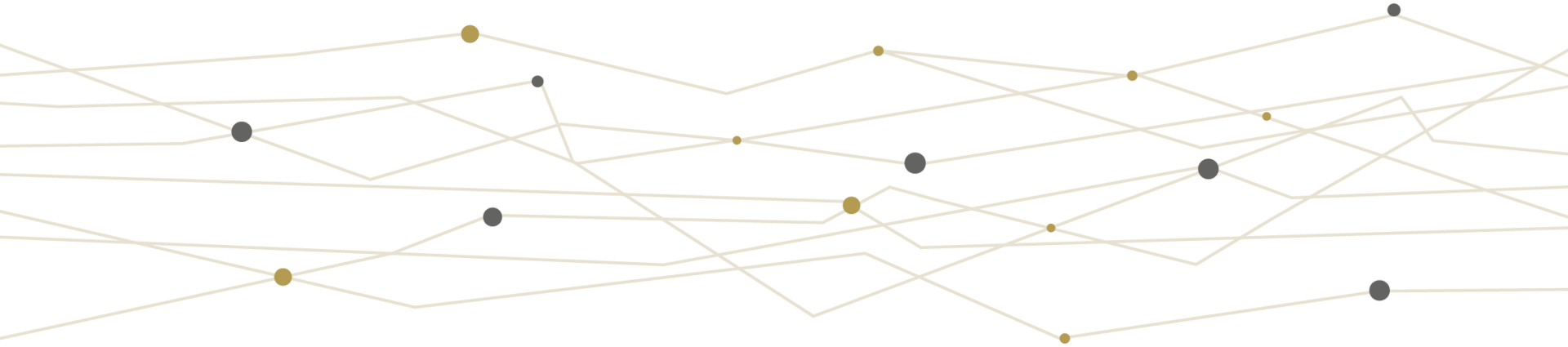

Case studies in EFSA pilot project

Case study 1: pesticide dossier

Active substance dossier for **clodinafop**:

- knoell received original a.s. dossier submitted by the applicant in 2002 in CADDY format and as well the renewal a.s. dossier submitted in 2013;
- Study summaries and reports were manually entered into IUCLID;
- **No confidential section** was provided --> some limited dummy data were used in the Identity section;
- Work was performed with IUCLID 6.4.14 on knoell server (specific testing in ECHA cloud e.g. report generator).

Case study 1: pesticide dossier in IUCLID

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Dashboard > Substances > Clodinafop-propargyl

Clodinafop-propargyl

e5fbc17b-5d6a-413e-a595-f156956a7a07

Submission Type: EU PPP Active substance information

EU PPP Active substance information

1. Identity of the active substance	8
2. Physical and chemical properties of the active substance	33
3. Further information on the active substance	8
4. Analytical methods	21
5. Toxicological and metabolism studies on the active substance	63
6. Residues in or on treated products, food and feed	56
7. Fate and behaviour in the environment	48
8. Ecotoxicological studies on the active substance	59
10. Classification and labelling of the active substance	2
11. Summary and evaluation	6

Dashboard > Mixtures / Products > Representative product

Representative product

db883e8b-e143-42be-a751-e81c1e3a8760

Submission Type: EU PPP Active substance application (representative product)

EU PPP Active substance application (representative product)

1. Identity of the representative plant protection product	4
2. Physical and chemical properties of the representative plant protection product	39
3. Data on application	9
4. Further information on the representative plant protection product	3
5. Analytical methods	5
6. Efficacy data	1
7. Toxicological studies	19
8. Residues in or on treated products, food and feed	9
9. Fate and behaviour in the environment	17
10. Ecotoxicological studies	27
12. Classification and labelling	2
13. Summary and evaluation	4

1 Identity of the representative plant protection product 4

1.1 (Cf. 1.3) Applicant

1.2 Producer of the representative plant protection product 1

1.3 Trade name or proposed trade name of the representative plant protection product 1

1.4 Detailed quantitative and qualitative information on the composition of the representative plant protection product 2

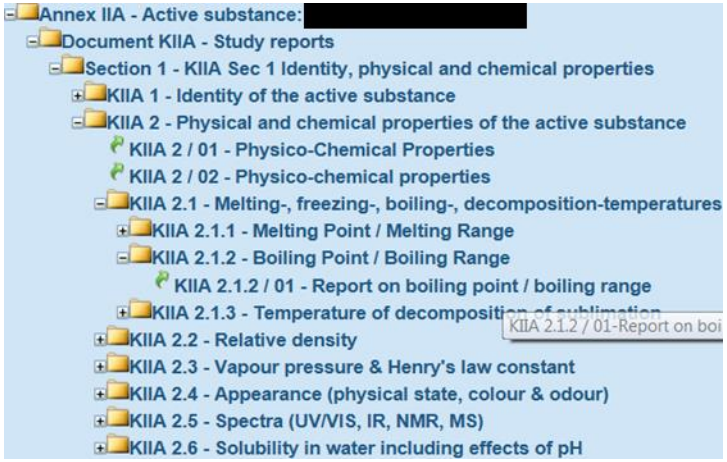
Linked metabolites

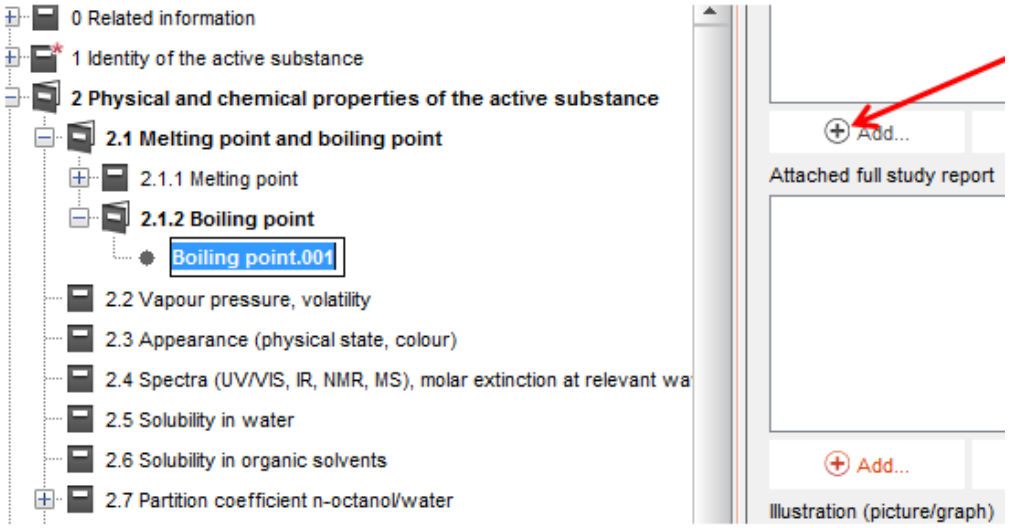
Detailed quantitative and qualitative information on the composition of

All datasets linked to the representative product dataset – the dossier is created from this file.

Preparation of the IUCLID dossier

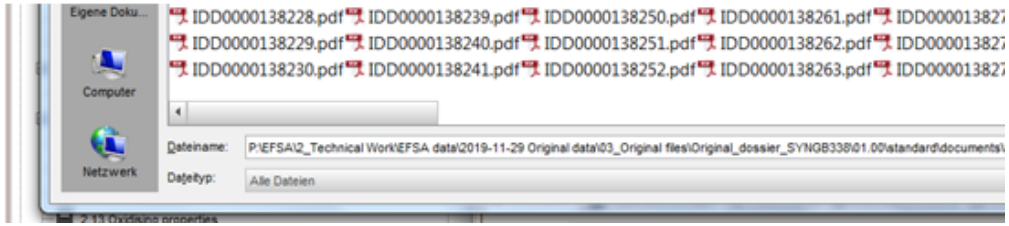
Data upload in IUCLID: all available study reports and study summaries were transferred manually from CADDY to IUCLID.





Manual migration of data is time consuming – data uploader software from CADDY to IUCLID would be very useful, also for transfer of text from M docs to IUCLID study summaries.

Choose attach full study report and enter the copied link without any cha



Case study 2: Micro-organism dossier

Dossier for ***Beauveria bassiana 147***:

- Submitted in 2013 and updated in 2014;
- **No confidential section** was provided --> some limited dummy data were used in the Identity section
  - ➢ No information on composition/metabolites is available;
- Work was performed with IUCLID 6.4.14 on knoell server (specific testing in ECHA cloud e.g. report generator);
- Data upload using individual files (word/pdf).

Micro-organism dossier preparation – Submission types

Microbial agent (MA part)

- Submission type available

EU PPP Microorganisms

1. Identity of the microorganism	4
2. Biological properties of the microorganism	5
3. Further information on the microorganism	3
4. Analytical methods	15
5. Effects on human health	20
6. Residues in or on treated articles, food and feed	6
7. Fate and behaviour in the environment	10
8. Effects on non-target organisms	21
10. Summary and evaluation	5

Microbial product (MP part)

- Submission type was not available yet (chemical PPP used instead)

EU PPP Active substance application (representative product)

1. Identity of the representative plant protection product	5
2. Physical and chemical properties of the representative plant protection product	38
3. Data on application	4
4. Further information on the representative plant protection product	2
5. Analytical methods	10
6. Efficacy data	2
7. Toxicological studies	10
8. Residues in or on treated products, food and feed	1
9. Fate and behaviour in the environment	1
10. Ecotoxicological studies	17
12. Classification and labelling	2
13. Summary and evaluation	2

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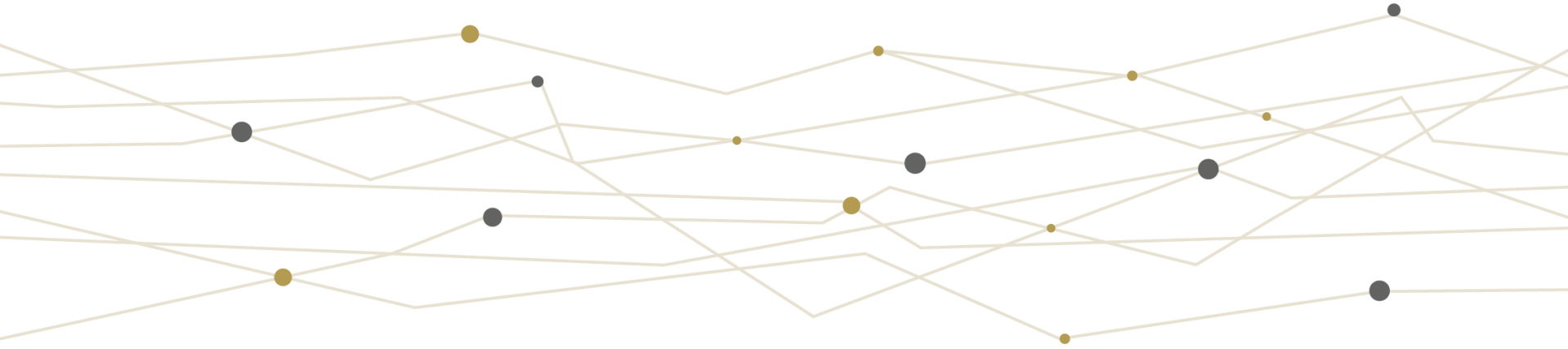


General findings

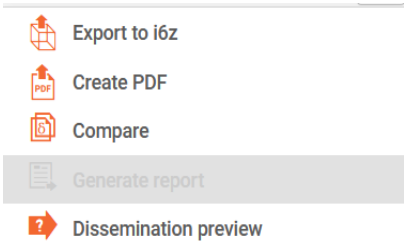
General findings for both case studies

- Preparation of the **applications for pesticides with IUCLID software is feasible** and after some improvements also considered to be suitable for an efficient collation of data in dossier format;
- **Advantage of IUCLID**: data entered in the relevant and defined fields, or pick-list are provided in **standardised formats**;
- IUCLID facilitates **simultaneous work** between various IUCLID users in cloud or server versions;
- The **annotation function** can be used during the commenting phase of the dossier evaluation;
- It was possible to use a large number of existing OHTs templates within IUCLID for the purpose of the pesticide dossier.

General findings for both case studies

- Organised content in IUCLID could be well used by **IUCLID plug-ins**:
  - Validation assistant – helpful in checking completeness of content

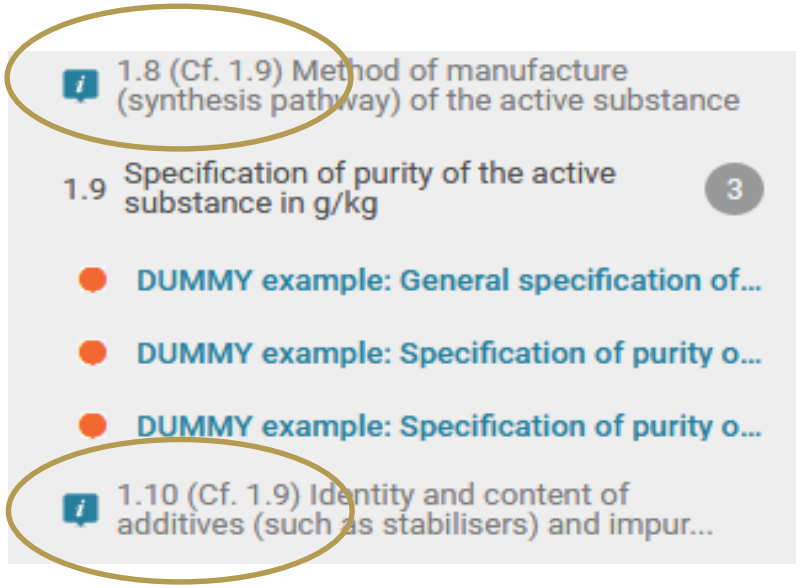
  - Report generator – to create automatically various reports, e.g. DAR, list of references
  - Dissemination preview
  - Fee calculator
  - Printing of dossier

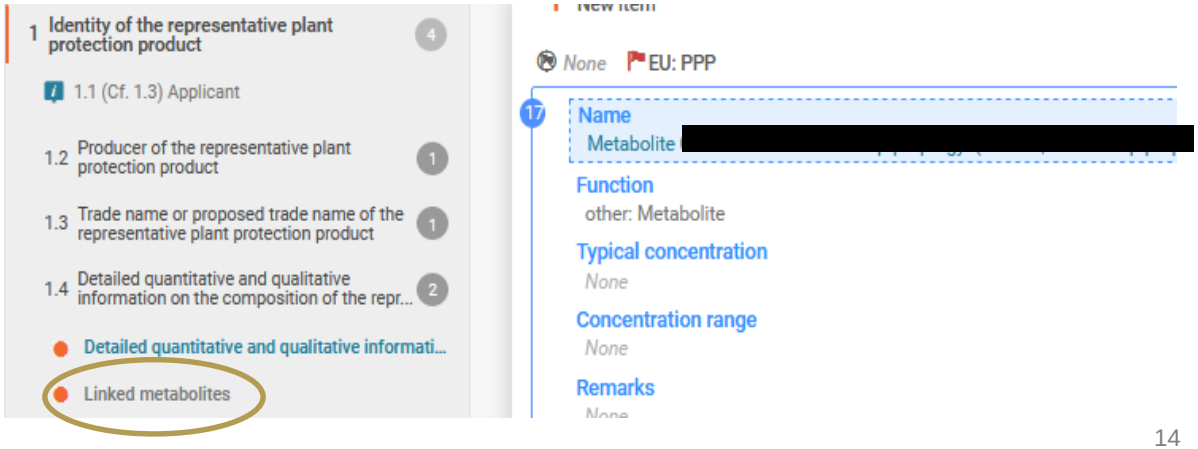


- For PPP submissions <u>important plug-ins are under development</u> – some plug-ins are expected in next IUCLID versions (e.g. 6.5 to be released at the end of October 2020)
  - REACH applications serve as a good example for using IUCLID capabilities
  - For BPR the use of plug-ins is limited.

IUCLID 6.4. weaknesses

- Some necessary **OHT templates are missing** within IUCLID;
- **Cross-references** used in IUCLID to link and guide the user to another location were somewhat burdensome;
- Presentation of data for **metabolites (or impurities)** – no dedicated solution in IUCLID 6.4.





IUCLID 6.4. weaknesses

- Template for **GAP table** was 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.);
- **Linking** of data between various datasets is not possible.

Open points – wish list for future

- Reference lists (format as given in SANCO/12580/2012– rev. 4);

Data Point	Author(s)	Year	Title Report No. Document No. Source (where different from company) GLP/ Officially recognised testing facilities[2,3] Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously used[1] Y/N If yes, for which data point?

- Indication of vertebrate study (Y/N), previously used (Y/N) and at which data point;
- Outcome of previous evaluation (see Appendix E of EFSA admin guidance): e.g. yes, evaluated and accepted …, no, not previously submitted, …
- Further possible tick boxes: study used for risk assessment, EU agreed endpoint in the context of PPP authorisations;
- More information about introduction of IUCLID, guidelines, timelines…

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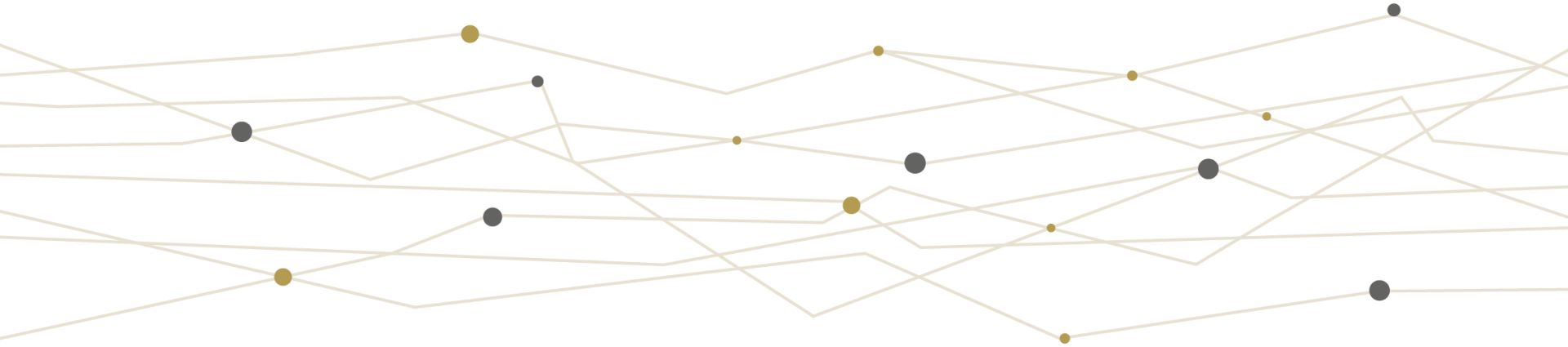
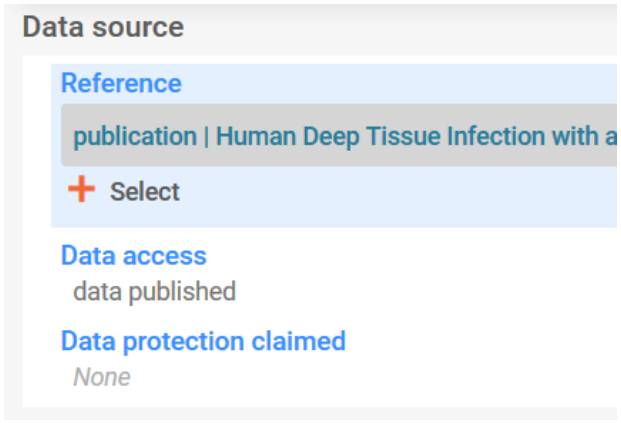
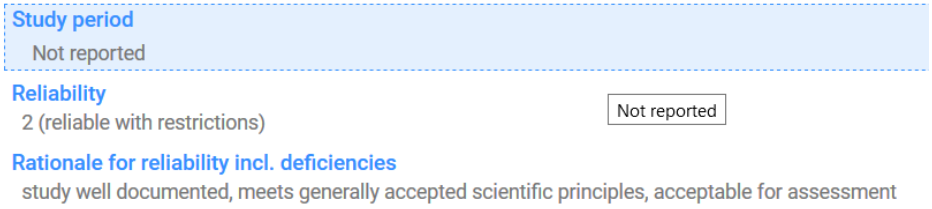


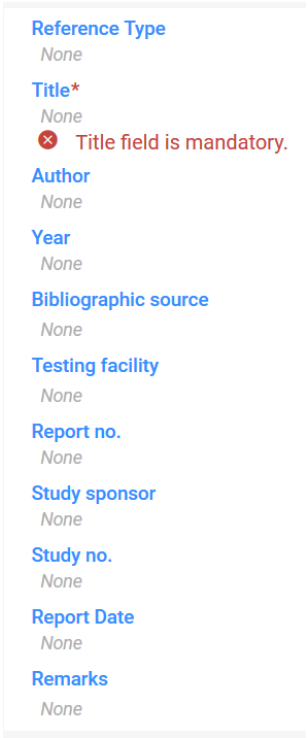
Special considerations for micro-organism dossier in IUCLID

Literature data

- Micro-organism dossier contained many literature references – IUCLID allows to enter data appropriately



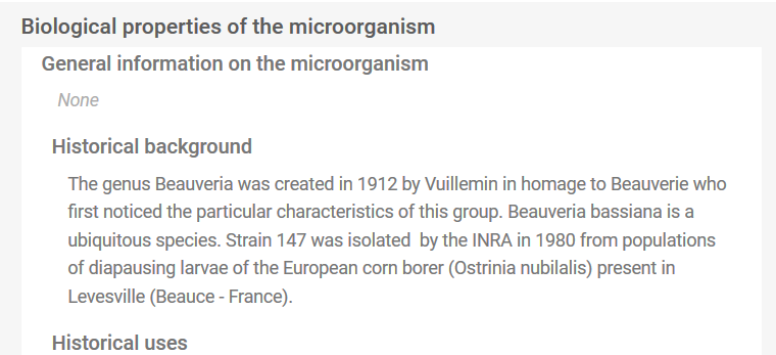




Biological properties – EU Micro-organism dataset

- Problematic presentation of biological properties in IUCLID

Study record template:



- Order of data points not in line with Reg. (EU) 283/2013
- Additional points (biocide related)
- Very difficult to find appropriate place

2.1, 2.4 , 2.6, 2.7, 2.8, 2.9, 2.5 Biological properties

Further issues

- Missing submission type for microbial (representative) product;
- Missing values, appropriate units CFU (colony forming units);

Dose descriptor	Effect level
LD50	> 1800000000 other: CFU/kg bw

- Missing appropriate guidelines for micro-organisms within specific fields such as picklists.

Test guideline + New item

#	Qualifier	Guideline	Version / remarks	Deviations
1	according to	other: EPA OPP 152A-12	1989	no

Bigger changes in IUCLID concerning PPP submissions are expected with new IUCLID 6.5 version.

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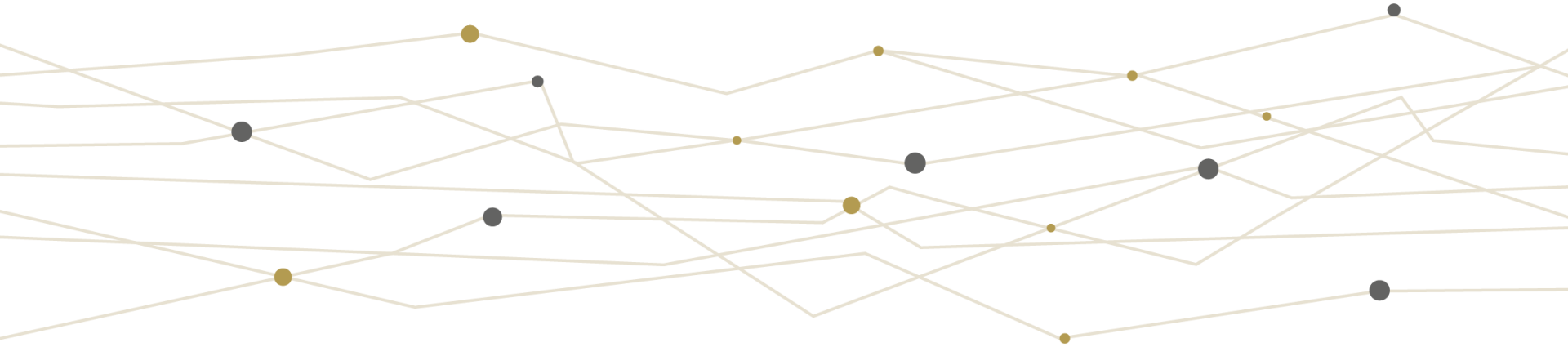

Time record

Preparation of dossier in numbers - disclaimer

- The overall time and related costs of the dossier preparation **do not fully refer to the true situation** for the following reasons:
  - The time recorded covered preparation of just one robust study summary per endpoint, whereas usually the dossiers contain more studies per endpoint that would also normally need to be summarised in the dossier;
  - The time recorded refers only to the inclusion into IUCLID of the available summaries and do not cover the scientific evaluation of the study reports. The available summaries were just transferred into IUCLID.
- We consider however that this information might be helpful as a **rough approximation of the future possible costs of the manual dossier transfer** from the current word format to the IUCLID format.

Preparation of dossier in numbers – *B. bassiana* 147

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IUCLID section	EU PPP Microorganism dataset the list of RSS & time needed*	
1. Identity of the microorganism	3 study summaries	20 h
2. Biological properties of the microorganism	3 study summaries	13 h
3. Further information on the microorganism	3 study summaries	14 h
4. Analytical methods	8 study summaries, 4 data waivings	15 h
5. Effects on human health	11 study summaries, 3 data waivings	50 h
6. Residues in or on treated products, food and feed	1 study summaries, 2 data waivings	15 h
7. Fate and behaviour in the environment	5 study summaries	12 h
8. Effects on non-target organisms	9 study summaries, 1 data waiving	17 h
Overall time	**43 study summaries, 10 data waivings: 156 h**	

IUCLID section	EU representative product dataset the list of RSS & time needed*	
1. Identity of the plant protection product	5 study summaries	9 h
2. Physical, chemical and technical properties of the plant protection product	9 study summaries, 19 data waivings	19 h
3. Data on application	4 study summaries	14 h
4. Further information on the plant protection product	2 study summaries	
5. Analytical methods	1 study summary, 7 data waivings	9 h
6. Efficacy data	1 study summary	12 h
7. Effects on human health	5 study summaries, 1 data waiving	13 h
8. Residues in or on treated products, food and feed	1 data waiving	11 h
9. Fate and behaviour in the environment	1 data waiving	7 h
10. Effects on non-target organisms	8 data waivings	12 h
Overall time	**27 study summaries, 37 data waivings: 106 h**	

* The time covered the preparation of the IUCLID study summaries, data waivings, endpoint summaries, IUCLID handling in these sections & intern communication.

Links

- Implementation of transparency regulation: https://www.efsa.europa.eu/en/stakeholders/transparency-regulation-implementation;

- Final report: Proof of concept pesticides dossier in IUCLID format, 9 July 2020 https://zenodo.org/record/3937381#.X4mm-dAzZPY

- Final report: Proof of concept pesticides dossier for micro-organism in IUCLID format, 24 July 2020 https://zenodo.org/record/4040679#.X4mnWNAzZPY

Contact us

knoell Germany GmbH

Dr. Katarzyna Bucior
Group Leader Chemistry & Analytics
Industrial Chemicals & Biocides
E-mail: kbucior@knoell.com
Tel: +49 621 718858 169

Christin Cramm
Manager Global Regulatory Affairs
Crop Protection
E-mail: ccramm@knoell.com
Tel: +49 214 20658 133

www.knoell.com