


# **Proof of concept pesticides dossier - Conclusions from building 2 dossiers**

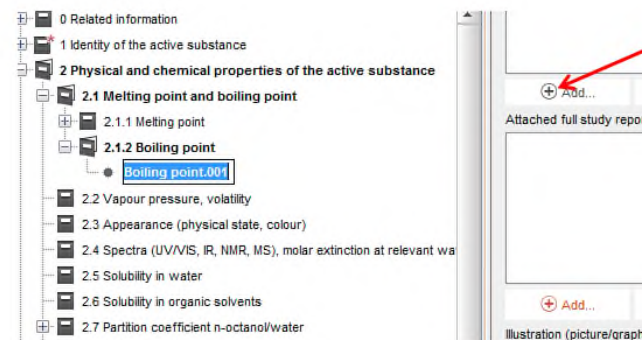
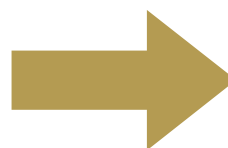
26.02.2020, Katarzyna Bucior, Christin Cramm,  
knoell Germany GmbH



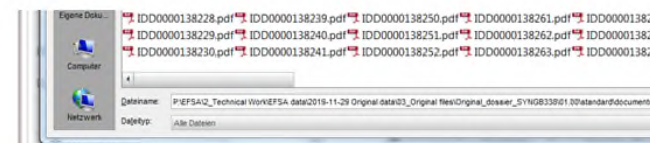
# Preparation of 2 dossiers - overview

# Preparation of the original dossier

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



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



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

## 5.3.1 Oral 28-day study

13/12/2019	28 days, rats, gavage (summary)	Last Modified: 20/02/2020 11:11
13/12/2019	28 days, rats, gavage	Last Modified: 13/12/2019 17:33
13/12/2019	28 days, rats, food	Last Modified: 13/12/2019 17:33
13/12/2019	28 days, mice, food	Last Modified: 13/12/2019 17:33
13/12/2019	28 days, dogs, food	Last Modified: 13/12/2019 17:33

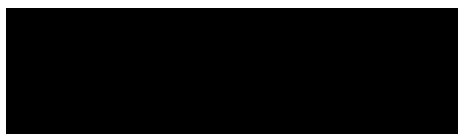
Manual migration of data is time consuming - IT data migration tool from Caddy to IUCLID would be very useful, also for transfer of text from M docs to IUCLID summaries

# 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:

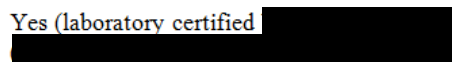


Guidelines:

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

GLP:

Yes (laboratory certified)



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

### 5.2.1 Oral

Study	●	(1987a) (summary)	Last Modified:19/02/2020 22:31
Study	●	(1991)	Last Modified:17/01/2020 16:24

- 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/m <sup>3</sup> , effe
Acute oral LD <sub>50</sub>	Rat 	
Acute oral LD <sub>50</sub>	Mouse	> 2000 mg/kg bw

### 5.2 Acute toxicity

Σ	Acute Toxicity	Last Modified:06/02/2020 12:17
---	----------------	--------------------------------

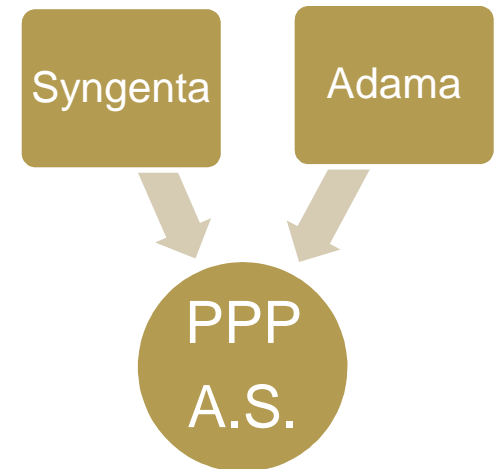
# Renewal of clodinafop pesticide dossier - the same a.s. and PPP

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

Clodinafop-propargyl 100 EC (TOPIK)	
Legal Entity	(EFSA Pilot) Knoell




**Adama:** “small dossier” with only confidential data

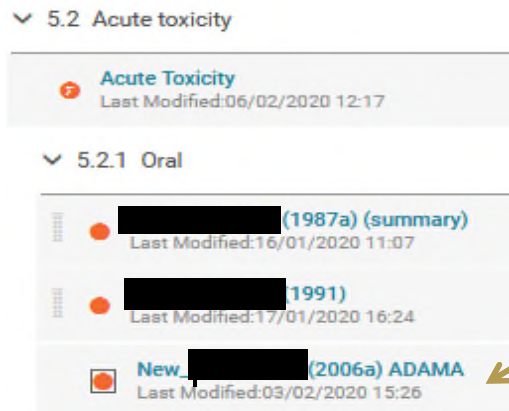
**Dossier size:**  
~1 MB

ADAMA Clodinafop-propargyl	
Legal Entity	(EFSA Pilot) Knoell

# 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 <a href="https://efsa.onlinelibrary.wiley.com/doi/10.2903/sp.efsa.2019.EN-1612">https://efsa.onlinelibrary.wiley.com/doi/10.2903/sp.efsa.2019.EN-1612</a>	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

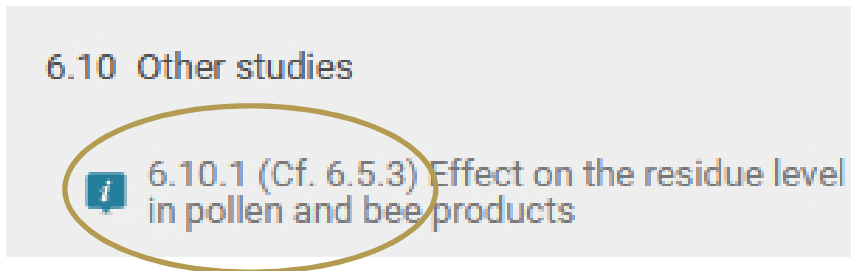
# IUCLID for pesticides – it is possible!

- 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 assistant
  - Dissemination preview (sanitized version)
- One dossier is just one file

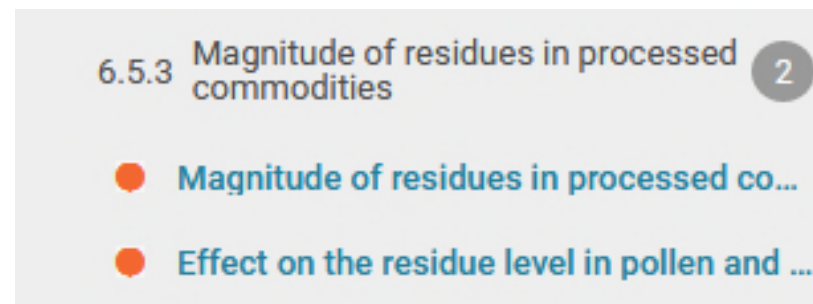
# Improvements – cross-references (Cf. ...)

## 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.

**1.8 (Cf. 1.9) Method of manufacture (synthesis pathway) of the active substance**

**1.9 Specification of purity of the active substance in g/kg** 3

- DUMMY example: General specification of...**
- DUMMY example: Specification of purity o...**
- DUMMY example: Specification of purity o...**

**1.10 (Cf. 1.9) Identity and content of additives (such as stabilisers) and impur...**

# 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

▼ 2.8 Technical characteristics of the representative plant protection product

2.8.1	2.8.1 Wettability_data waiving Last Modified:23/01/2020 18:31
2.8.2	2.8.2 Persistent foaming NOT SUBMITTED FOR RENEWAL [REDACTED] (1999) (summary) Last Modified:23/02/2020 20:53
2.8.2	2.8.2 Persistent foaming NEW_Gerhardt P. (2004) Last Modified:14/02/2020 08:27
2.8.3.1	2.8.3.1 Suspensibility_data waiving Last Modified:23/01/2020 18:31

– 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.

### ▼ 7.2 Data on exposure

Endpoint Summary	Last Modified:21/02/2020 09:12
NOT SUBMITTED FOR RENEWAL [REDACTED] (1995)	Last Modified:13/12/2019 17:33
NOT SUBMITTED FOR RENEWAL [REDACTED] (1994)	Last Modified:13/12/2019 17:33
NOT SUBMITTED FOR RENEWAL [REDACTED] (1993)	Last Modified:13/12/2019 17:33
Exposure related observations in humans	Last Modified:20/02/2020 10:55

**Recommendation: to add the relevant subpoints in IUCLID**

- ## 8 Ecotoxicological studies on the active substance

### 8.1 Effects on birds and other terrestrial vertebrates

## 8.2 Effects on aquatic organisms

### Aquatic toxicity

Last Modified:10/02/2020 11:28

15

# 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)

## ▼ 5.8.3 Endocrine disrupting properties

+ New ▼ 5

+ New document

📄 Copy from existing

 **New\_EPS Endocrine disrupting properties**  
Last Modified:11/02/2020 12:52

 **New\_ [REDACTED] (2015) NO REPORT**  
Last Modified:03/02/2020 14:55

- 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

## ▼ 7.2 Data on exposure

+ New ▼ 5

+ New document

📄 Copy from existing

Endpoint Summary  
Last Modified:21/02/2020 09:12

NOT SUBMITTED FOR RENEWAL\_ [REDACTED] (1995)  
Last Modified:13/12/2019 17:33



# Linking of metabolites

- Current linking of metabolites:

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 repr... (2)

Detailed quantitative and qualitative informati...

Linked metabolites

NEW ITEM

None EU: PPP

17

Name  
Metabolite [redacted] Clodinafop-propargyl (isom... | Clodinafop-propargyl)

Function  
other: Metabolite

Typical concentration  
None

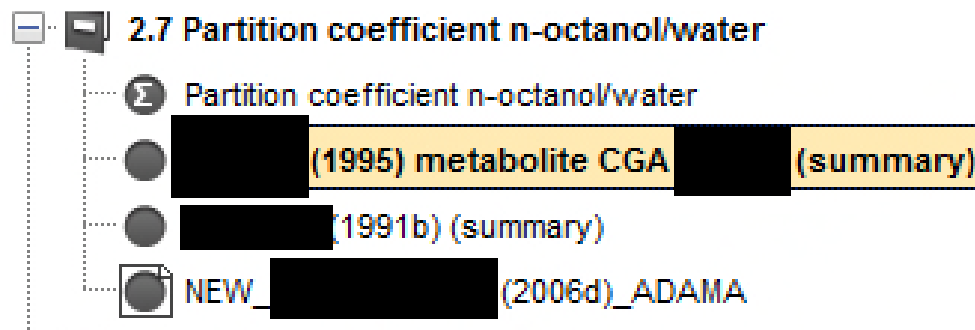
Concentration range  
None

Remarks  
None

- 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.:

Partition coefficient type  
octanol-water

Test material

Test material information

metabolite CGA [REDACTED] X

- 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”

## General Information

### Name

DUMMY example: Clodinafop-propargyl

### Type of composition

legal entity composition of the substance

### State / form

solid: particulate/powder

### Description

Confidential business information (CBI)

Declaration:

We, applicant claim the corresponding below information as confidential in accordance with Art. 63 of Regulation 1107/2009:

References:

The specifications summarized below refer to latest 5 batch analysis study of the test item.

# Some other recommendations & problems

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

✓ EU: PPP-[Plant Protection Products Directive 91/414/EEC] ✓

- 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 possibility to add the justification, why the data should be treated as protected or why they are not protected 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.

**Thank you for your  
attention!  
QUESTIONS?**