Changes to OHTs

TG IUCLID

26&27 FEB 2020

Toxicity to Terrestrial Arthropods OHT 50.2

Modifications to OHT needed and separate summary documents for Bees and Other Non-target Arthropods

- Bees (pollinators)
  - Tier I - LD_{50} and NOED values and potentially differentiate between the types of test i.e. acute oral, acute contact, chronic and the species
    (separate section or separate summary)
  - Tier II / III – could have a field / fields to indicate the major effects e.g. mortality, behaviour, brood development but also could just have the standard text fields (Key Information, Additional information)
    (separate section or separate summary)
- Non-target arthropods
  - Tier I EC_{50}, LR_{50}, ER_{50} values (separate section or separate summary)
  - Tier II / III EC_{50}, $LR5_{0}$, ER_{50} values (separate section or separate summary)

Proposal by NZ for Review

Effectiveness against target organisms and intended uses OHT 88

- Target organisms: use of EPPO codes
- Function addressed: add new terms e.g. plant growth regulators
- Product types: how to harmonise between Biocides and Pesticides?
- Method of application: add terms starting from application methods in EFSA guidance
- Mode of action: add new terms (see HRAC, FRAC, IRAC, other)
- Details on application: link to GAP of intended use
- Is an additional summary document needed?

Guidance on Pesticides Exposure Assessment of Operators, Workers, Residents and Bystanders (Under review)

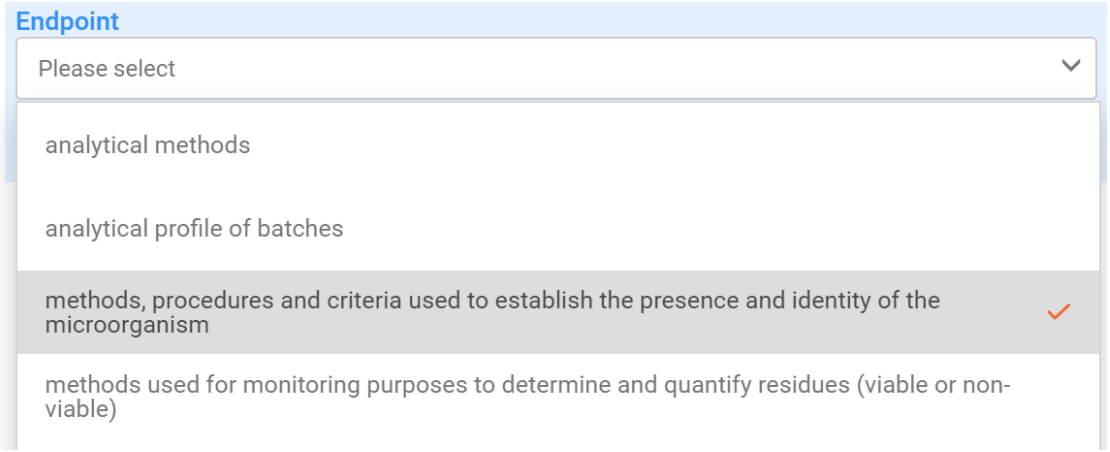
Efficacy data OHT 89

- Check latest EPPO guidelines are included in the Guidelines list
- Research facility / Officially Recognised Organisation for conducting field trials (NoS?)
- Efficacy assessment and minimum effective dose tables to be revised (including units)
- Method of application: link to GAP information

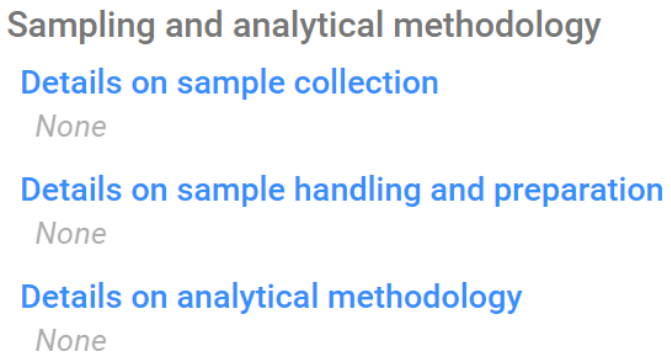
Alignment with EPPO Database on PP1 Standards - Efficacy Evaluation of Plant Protection Products?

AnalyticalMethods (OHT 87)

SECTION 4.	***Analytical methods***
Introduction	
4.1.	Methods used for the generation of pre-approval data
4.1.1.	Methods for the analysis of the active substance as manufactured
4.1.2.	Methods for risk assessment
4.2.	Methods for post-approval control and monitoring purposes

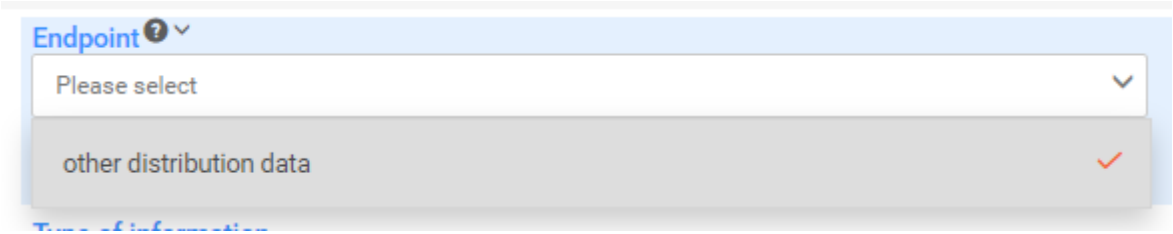


Need to link analytical methods in studies?



Appendix D - Template for the overview table for analytical methods used for risk assessment

Other Distribution Data (OHT 37)



Add endpoints

7.1.4.1. Column leaching studies

7.1.4.1.1. Column leaching of the active substance

7.1.4.1.2. Column leaching of metabolites, breakdown and reaction products

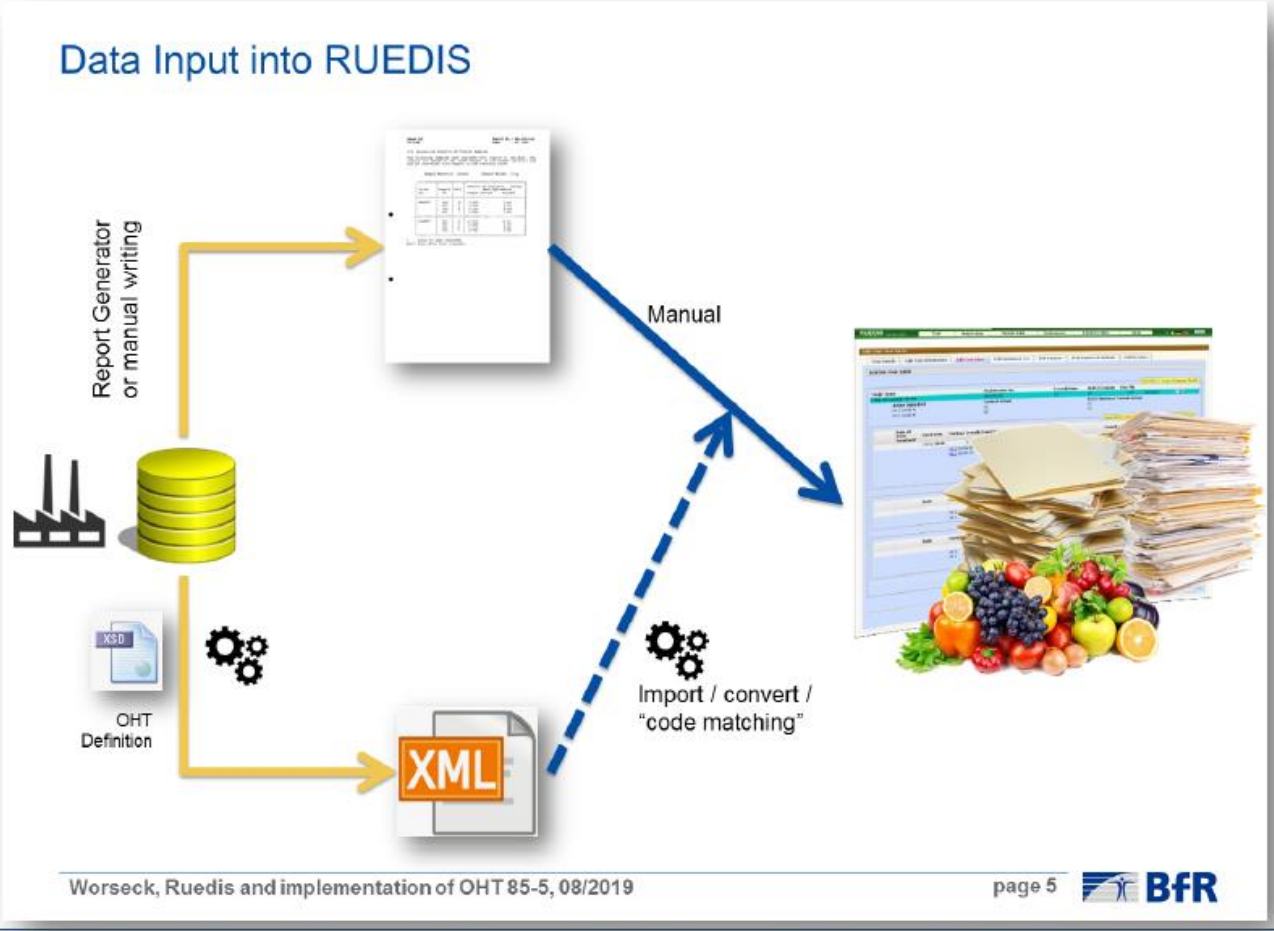
7.1.4.2. Lysimeter studies

7.1.4.3. Field leaching studies

The template is very basic – the POC dossier provides examples of how the information should be presented

The OHT 85-5 project

Project partner have interest to support this project and to build up an informational flow for residue data on the raw data level



Guidelines added for the EU PPP Microorganisms (substance)

- OPPTS 885.3050 Acute Oral Toxicity/Pathogenicity (EPA 712–C–96–315)
- OPPTS 885.3100 Acute Dermal Toxicity/Pathology (EPA 712–C–96–316)
- OPPTS 885.3150 Acute Pulmonary Toxicity/Pathogenicity (EPA 712–C–96–318)
- OPPTS 885.3200 Acute Injection Toxicity/Pathogenicity (EPA 712–C–96–318)
- OPPTS 885.3650 Reproductive/Fertility Effects (EPA 712–C–96–324)
- OPPTS 885.3500 Cell Culture (EPA 712–C–96–321)
- OPPTS 885.3600 Subchronic Toxicity/Pathogenicity (EPA 712–C–96–232)

Changes to other IUCLID documents and proposal for new summary records

Summary records – level of granularity

Option 1

ENDPOINT_SUMMARY_RECORD.PredictedEnvironmentalConcentrations

Option 2

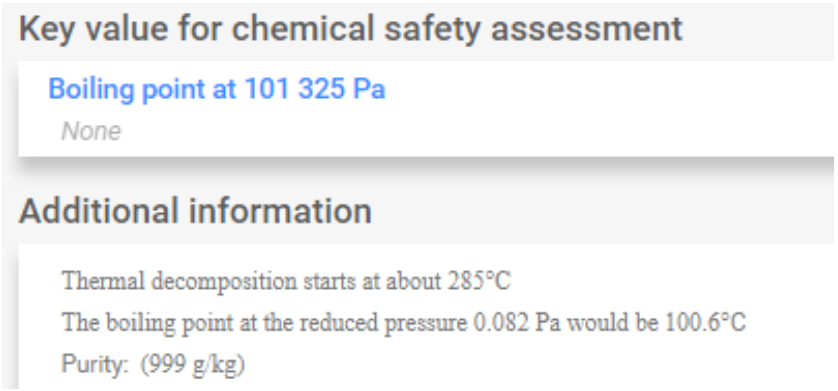
ENDPOINT_SUMMARY_RECORD.PredictedEnvironmentalConcentrationsSoil

ENDPOINT_SUMMARY_RECORD.PredictedEnvironmentalConcentrationsWater

ENDPOINT_SUMMARY_RECORD.PredictedEnvironmentalConcentrationsAir

Boiling Point 2.1.2 (AS)

- New summary for the Sublimation temperature (OR extension of the existing summary for the Boiling point)



Toxicological and metabolism studies on the active substance 5 (AS)

Description of key information

ADI = 0.003 mg/kg bw/day (2 year rat, oral)

No change is proposed from the existing EU end-point value of 0.003 mg/kg body weight/day for clodinafop.

AOEL = 0.026 mg/kg bw/day (1 year dog, oral)

No change is proposed from the existing EU end-point value of 0.026 mg/kg body weight/day for clodinafop.

ARfD = 0.25 mg/kg bw/day (2 -generation reproduction and dev tox in rat)

No change is proposed from the existing EU end-point value of 0.05 mg/kg body weight/day for clodinafop.

Can this be derived from sub section summaries?

AcuteToxicity 5.2

Parameter	Species	Result	Classification according to Regulation (EC) No.1272/2008
Acute oral LD50 [xxx, 1987a]	Rat	>1829 mg/kg bw (males 1392 mg/kg bw, females 2271 mg/kg bw)	H302
Acute oral LD50 [xxx, 2006a]	Rat	>2000 mg/kg bw (males and females)	None
Acute oral LD50 [xxx, 1991]	Mouse	>2000 mg/kg bw	None
Acute dermal LD50 [xxx, 2006b]	Rat	>2000 mg/kg bw	None
Acute dermal LD50 [xxx, 1987b]	Rat	>2000 mg/kg bw	None
Acute inhalation [xxx, 1987c]	Rat	>2.325 mg/L (maximum attainable concentration)	None
Acute skin irritation [xxx, 1987a]	Rabbit	Non irritating	None
Acute skin irritation [xxx, 2006a]	Rabbit	Non irritating	None
Acute eye irritation [xxx, 1987b]	Rabbit	Non- irritating	None
Acute eye irritation [xxx, 2006b]	Rabbit	Non- irritating	None
Skin sensitisation [xxx, 1987]	Guinea Pigs	Sensitiser	H317
Skin sensitisation [xxx, 2006c]	Guinea Pigs	Non-sensitiser	None
Phototoxicity [xxx, 2014]	In vitro 3T3 NRU Phototoxicity Test	Not phototoxic	None

Add Key value for chemical safety assessment for acute endpoints skin irritation, eye irritation and skin sensitisation

New summary needed in section 5.5 (AS) or Amendment of Carcinogenicity 5.5.2

Long-term toxicity and carcinogenicity (Regulation (EU) N°283/2013, Annex Part A, point 5.5)

Long-term effects (target organ/critical effect)	Rat & mouse: liver (increased ALT/AST and hepatocellular hypertrophy)	[redacted]
Relevant long-term NOAEL	2-year, rat: 3 mg/kg bw per day 18-month, mouse: 10 mg/kg bw per day	
Carcinogenicity (target organ, tumour type)	Rat: benign liver tumours Mouse: no tumours *Substance* is unlikely to pose a hazard to humans	[redacted]
Relevant NOAEL for carcinogenicity	2-year, rat: 3 mg/kg bw per day; 18-month, mouse: 10 mg/kg bw per day	

Nature of residues and methods of analysis in livestock 6.4 (AS)

Livestock (available studies)	Animal	Dose (mg/kg bw/d)	Duration (days)	Comment/Source
	Laying hen			
	Lactating ruminants			e.g. Goat, cow, sheep
	Pig			
	Fish			

Time needed to reach a plateau concentration in milk and eggs (days)	Milk:	Comment
	Eggs:	Comment
Metabolism in rat and ruminant similar	yes/no/inconclusive/not triggered	Comment
Can a general residue definition be proposed for animals?	yes/no/inconclusive/not triggered	Comment
Animal residue definition for monitoring (RD-Mo)	<RD> (tentative) [metabolism group 1/tissue]: <RD> [metabolism group 2/tissue]: <RD>	
Animal residue definition for risk assessment (RD-RA)	<RD> (tentative) [metabolism group 1/tissue]: <RD> [metabolism group 2/tissue]: <RD>	
Fat soluble residues		
Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)		

Modification of AdditionalInformationOnResiduesInFoodAndFeedingstuffs?

Animal burden calculation

"OECD Guidance Document, Series on testing and assessment No 64 and Series on pesticides No 32" and "OECD Guidance Document on Residues in livestock, Series on Pesticides No 73"

Cattle						Sheep					
Beef	500 kg 12 kg		Dairy	650 kg 25 kg		Ram/Ewe	75 kg 2.5 kg		Lamb	40 kg 1.7 kg	
	mg/kg bw/d	%		mg/kg bw/d	%		mg/kg bw/d	%		mg/kg bw/d	%
	mg/kg bw/d			mg/kg bw/d			mg/kg bw/d			mg/kg bw/d	

ExpectedExposureAndProposedAcceptableResidues 6.9 (AS)

ADI	X mg/kg bw per day (source)
TMDI according to EFSA PRIMo	Highest TMDI: XX% ADI (MS, diet)
NTMDI, according to (to be specified)	Highest NTMDI: XX% ADI (MS, diet)
Highest IEDI, according to EFSA PRIMo (rev.x)	**Scenario 1 without risk mitigation measures:** xx% ADI (diet) Contribution of crops assessed: Crop1: x% of ADI Crop2: x% of ADI Crop3: x% of ADI **Scenario 2 with risk mitigation measures:** 36% ADI (diet) Contribution of crops assessed: Crop1: x% of ADI Crop2: x% of ADI Crop3: x% of ADI
NEDI (% ADI), according to (to be specified)	Highest NEDI: XX% ADI (MS, diet)

Pesticide Residue Intake Model- EFSA PRIMo revision 3.1

Proposed residue definitions and maximum residue levels 6.7 (AS)

Commodity	Region/ Indoor [a]	Residue levels observed in the supervised residue trials (mg/kg)	Comments/Source	Calculated MRL (mg/kg)	HR [b] (mg/kg)	STMR [c] (mg/kg)	CF [d]
Intended uses in MRL application							
	NEU	**Mo:** - **RA:** -	Residue trials on <crop> compliant with GAP. Reduced number of trials is sufficient since, also considering metabolism studie(s), a zero residue situation is expected.				
	NEU	**Mo:** - **RA:** -					
Summary of data on residues in pollen and bee products (Regulation (EU) No 283/2013, Annex Part A, point 6.10.1)							
	NEU	**Mo:** - **RA:** -					

* Indicates that the MRL is proposed at the limit of quantification.

Mobility in Soil 7.1 (AS)

Mobility in soil column leaching active substance (Regulation (EU) N° 283/2013, Annex Part A, point 7.1.4.1.1 and Regulation (EU) N° 284/2013, Annex Part A, point 9.1.2.1)

Column leaching

Elution (mm): *x* mm Time period (d): *x* d
Leachate: *x* % total residues/radioactivity in leachate *x* % active substance, *x* % *Met I*,… *x* % *Met VII* >*x* % total residues/radioactivity retained in top *x* cm Koc (mL/g) =*(When it has not been possible to determine it by batch sorption experiments).*

Mobility in soil column leaching transformation products (Regulation (EU) N° 283/2013, Annex Part A, point 7.1.4.1.2 and Regulation (EU) N° 284/2013, Annex Part A, point 9.1.2.1)

Column leaching

Elution (mm): *x* mm Time period (d): *x* d
Leachate: *x* % total residues/radioactivity in leachate *x* % active substance, *x* % *Met I*,… *x* % *Met VII* >*x* % total residues/radioactivity retained in top *x* cm Koc (mL/g) =*(When it has not been possible to determine it by batch sorption experiments).*

Location:

Study type (e.g. lysimeter, field): *lysimeter*

Soil properties: texture, pH = , OC= , MWHC =

Dates of application :

Crop : /Interception estimated:

Number of applications: **x** years, **x** applications per year

Duration.

Application rate: **x** g/ha/year

Average annual rainfall (mm): **x** mm

Average annual leachate volume (mm): **x** mm

% radioactivity in leachate (maximum/year): **x** % AR

Individual annual maximum concentrations (e.g. 1st, 2nd, 3rd yr): **x** µg/L active substance, **x** µg/L *Met I*, …*x*µg/L *Met VII*. Unidentified radioactivity, no of components, *x* µg/L parent equivalents.

Individual annual average concentrations (e.g. 1st, 2nd, 3rd yr): *x* µg/L active substance, *x* µg/L *Met I, x*µg/L … *Met VII*. Unidentified radioactivity, no of components, *x* µg/L parent equivalents.

Amount of radioactivity in the soils at the end of the study = % AR; *XX* % AR as parent, *XX* % AR as *Met X*

BiodegradationInWaterAndSedimentSimulationTests 7.2.2.3 (AS)

Water / sediment study (Regulation (EU) N° 283/2013, Annex Part A, point 7.2.2.3 and Regulation (EU) N° 284/2013, Annex Part A, point 9.2.2)

Parent	Distribution (*e.g. max in water x after n d. Max. sed x % after n d*)									
Water / sediment system	pH water phase	pH sed [a)]	t. °C	DT_{50} /DT_{90} whole sys.	St. (χ^2)	DT_{50} /DT_{90} water	St. (χ^2)	DT_{50} /DT_{90} sed	St. (χ^2)	Method of calculation
Geometric mean at 20°C[b)]										

[a)] Measured in [medium to be stated, usually calcium chloride solution or water]
[b)] Normalised using a Q10 of 2.58

Fate and behaviour in air 7.3 (AS)

Direct photolysis in air	*Not studied - no data requested* *or* *@Latitude: ..... Season: ..... DT_{50}.....*
Photochemical oxidative degradation in air	DT_{50} of *x* hours derived by the Atkinson model (version *x.x*). OH (*12 or 24 h*) concentration assumed = *xxx*
Volatilisation	from plant surfaces (BBA guideline): *<x* % after *x* hours
	from soil surfaces (BBA guideline): *negligible after x hours*
Metabolites	

7.3.3. ***Local and global effects***

For substances that are applied in high amounts, the following effects shall be considered:

- global warming potential (GWP);
- ozone depleting potential (OPD);
- photochemical ozone creation potential (POCP);
- accumulation in the troposphere;
- acidification potential (AP);
- eutrophication potential (EP).

Transport by Air in case of highly volatile substances?

Definition of the residue (soil) 7.4 (AS)

Definition of the residue for monitoring (Regulation (EU) N° 283/2013, Annex Part A, point 7.4.2) Ecotoxicologically relevant compounds[1]

Compartment	
soil	Parent (state name), Metabolite 1 (state name)
water	Parent (state name), Metabolite 1 (state name)
sediment	Parent (state name), Metabolite 1 (state name)
groundwater	Parent (state name), Metabolite 1 (state name)

[1] metabolites are considered relevant when, based on the risk assessment, they pose a risk comparable or higher than the parent

EcotoxicologicalInformation 8.1 (AS)
(plus summary for birds and summary for mammals)

Acute risk assessment

Acute risk is assessed by comparing the relevant DDD from Table 10.1-4 with the appropriate LD50endpoint (summarised in Table 10.1-2) to give an acute Toxicity: Exposure Ratio (TERA):

The resulting TERAvalues for each crop grouping are given in the table below.

Table 10.1.1-7: Screening step - Acute risk (TERA) to birds fromclodinafop

Test substance	Crop group	Indicator species	LD50 (mg a.s./kg bw)[a]	DDD (mg a.s./kg bw/day)	TERA
Clodinafop	Cereals	Small omnivorous bird	[redacted]		

[a]Based on the geometric mean of acute toxicity studies conducted with the mallard duck,bobwhite quailand the canary

Hazard for terrestrial organisms

Soil

Hazard assessment conclusion

None

PNEC value

None

Assessment factor

None

Extrapolation method

None

Explanation for hazard conclusion

None

Marine water

Hazard assessment conclusion

None

PNEC value

None

Assessment factor

None

Extrapolation method

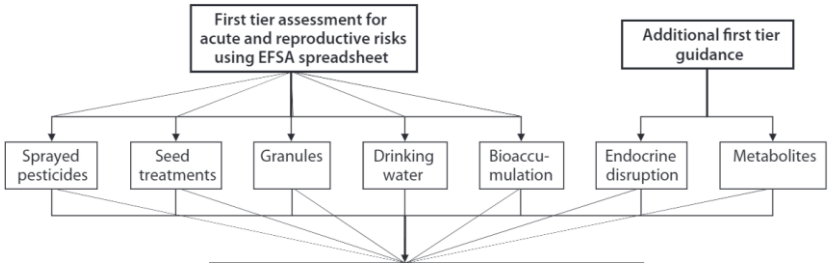
None

PNEC marine water (intermittent releases)

None

Explanation for hazard conclusion

None



Risk Assessment for Birds and Mammals

Endocrine Disruptors 8.1.5 (AS)

Table 3: Selection of relevant scenario

Adversity based on T-mediated parameters	**Positive mechanistic OECD CF level 2/3 Test**	**Scenario**	**Next step of the assessment**	**Scenario selected** *(indicate with an "x" the scenario selected based on the assessed lines of evidence)*
No (sufficiently investigated)	Yes/No	1a	Conclude: ED criteria not met because there is not "**T-mediated**" adversity	
Yes (sufficiently investigated)	Yes/No	1b	Perform MoA analysis	e.g. X
No (not sufficiently investigated)	Yes	2a (i)	Perform MoA analysis (additional information may be needed for the analysis)	
No (not sufficiently investigated)	No (sufficiently investigated)	2a (ii)	Conclude: ED criteria not met because no **T-mediated endocrine activity** observed	
No (not sufficiently investigated)	No (not sufficiently investigated)	2a (iii)	Generate missing level 2 and 3 information. Alternatively, generate missing "EATS-mediated" parameters. Depending on the outcome move to corresponding scenario	
Yes (not sufficiently investigated)	Yes/No	2b	Perform MoA analysis	

Appendix I - Template for presentation of the assessment of endocrine disrupting properties

Effects on other terrestrial organisms 8.7 (AS)

Additional studies (MA 8.7 & MP 10.7; OECD IIM 8.11 & IIIM 10.7)

Effects on biological methods for sewage treatment 8.8 (AS)

Effects on biological methods for sewage treatment (Regulation (EU) N° 283/2013, Annex Part A, point 8.8)

Test type/organism	end point
Activated sludge	
Pseudomonas sp	

Literature Data 9 (AS)

Summary of the review	Number	Justification
Total number of summary records retrieved from search		
Total number of summary records retrieved after removing duplicates from all database searches		
Number of summary records excluded after rapid assessment for relevance (by title/abstract)		
Number of studies excluded from the risk assessment after detailed assessment of full-text documents (i.e. not relevant)		See table 1
Number of studies not excluded for relevance after detailed assessment (i.e. reliable studies and studies of unclear reliability)		See tables 2 and 3
Number of studies included in the RAR/DAR as supporting information		

As defined in Appendix to Further guidance on performing and presenting the literature search

Changes to EU PPP Active Substance Information

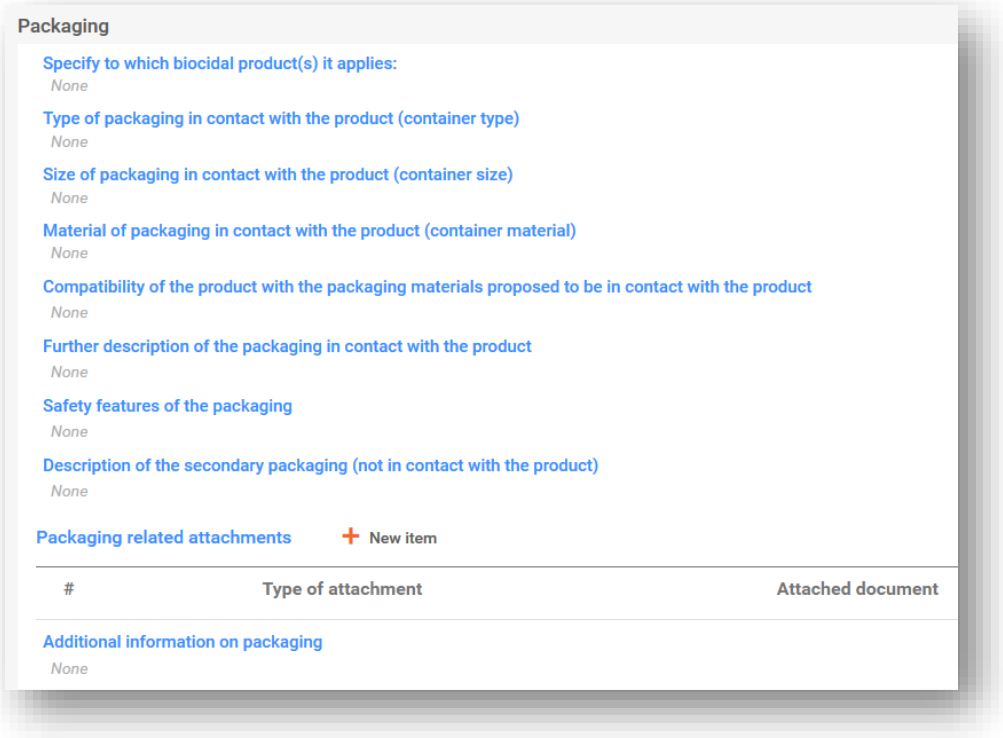
- Acute toxicity: other routes (OHT 63) – move from 5.2.8 to 5.3.3.3?
- Respiratory sensitisation (OHT 66-2) – remove?
- Metabolism of residues in crops and in rotational crops (OHT 85-3) move from 6.6 to 6.2?
- Henry's Law Constant (OHT 35) move from 7.6.2 to 2.2?
- Bioaccumulation: terrestrial (OHT 33) move from 7.6.1 to 8.4?
- 10.2 DSD – DPD remove?
- 3.1 Use of the active substance – remove flexible record?

ProtectionMeasures 4.1 (PPP)

- New section on safety intervals
- Pre-harvest
- Re-entry (livestock / workers)
- Withholding period
- Waiting period (application – handling / application – sowing)
- More generic use of language applicable to biocides and pesticides

Packaging 4.4 (PPP)

- Possibility to report different packaging sizes for one packaging material inside one document



Question:
Should the repeatable entry include all the fields related to packaging?

Further information, Efficacy 6 (PPP)

Further information, Efficacy

Effectiveness (Regulation (EU) N° 284/2013, Annex Part A, point 6.2)

Brief statement on whether representative uses GAPs are supported

Adverse effects on field crops (Regulation (EU) N° 284/2013, Annex Part A, point 6.4)

Brief statement on whether representative uses GAPs are supported

Observations on other undesirable or unintended side-effects (Regulation (EU) N° 284/2013, Annex Part A, point 6.5)

Brief statement on whether representative uses GAPs are supported

Data on Exposure 7.2 (PPP)

Exposure assessment

Substance	0	Formulation =	Application rate- kg a.s. /ha	#DIV/0!
Scenario	/ / /			Buffer = 2-3
Percentage Absoprtion	Dermal for product = 100	Dermal for in use diluation = 100	Oral = 100	Inhalation = 100
RVNAS	mg/kg bw/day		RVAAS	mg/kg bw/day
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days

Operator Model		Mixing, loading and application AOEM		
Potential exposure	Longer term systemic exposure mg/kg bw/day		#N/A	% of RVNAS
	Acute systemic exposure mg/kg bw/day		#N/A	% of RVAAS
Mixing and Loading		Gloves = Chemical resistant gloves	Clothing = Certified protective coverall	RPE = None
Application		Gloves = Chemical resistant gloves	Clothing = Certified protective coverall	RPE = FP1, P1 and similar
Exposure	Longer term systemic exposure mg/kg bw/day		#N/A	% of RVNAS

Guidance on Pesticides Exposure Assessment of Operators, Workers, Residents and Bystanders (Under review) and Others

Dermal Absorption 7.3 (PPP)

Table 5: Template with minimum information on dermal absorption studies to be presented in assessment reports

***In vitro* and *in vivo* studies**
Material/product tested (name/code number)
Type of formulation
Concentration of active substance in the formulation
Vehicle used (if any)
Dilution rates
Surface area dose in micrograms of active substance per cm^2
Exposure time
Sampling duration (time of last sample)
Animal species/strain and skin sample source/application site
Group size/number of replicates/donor's ID for replicate
Total recovery (individual values for replicates, mean values ± SD)

Guidance on dermal absorption

EnvironmentalFateAndPathways 9 (PPP) Estimation of concentrations

PEC soil (Regulation (EU) N° 284/2013, Annex Part A, points 9.1.3 / 9.3.1)

Parent Method of calculation	DT_{50} (d): *x* days Kinetics: *SFO* Field or Lab: *representative worst case from field studies.*
Application data	Crop: *wheat* Depth of soil layer: *5cm or 20cm* Soil bulk density: *1.5g/cm³* % plant interception: *Pre-emergence therefore no crop interception* Number of applications: *x* Interval (d): *x* Application rate(s): *x* g a.s./ha

Soil, Ground water, Surface water, Sediment, Air

Relevance of metabolites in ground water 9 (PPP) Document N4

Guidance document on the assessment of the relevance of metabolites in groundwater of substances

Changes to EU PPP Active Substance application (representative product)

- 3. Application rate and concentration of the active substance – remove?

Metabolism, distribution and expression of residues 6.2 (AS)

Crop field trials

Study ref.	Trial ref.	Crop	variety	Country	Location	g a.s./ha T1	T2	T3	T4	T5	T6	T7	T8
R-24957/R-24957A	S08-00769-01	Apple	Delicious	DE	[redacted]	[redacted]							
R-24957/R-24957A	S08-00769-02	Apple	Golden	FR									
R-24957/R-24957A	S08-00769-03	Pear	Lucas	DE									
R-24957/R-24957A	S08-00769-04	Pear	Lucasowka	PL									
R-24957/R-24957A	S08-00769-05	Apple	Elstar	DE									
R-24957/R-24957A	S08-00769-06	Apple	Gloster	PL									
R-27555	S10-00609-01	Apple	Elstar	DE									
R-27555	S10-00609-02	Apple	Tentation	FR									
S10-00610	S10-00610-01	Apple	Golden	ES									
R-24961/R-24961A.	S08-01351-01	Pear	Pyuco	IT									
R-24961/R-24961A.	S08-01351-02	Apple	Golden	ES									
R-24961/R-24961A.	S08-01351-03	Pear	William	FR									

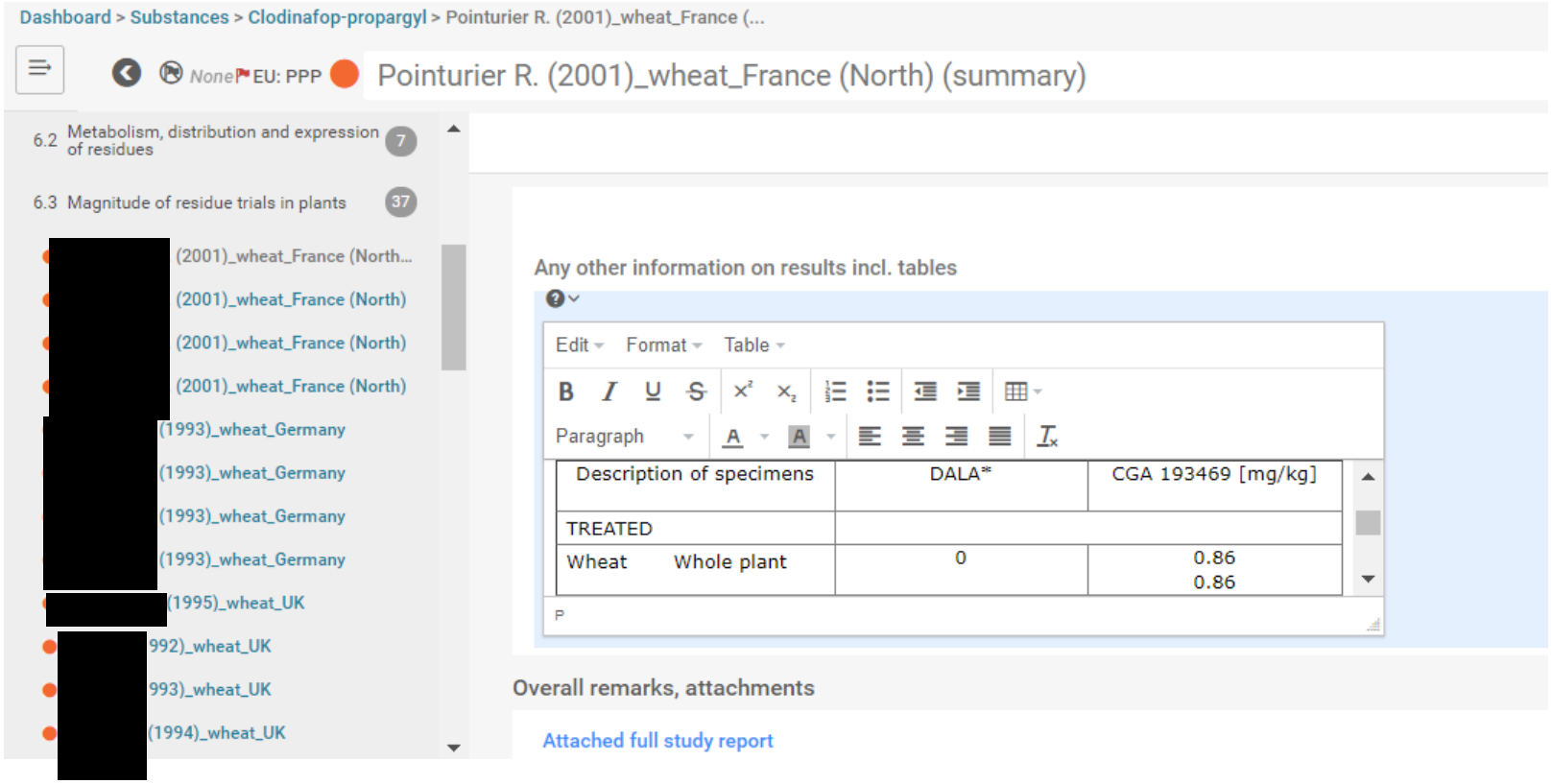
Consider export to RUEDIS database

Combination of data

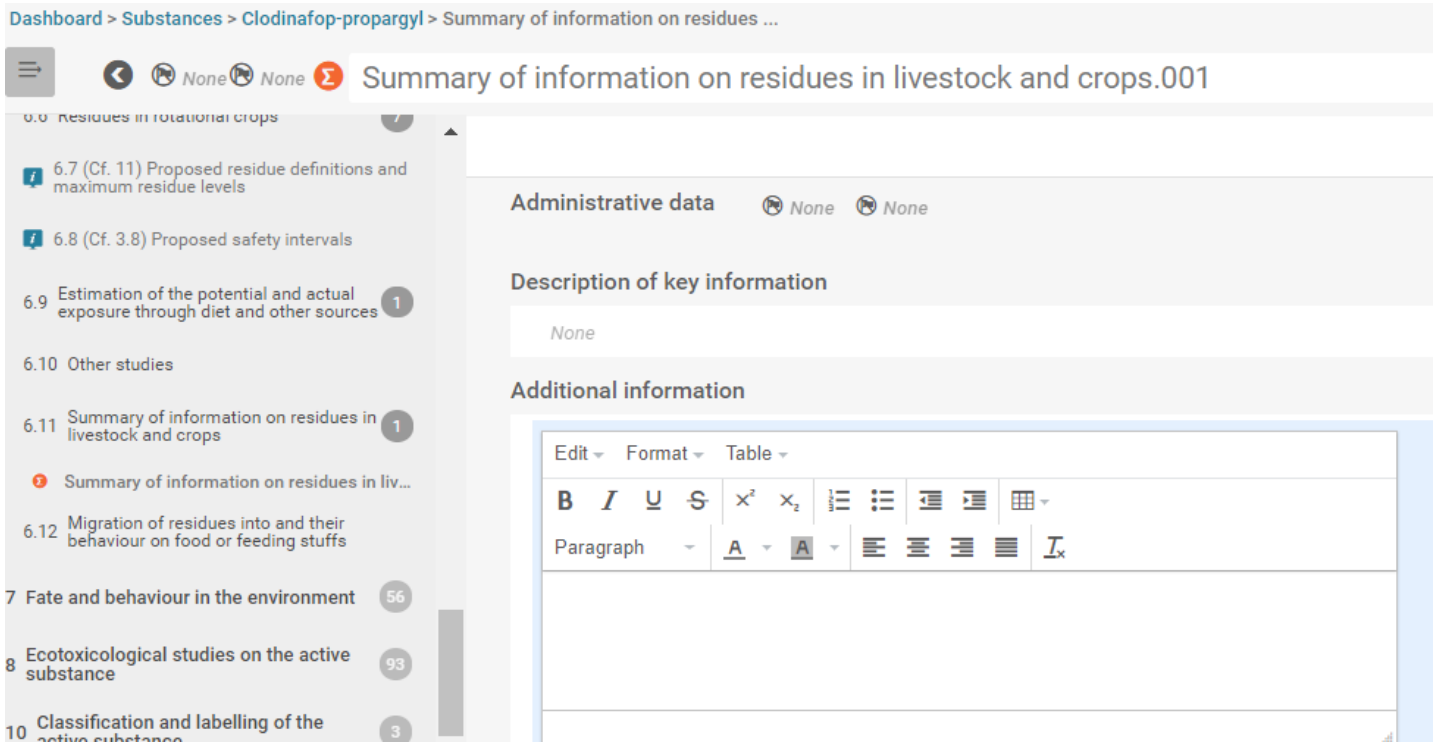
Appendix G of "Administrative guidance on submission of dossiers and assessment reports for the peer-review of pesticide active substances "

- Metabolism in primary crops - OECD Test Guideline 501
- Metabolism in Rotational crops - OECD Test Guideline 502
- Metabolism in livestock - OECD Test Guideline 503
- Crop field trials - OECD Guideline + 509 OECD Guidance Document on crop field trials

Combination/Aggregation of data



Possible solution



When to use a summary document, when to use a report and when to use CSV/XML attachments?