



## **Section 4 (analytical methods) and OHT 87 Considerations on a path forward**

**7<sup>th</sup> Pesticide Steering Network meeting  
19-20<sup>th</sup> June 2023, Parma (IT) and online**

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(on behalf of European Crop Care Association – ECCA)**

# Section 4 and OHT 87 – some considerations



## ► In dossier section 4, summaries of all analytical methods are provided:

- Active substance
- Impurities
- Residue methods
  - Crops
  - Livestock
  - Body fluids
  - Soil
  - Water
  - Air
  - Etc.

In IUCLID: Huge dossier section with no substructure

# Section 4 and OHT 87 – some considerations



4 Analytical methods	
>	EPS_CA 4.1.1 Methods for the analysis of the active substance as manufactured
>	EPS_CA 4.1.2.(a)_Quinmerac_methods_for_risk_assessment_environmental_fate
>	EPS_CA 4.1.2.(b)_Quinmerac_methods_for_risk_assessment_efficiency_Data waiving
>	EPS_CA 4.1.2.(c)_Quinmerac_methods_for_risk_assessment_toxicology
>	EPS_CA 4.1.2.(d)_Quinmerac_methods_for_risk_assessment_bystander_exposure_Data waiving
>	EPS_CA 4.1.2.(e)_Quinmerac_methods_for_risk_assessment_residues
>	EPS_CA 4.1.2.(f)_Quinmerac_methods_for_risk_assessment_ecotoxicology
>	EPS_CA 4.1.2.(g)_Quinmerac_methods_for_risk_assessment_physical_and_chemical_property_Data waiving
>	EPS_CA 4.2_Quinmerac_methods_for_post-approval_control_and_monitoring
>	CA 4.1.1 (a)_Quinmerac_Determination of the pure active substance in the active substance as manufactured_Data waiving
>	CA 4.1.1 (b)_Quinmerac_Determination of relevant impurities and additives (such as stabilisers) in the active substance as manufactured_Data waiving
>	CA 4.1.1 (b)_Quinmerac_Determination of significant impurities in the active substance as manufactured_data waiving
>	4.1.2.(a)_2001_Quinmerac_environmental_fate_soil_analytical method 470_(2001/1000974; 2006/1031794; 2015/1249140)
>	4.1.2.(a)_1992_Quinmerac_environmental_fate_soil_(1992/12115)
>	4.1.2.(a)_1992_Quinmerac_environmental_fate_soil_(1992/11914)
>	4.1.2.(a)_1985_Quinmerac_environmental_fate_CaCl2_soil_(1985/10042; 2006/1009575)
>	4.1.2.(a)_1993_Quinmerac_environmental_fate_soil_(1993/1000734)
>	4.1.2.(a)_2020_Quinmerac_environmental_fate_soil_(09F02033-02-VMS)
>	4.1.2.(a)_1097_Quinmerac_environmental_fate_water_(1097/10294)

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4 Analytical methods	
>	242d7643-4526-41ec-af35-76a41ad32b26
>	7e892efe-68ab-405e-b16e-418b25a33946
>	ad521169-a886-485d-994e-9d5b53ede29f
>	a8d33a4c-4334-421e-8816-8ec3e00e5fc3
>	0ce1f46a-dfa0-4ec8-b771-42310c03e3f1
>	f62bda4e-04c9-4d30-806b-36af13a17c00
>	2d040708-ce37-4e43-acba-140afaa53e68
>	c0f193c8-647e-4376-8973-6fbfe9c2cd6
>	7f1c6850-9a42-474a-97cc-3ddfc5c9c5d
>	242a1e4a-b94b-48e8-a120-31d47ab29392
>	66c3c1d1-9345-474b-b946-138ceb4751fa
>	c1a6264e-b81a-4a59-831e-98ef71a08bae
>	29630d6a-ec45-4fad-944c-62cdceac934c
>	02e8a7ee-0aa9-42b2-9481-3c694bac77d5
>	0ca46a2c-e2b8-47f4-9d17-bbc26596cb98
>	d63cc68e-554b-4513-b577-f3a3c4f1dc04

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Example – AI Renewal dossier (BASF test server: 83 entries)

Example – AI Renewal dossier (Public IUCLID: 42 entries)

Challenging for preparation and assessment  
Proposal for discussion: Split in accordance with the relevant EU Regulation

# Section 4 and OHT 87 – some considerations



## 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

determination of non-isotope-labelled residues in all points:

used in support of environmental fate studies;

- (b) in soil, water and any additional matrices used in support of efficacy studies;
- (c) in feed, body fluids and tissues, air and any additional matrices used in support of toxicology studies;
- (d) in body fluids, air and any additional matrices used in support of operator, worker, resident and bystander exposure studies;
- (e) in or on plants, plant products, processed food commodities, food of plant and animal origin, feed and any additional matrices used in support of residues studies;
- (f) in soil, water, sediment, feed and any additional matrices used in support of ecotoxicology studies;
- (g) in water, buffer solutions, organic solvents and any additional matrices used in the physical and chemical properties tests.

EU Regulation 283/2013 foresees different subsections

# Section 4 and OHT 87 – some considerations



## Relevant guidelines analytical method – applicant view

Technical Material and Preparations - Analytical methods for Annex II (part A, Section 4) and Annex III (part A, Section 5) SANCO/3030/99 rev.5 - 22 March 2019

US EPA 830 series

Residues Analytical Methods for Risk Assessment and Post-approval Control and Monitoring Purposes - SANTE/2020/12830. Rev 2 – 14 February 2023

Technical Guideline on the Evaluation of Extraction Efficiency of Residue Analytical Methods – SANTE/2017/10632. Rev.5 – 11 May 2023

Working document on the summing up of LOQs in case of complex residue definitions - SANCO/12574/2014 rev.5.1, 30 November-1 December 2015

OECD Guidance on Pesticide Residue Analytical Methods (2007, No. 72)

US EPA 860 series

# Section 4 and OHT 87 – some considerations



## Relevant guidelines analytical method – applicant view

## **8. Appendix 3**

### **SUMMARY OF REQUIRED VALIDATION**

Sample/purpose	Analyte consideration	Recovery	Precision	LOQ	Linearity	Interference	Specificity	Confirmatory of identity
Technical active substance	Active substance	Not required	Minimum 5 independently weighed samples determination at the same conc.	Not required	Range appropriate to the lowest and highest nominal concentration of the analyte $\pm 20\%$ . Range in % w/v and w/w Duplicate (independently weighed samples) determination at 3 conc or single determination at 5 conc $r \geq 0.99$	Interferences from impurities in a.s. $< 3\%$ of the total peak measured for the target analyte	For a.s. specified as being optically pure or ratio of isomer set , the method must support this	not required
	Significant impurities/relevant impurities and additives	Recoveries determined at levels appropriate to the material specification 2 independent recoveries (i.e. 2 weighings). Standard addition is an acceptable method of determining recoveries of impurities and additives	Minimum 5 independently weighed samples determination at the same conc.	Not required. However, the method has to be validated at least at specifications level for significant impurities and at least at 20% less for relevant impurities.	Range appropriate to the lowest and highest nominal concentration of the analyte $\pm 20\%$ . Range in % w/v and w/w Duplicate (independently weighed samples) determination at 3 conc or single determination at 5 conc $r \geq 0.99$	Interferences from impurities in a.s. $< 3\%$ of the total peak measured for the target analyte	Addressed to the extent that the technical active substance or technical concentrate is properly characterised	Must be addressed for impurities if the primary method is not highly specific and no identity data provided (i.e. mass spectrum)
Section references	4.2	4.1.1(iii) 4.1.2 (ii)	4.1.1(iv) 4.1.2(iv)	4.1.2(v)	4.1.1(ii) 4.1.2(ii)	4.1.1(i) 4.1.2(i)	4.1.1(i) 4.1.2(i)	4.1.3

## Appendix 2: List of methods required

**Table A2: Completeness check of analytical methods for post-approval control and monitoring purposes**

Today: Different guideline requirements for product chemistry and residue chemistry  
Future (after revision of OECD GD): More differences expected

# Section 4 and OHT 87 – some considerations



## OHT 87 – findings (IUCLID 6.7, including points raised by J. Juanes)

**OHT 87 - final draft proposal**

efsa European Food Safety Authority

- ✓ Structure improved including **4 sections** (Materials&Methods; Results):
  - Principles of analytical methods (i.e., primary method)
  - Enforcement
  - Confirmatory
  - Independent Laboratory Validation
- ✓ Proposal to have **Dynamic Content Rules** (DCR) for "Methods class" picklist;
- ✓ **Structured table** for reporting values on:

Results and discussion		Header 1										
Recovery	Analyte	Matrix	MSW/ M2	Formulation level (mg/kg)	Units	Number of replicates	Range recovery (%)	Mean recovery (%)	RSD (%)	Remarks	Recal.	
Data type:	Link to entity	Text	Numeric range	Decimal	Picklist	Integer	Numeric range	Decimal	Decimal	Text		
LOQ/LOD	Analyte	Matrix	Limit of quantification (mg/kg)	Limit of detection (mg/kg)	Units		Remarks	LOQ/LOD				
Data type:	Link to entity	Text	Decimal	Decimal	Picklist	Text						
Calibration	Analyte	Standards	Matrix	MSW/ M2	Calibration range (mg/kg)	Units	Calibration equation	Calibration coefficient (1)	Calibration coefficient (2)	Number of replicates	Remarks	Cal.
Data type:	Link to entity	Picklist multiple	Text	Numeric range	Numeric range	Picklist	Text	Decimal	Decimal	Integer	Text	
- ✓ Improving the use of **CSV uploader**.

Analytical (primary) method

Instrument / detector

Residue method

Extraction and clean-up

Flow diagram

Further details on analytical method

Enforcement method (if applicable)

Instrument / detector for enforcement method

Residue method

Extraction and clean-up

Flow diagram

Further details on enforcement method

Confirmatory method (if applicable)

Instrument / detector for confirmatory method

Residue method

Extraction and clean-up

Flow diagram

Details on ILV

Any other information on materials and methods incl. tables

Pick list selection available for method  
Dynamic content rules not established: Repetition of contents

# Section 4 and OHT 87 – some considerations



## OHT 87 – findings (IUCLID 6.7, including points raised by J. Juanes)

Results and discussion

Results using analytical (primary) method

Recovery	+ New item	Import file	#	Analyte	Matrix	MRM/ m/z	Fortificatio...	Number rep...	Range reco...	Mean recov...	RSDr (%)	Remarks	Actions
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Only applies to MS/MS methods

Additional details on recovery results

Repeatability

Repeatability	+ New item	Import file	#	Analyte	Matrix	Number repli...	Mean content	RSD (%)	RSDr (%)	Horrat value	Remarks	Actions
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Not required for Residues

LOQ/LOD

LOQ/LOD	+ New item	Import file	#	Analyte	Matrix	Limit of quantification	Limit of detection	Remarks	Actions
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Not required for PC

Calibration

Calibration	+ New item	Import file	#	Analyte	Standards	Matrix	MRM/ m/z	Calibratio...	Calibratio...	Correlatio...	Correlatio...	Number re...	Remarks	Actions
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Matrix effects (%)

Must be by analyte

Matrix effects remarks

After adaption: OHT 87 not suitable;  
Suggestion: Split between product chemistry (4.1.1 and 4.1.2 / 4.2)

# Section 4 and OHT 87 – some considerations



## ► Conclusion and proposal on path forward:

- Establish substructure as foreseen in Reg. 283/2013
- Discuss with OECD to separate Endpoint Study Record (OHT-87) for
  - Product chemistry methods
  - Residue analytical methods
- If agreed: Continue to develop further both method OHTs including
  - Differentiation of fields / contents by method type (according to data requirements listed in guidelines)
  - Inclusion of suitable picklists / drop down lists
  - Upload functionality for new dossiers
  - Functionality check

Without considerable modifications of OHT 87: Update of validation rules not considered as feasible