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

7th Pesticide Steering Network meeting
19-20th June 2023, Parma (IT) and online

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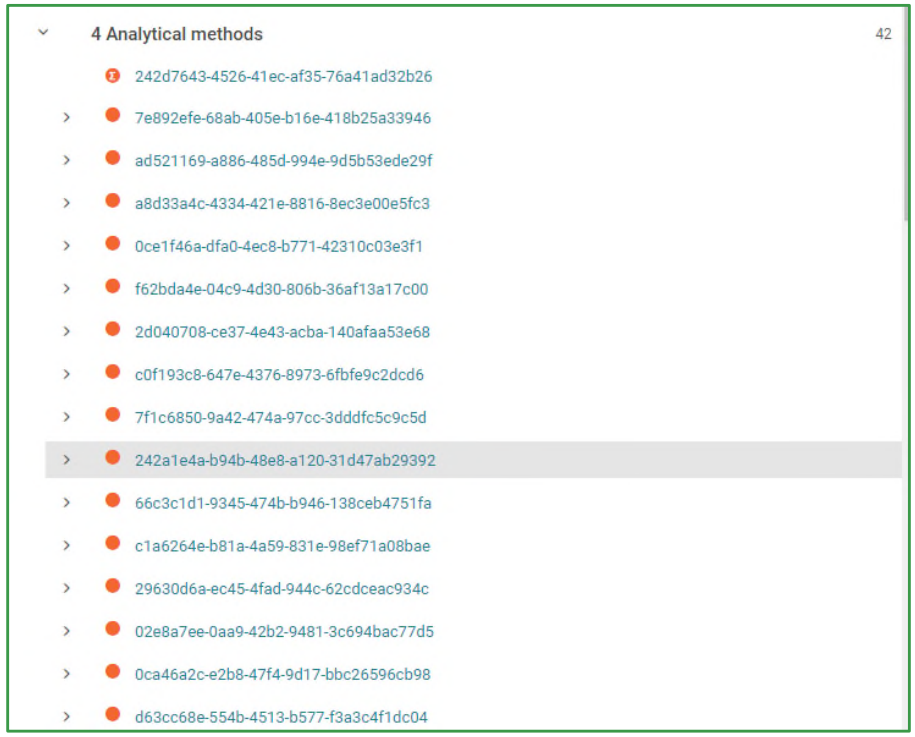
Section 4 and OHT 87 – some considerations

- **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



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
oints:

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 ± 20%. Range in % w/v and w/w Duplicate (independently weighed samples) determination at 3 conc or single determination at 5 conc r>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 ± 20%. Range in % w/v and w/w Duplicate (independently weighed samples) determination at 3 conc or single determination at 5 conc r>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 (iii)	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

Matrix group / crop group	Residue definition for monitoring	LOQ	Methods		
			Primary method	Confirmatory method	Independent lab validation
					Not necessary
					Not necessary
Air					Not necessary
Body fluids					Not necessary
Body tissues					Not necessary

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

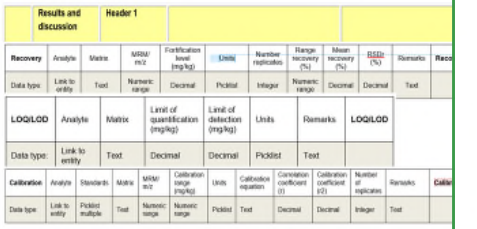
Section 4 and OHT 87 – some considerations

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:
  - *Recovery*
  - *LOQ/LOD*
  - *Calibration*
- ✓ Improving the use of **CSV uploader**.



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

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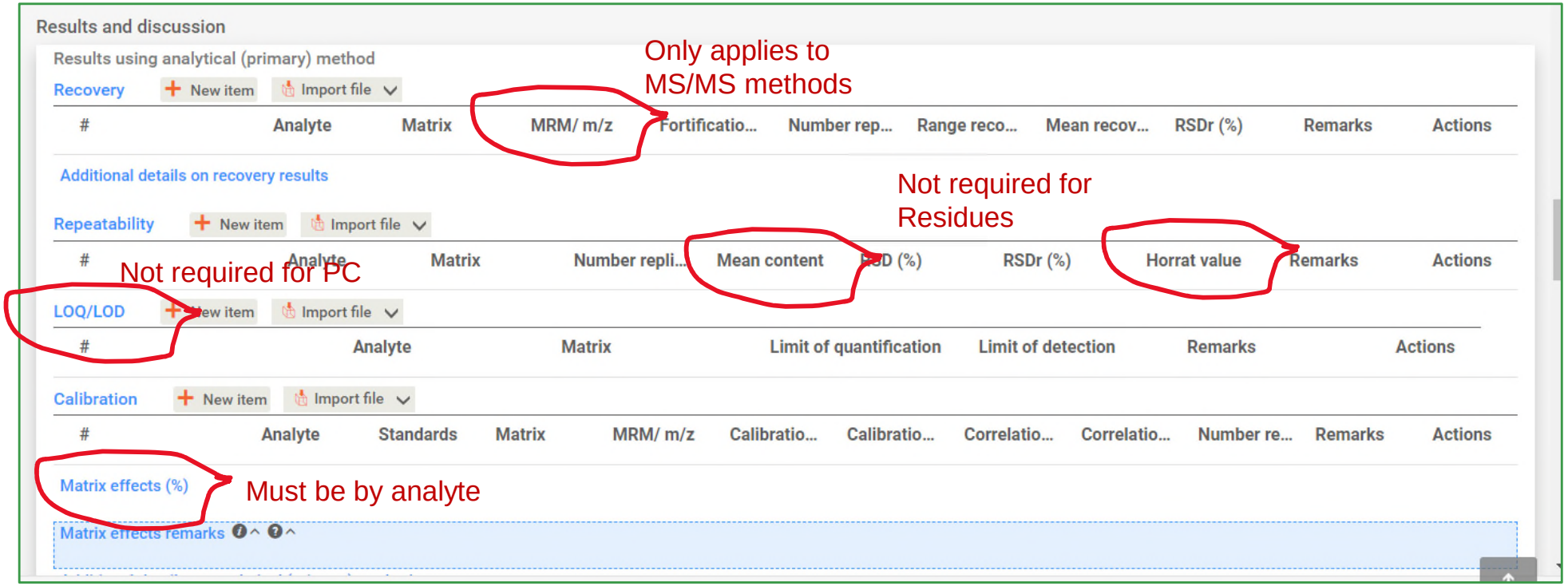
OHT 87 – findings (IUCLID 6.7, including points raised by J. Juanes)



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