



Bundesamt für  
Verbraucherschutz und  
Lebensmittelsicherheit



WAGENINGEN  
UNIVERSITY & RESEARCH



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European Union

# Changes in European Food Control – Challenges - and Solutions of the EURL Network

## Networking and Information Exchange....



# Networking, Contact and Information Exchange....



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<https://eurl-residues.eu/>

Legislation and Guidance

Access to individual information / websites of the three VMPR EURLs

Current information

## Tolerance Limits for Coccidiostats

Many coccidiostats are authorised as feed additives and maximum levels (MLs) for the unavoidable carry-over into food have been established along maximum residue limits (MRLs). Since the authorisation as feed additive is limited to a certain time period, the applicability of MLs frequently changes. Furthermore, MLs are usually provided for a large variety of species and may also differentiate within a species (e.g. differentiation between chicken for laying and chicken for fattening). The EURL Berlin would like to support the laboratory network in the implementation of the legislation by providing an overview of the tolerance limits for all relevant coccidiostats. The document is regularly updated. The [current version](#) is 1.5 and can be downloaded from the sub-page ['Guidance Documents'](#).

# Topics



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## Developments in Legislation

## Tools for Method Development and Validation

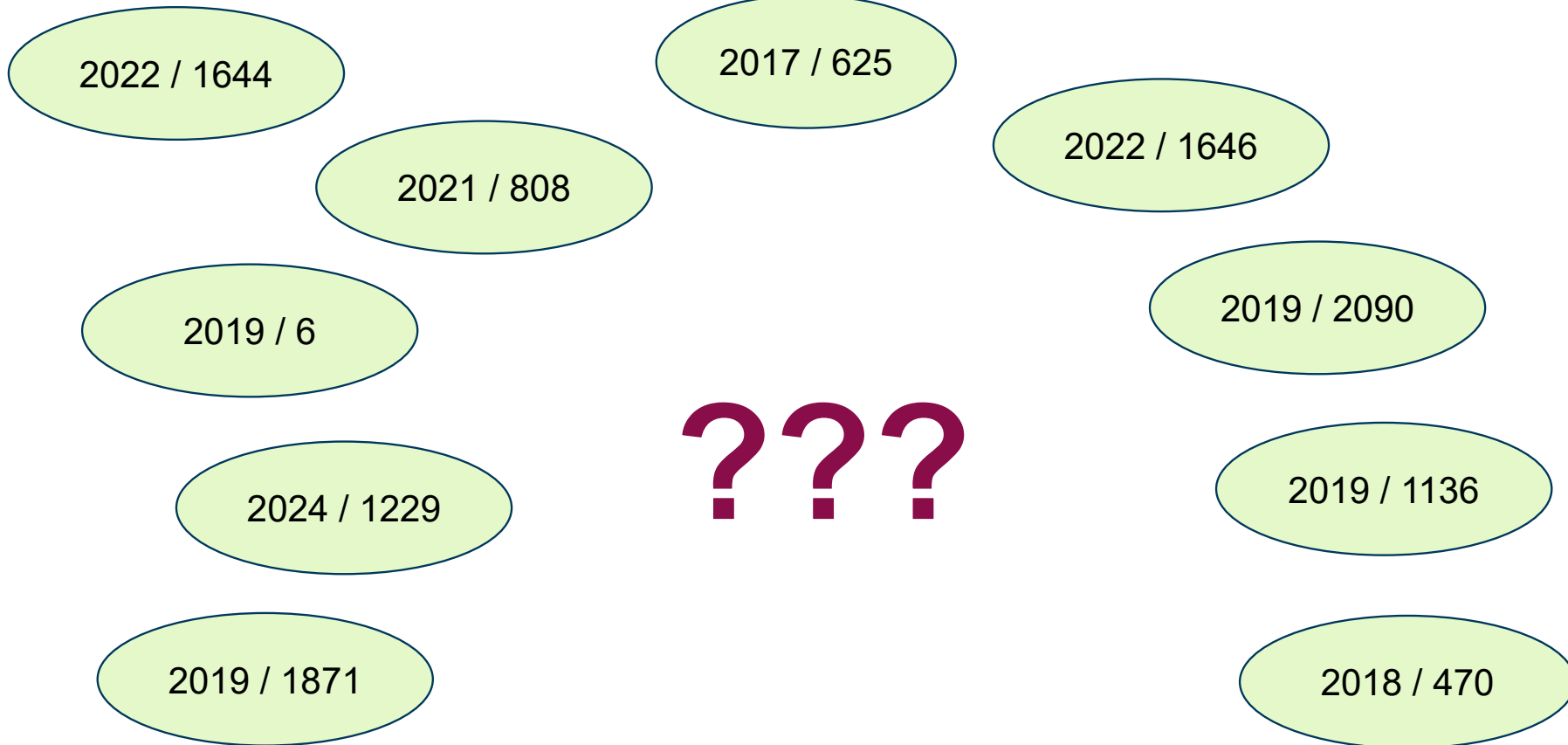
## Projects for Harmonisation and Support

<https://stock.adobe.com/de/free>

# Developments in EU Food Legislation



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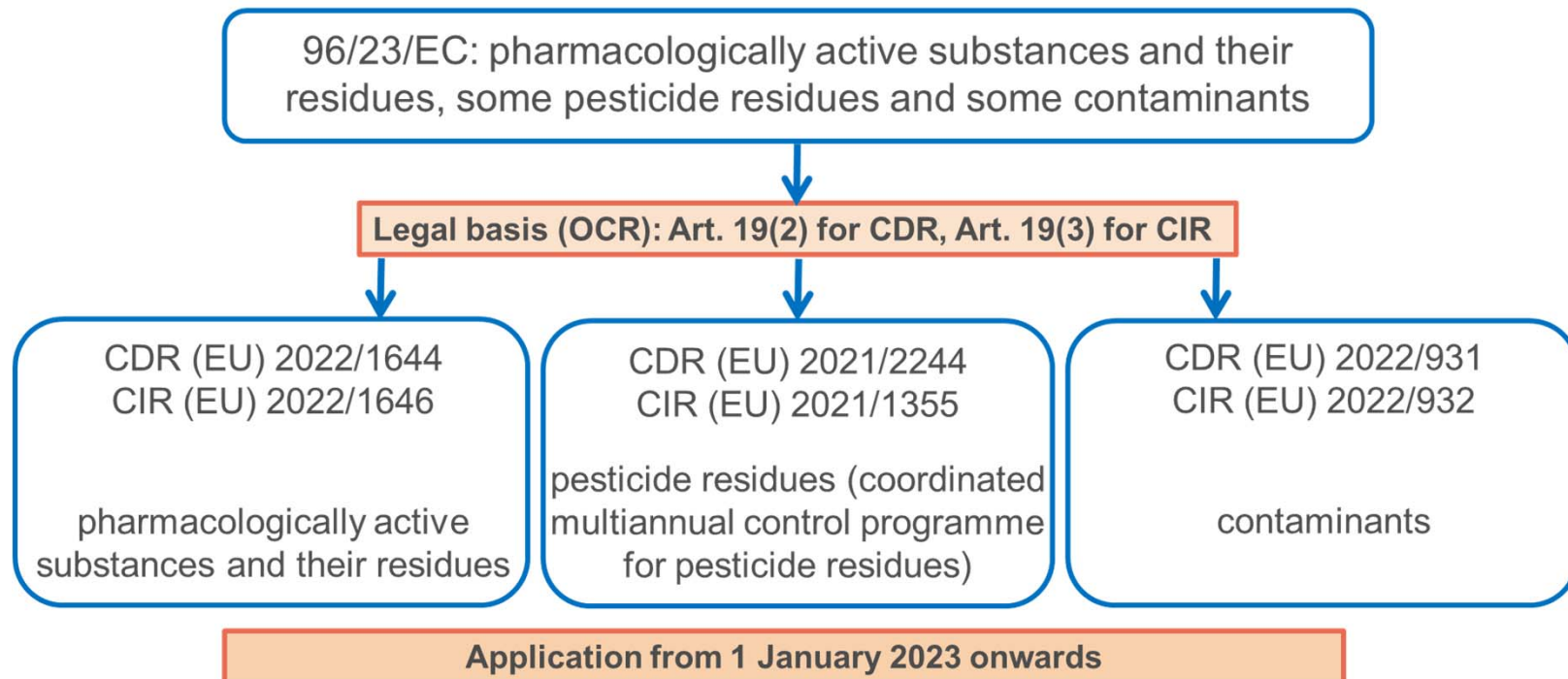


???

# Developments in legislation

## Council Directive 96/23/EC and Regulation (EU) 2017/625

The provisions on monitoring of residues of VMP provided for in 96/23/EC shall continue to apply until 14 December 2022 (transitional measure provided in Article 150)



# Residue Control Programmes



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## COMMISSION IMPLEMENTING REGULATION (EU) 2022/1646 (control plans)

- (a) a ‘national risk-based control plan’  
individual risk assessment required
- (b) a ‘national randomised surveillance plan (10 – 1425 samples)’  
discover new risks / HRMS techniques
- (c) a ‘national risk-based control plan for third-country imports’  
inclusion of processed food

**New way of reporting data to EFSA**

**For control plans 2027 methods validated according to CIR (EU) 2021/808 has to be ready !**

# Combinations of substance groups and commodity groups (NRL Survey)



in light green: boxes with crosses in CIR (EU) 1644/2022

in light yellow : boxes were crosses were removed compared to the first version of CIR (EU) 1644/2022;

in dark green: boxes with crosses in CIR (EU) 1644/2022 considered as very important by the EURLs (major species, high sample numbers)

## B-Substances

<u>Substance group</u>	<u>Bovine, ovine and caprine</u>	<u>Porcine</u>	<u>Equine</u>	<u>Poultry</u>	Aquaculture (finfish, crustaceans and other aquaculture products)	Raw bovine, ovine and caprine milk	Hen eggs and other eggs	Rabbits, farmed game, reptiles and insects	Honey
B1a Antimicrobial substances	9	7	3	8	8	11	7	3	6
B1b Insecticides, fungicides, anthelmintics and other antiparasitic agents	9	8	4	5	8	9	3	3	0
B1c Sedatives	11	11	7	2	3	3	1	1	0
B1d Non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids and glucocorticoids;	9	6	7	4	2	10	2	3	0
B1e Other pharmacologically active substances	0	0	0	0	0	0	1	0	0
B2 Coccidiostats and histomonostats, for which maximum levels and maximum residue limits are set under Union legislation	8	7	2	8	1	4	10	2	0



## Clarification as regards A3b and B1b substances

- **Group A – Prohibited or unauthorised pharmacologically active substances in food-producing animals**
- 3. Pharmacologically active substances, not listed in Table 1 of the Annex to Regulation (EU) No 37/2010 or substances not authorised for use in feed (Regulation (EU) No 1831/2003) :

**(b) Plant protection products** Regulation (EU) No 1107/2009  
**biocides** Regulation (EU) No 528/2012

- **B1: Pharmacologically active substances listed in Table 1 of the Annex to Regulation (EU) No 37/2010:**
  - **(b) Insecticides, fungicides**, anthelmintics and other antiparasitic agents
- **Validation of analytical methods (matrices of animal origin)**



**Validation procedures for pesticide residues as well as for VMPPR can be used**

# Evaluation of risks ....



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## Report for 2023 on the results from the monitoring of residues of veterinary medicinal products in live animals and animal products

Published: 25 February 2025 | Approved: 19 February 2025

Share:

Complete report :  
<https://www.efsa.europa.eu/en/supporting/pub/en-9297>

Report for 2023 available !

New substance group classification – limited comparability

Reporting of all results is welcome !

# European Residue Control Programme

## Plan 1 results

Contents

Meta data

Substance group	Samples analysed	Non- compliant samples (%)	Non- compliant results
<b>A</b>	<b>225635</b>	<b>0.09</b>	<b>257</b>
A1c (Steroids)	34994	0.33	127
A2 (banned substances, 37/2010, table 2, e.g. CAP)	87959	0.04	33
<b>B</b>	<b>156769</b>	<b>0.14</b>	<b>257</b>
B1a (Antibacterial substances)	144467	0.15	243
B1b (dual use)	35824	0.06	23
B1c (sedatives)	7263	0.04	3
B1d (NSAIDs, corticosteroids)	34695	0.22	85
B2 (Coccidiostats)	15298	0.09	14
B3 (environmental contaminants)	XX	XX	XX
<b>Total</b>	<b>284850</b>	<b>0.15</b>	<b>514</b>

# Amendment of Reg. 37/2010 - processed food



**The proposal is to add a new Article to Reg. 37/2010 concerning the use of MRLs also for processed or compound products**

## **EURL systematic literature study**

- **Research into the effects of processing steps on the veterinary drug residues is often lacking.**
- **Besides the effects of processing, degradation products from veterinary drug residues, formed during processing have not been identified in most cases**
- **No general processing factor can be set for all processed food - analyte combinations. It needs to be assessed for every case individually.**
- **Clarification how to with products in which an accumulation of the analyte is to be expected (e.g. cheese, dried products).**

# Changes in CIR (EU) 2021/808 vs CD (EU) 2002/657



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<https://eurl-residues.eu/>

EURL Portal - FAQ

**EURLs for Residues of Veterinary Medicinal Products**

HOME EURL PORTAL EURL ANSES EURL BVL EURL WFSR  Search

FAQ

- » What are the tasks of the EURLs? +
- » Where do I find information on the EURLs' current objectives? +
- » Where can I find information if I plan to import goods into the EU? +
- » Where can I find an introduction into the requirements of CIR 2021/808? -

During a webinar initiated by the School for Advanced Residue Analysis in Food (SARAF) the heads of the three EURLs active in the field of veterinary drug residue analysis presented an [overview of changes](#) from CD 2002/657 to CIR 2021/808. They also gave guidance on the validation of confirmation methods using the [conventional](#) and the [alternative](#) approach and presented the state of play for the guidance document on [screening method validation](#).

- » Where can I find information on current developments regarding the implementation of Reg. (EU) 2017/625? +

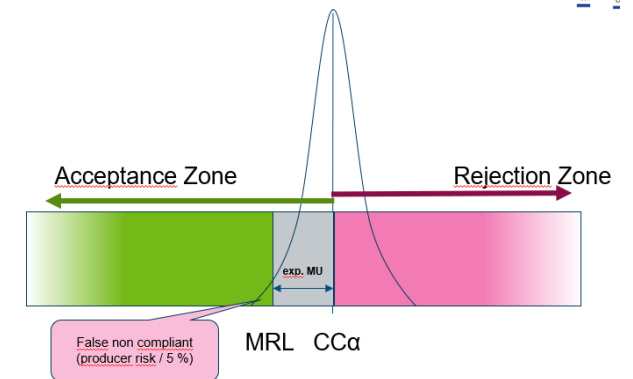
[https://eurl-residues.eu/wp-content/uploads/2022/05/3-CIR\\_2021\\_808\\_Overview\\_Changes\\_J\\_Polzer.pdf](https://eurl-residues.eu/wp-content/uploads/2022/05/3-CIR_2021_808_Overview_Changes_J_Polzer.pdf)

# Changes in CIR (EU) 2021/808 vs CD (EU) 2002/657



## Main aspects :

- Keeping  $CC\alpha$  concept / Revised calculations
- Addressing measurement uncertainty / ongoing QA (ISO 17025)
- Revised definition of  $CC\beta$  (relevance for screening)
- Absolute recovery / Matrix effects
- Revised Suitable analytical techniques
- Extended HRMS requirements (mass accuracy)
- Identification criteria (ion ratio / RT)



Classification of analytical methods by the performance characteristics that have to be determined

Method	Confirmation		Screening		
	Qualitative	Quantitative	Qualitative	Semi-quantitative	Quantitative
Substances	A	A, B	A, B	A, B	A, B
Identification in accordance with 1.2	x	x			
CCα	x	x			
CCβ	-		x	x	x
Trueness		x			x
Precision		x		(x)	x
Relative matrix effect/absolute recovery *		x			x
Selectivity/Specificity		x	x	x	x
Stability *		x	x	x	x
Ruggedness		x	x	x	x

## Tools for Method Development and Validation



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Data bases

Workshops and  
Training

Templates

NRL / EURL  
Working groups

Guidance docs

Email support /  
Networking

## Which Guidance is available ?



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<https://eurl-residues.eu/>

### EURLs for Residues of Veterinary Medicinal Products

HOME EURL PORTAL EURL ANSES EURL BVL EURL WFSR

#### Guidance Documents

The EURL Guidance Documents to Commission Implementing Regulation (EU) 2021/808 shall provide technical instructions for official control laboratories active in the field of veterinary drug residue analysis according to Regulation (EU) 2017/625. The documents' status will be that of associated documents to CIR (EU) 2021/808, representing the EURLs' interpretation of this document. Following the EURL Guidance Documents minutely will not be mandatory and different implementations are possible. However, a comparable level of quality must be achieved if deviation from the approaches outlined in the EURL Guidance Documents is intended.

Before the adoption of an EURL Guidance Document, an initial draft is prepared. From this, an EURL consolidated version is prepared which is then presented to the NRLs for discussion. The NRLs' comments are evaluated by the EURLs and the document amended before the publication of a first version. The EURL Guidance Documents are seen as 'living' documents and NRLs are welcome to submit their feedback in order to further improve the quality of the EURL Guidance Documents.

Currently, six technical EURL Guidance Documents have been published or are currently discussed:

- EURL Guidance Document on the quality control during routine analysis (ongoing method performance verification); finalised ([version 1.2](#))
- EURL Guidance Document on confirmation method validation; finalised ([version 1.1](#))
- EURL Guidance Document on the extension of methods; finalised ([version 2.0](#))
- EURL Guidance Document on validation of screening methods; finalised ([version 1.1](#))
- EURL Guidance Document on standard addition in the field of the analysis of residues of pharmacologically active substances; finalised ([version 1.1](#), [Spreadsheet MSA](#))
- EURL Guidance Document on the validation of HRMS methods

The screenshot shows the website interface for EURLs for Residues of Veterinary Medicinal Products. At the top, there is a navigation bar with links for HOME, EURL PORTAL, EURL ANSES, EURL BVL, and EURL WFSR. A search bar is located on the right. A dropdown menu is open under 'EURL PORTAL', showing options for LEGISLATION, GUIDANCE DOCUMENTS (which is highlighted), EVENTS, NETWORK, and FAQ. Below the menu is a map of Europe with several orange location markers. At the bottom of the map, there is a copyright notice: 'network, © OpenStreetMap contributors, License: https://www.openstreetmap.org/copyright'. Below the map, there are three dots indicating a carousel. The main content area below the map is titled 'Tolerance Limits for Coccidiostats' and contains text about maximum residue limits (MRLs) and maximum levels (MLs) for feed additives.

EURL guidance on minimum method performance requirements (MMPRs) for specific pharmacologically active substances in specific animal matrices; finalised (version 2.1) – **presently under revision**



# Tools for Method Development and Validation

## Minimum Method Performance Requirement (MMPR) Clarification of method requirements – “level of interest”

Laboratories should ensure  $CC\beta$  for screening methods  $< \text{MMPR}$   
 $CC\alpha$  for confirmatory methods

Rules for B-substances without MRL in a specific matrix or species:

**the MMPR is 1/4th of the cascade MRL**

(This requires in principle a **spike level of down to 0.1 times the cascade MRL** - where analytically feasible)

All Substances in table 1 of CR (EU) 37/2010 count as B-substances (also in case of “restrictions”)

Exception : Council Directive 96/22/EC substances

# Tolerance Limits for coccidiostats and dual use substances



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Sub Group	Substance	Tolerance limits (µg/kg)							Legal requirements	
		Species	Eggs	Milk	Liver	Kidney	Muscle	Fat (skin/fat)		Other
Chemical coccidiostats	<b>Clazuril (a)</b>	Pigeon (a)	no MRLs required							Commission regulation 37/2010
	<b>Decoquinate (a,b,c,f)</b>	Chicken for fattening (b)	no MRLs required							Commission implementing regulation (EU) 2021/2094
		Bovine (a)	no MRLs required							Commission Regulation 37/2010
		Ovine (a)	no MRLs required							Commission Regulation 37/2010
		Non-target / Other than chickens for fattening, bovine and ovine except dairy animals	20		20	20	20	20	20	20
	<b>Diclazuril (a,b,c,d,e)</b>	Poultry (a,e)			1500	1000	500	500		Commission regulation 37/2010
		Chicken for fattening, broiler (b)			1500	1000	500	500		Commission regulation 1118/2010
		Chickens reared for laying (b)			1500	1000	500	500		Commission implementation Regulation (EU) 667/2013
		Young hen (b)			1500	1000	500	500		Commission regulation 667/2013 with reference to CR
		Mast and breeding guinea fowl (b)			1500	1000	500	500		Commission regulation 169/2011
		Turkey for fattening (b)			1500	1000	500	500		Commission regulation 888/2011
		<b>Pheasants (b)</b>			<b>1500</b>	<b>1000</b>	<b>500</b>	<b>500</b>		<b>Commission regulation 2023/2733</b>
		Rabbit (a,b)			2500	1000	150	300		Commission regulation 37/2010 Commission regulation 2015/1417
		Ruminants (a)	no MRLs required							Commission regulation Nr. 37/2010
		Porcine (a)	no MRLs required							Commission regulation Nr. 37/2010
Non-target / Other than chickens for fattening, turkeys for fattening, guinea fowl, rabbits for fattening and breeding, ruminants and porcine	2	5	40	40	5	5	5	5	Commission regulation Nr. 610/2012	
<b>DNC (Nicarbazin) (b,c)</b>	<b>Chicken for fattening, chicken reared for laying (max age 16 weeks) and turkey for fatten</b>			15000	6000	4000	4000 (skin/fat)		Commission regulation 875/2010 and Commission reg	
	Non-target / Other than chickens for fattening, <b>chicken for reared laying and turkey (not included/Gap)</b>	300	5	300	100	50	50	50	Commission regulation Nr. 610/2012 and Commission re	
<b>Halofuginone (a,f,c)</b>	Bovine (a,f)			30	30	10	25		Commission regulation 37/2010	
	Chicken for fattening, turkeys for fattening and turkeys reared for breeding (b)			50	40	3	10		Commission Implementing Regulation (EU) 2024/231	
	Non-target / Other than chickens for fattening, turkeys and bovine except dairy cattle	6	1	30	30	3	3	3	Commission regulation Nr. 124/2009	
<b>Fluralaner (a)</b>	Poultry (a)	1300		650	420	65	650		Commission regulation 37/2010	
	Fin fish					65			Commission regulation 37/2010	
<b>Teflubenzuron (a)</b>	Salmonids (a) (muscle and skin in natural proportions)					500			Commission Regulation 37/2010	

Extract of „Tolerance-limits-for-coccidiostats\_V1\_5\_\*.xls“

# Almanac Data Base



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## Collection of **method information** – an EURL task (harmonisation of methods – Article 94)



ALMANAC - AnaLYtical Method  
vAlidation dAta Collection

EU and  
National  
Reference  
Laboratory  
for Residues



- **Laboratories have an overview of all their method data, data can be continuously updated**
- **Search for NRLs analysing a compound of interest**
- **Overview of analytical spectrum of other labs**
- **Find labs with whom to discuss specific analytical problems, EURL can help with establishing contact**

[Home](#)

## NRL entries

NRL entries

RFL entries

▼ FILTER

Laboratory: Choose...

Group: B1b x

Substance group: B1b\_antiparasitic agents x

Substance: febantel x

Matrix: internal organs (liver) - i (l) x

Species: Choose...

Technique: LC-MS/MS x |

Screening:  Yes  No  Both

Confirmation:  Yes  No  Both

# Data Base for VMP Substances



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Home My account Log out

Federal Office of Consumer Protection and Food Safety

## ALMANAC - AnaLYtical Method vAlidation dAta Collection

used in the NRLs of the European Union for the substance groups A1, A2c, A3b, A3d, A3e, A3f, A3g, B1b, B1c, B1d, B1e, B2 and in the German Routine Field Laboratories for all substance groups of Annex I, CDR (EU) 2022/1644

EU and National Reference Laboratory for Residues

Home

**all fields are open for search**

COLOR AND GROUP LEGEND

ON Main information ON Legal aspects ON General chemical information ON Analytical information (HRMS) ON Analytical information (LRMS) ON Standard information ON Solubilit ON C

Search...

Changed	Pharmacologically Active Substance	Internal Standards	Main Compound	CAS Number	Compound Group	Substance group (2022/1644)	EFSA Code	NRCP	MRL/ML/MMPR/RPA	Legal Requirements	IUPA
5/14/2024	Clenbuterol	Clenbuterol-D9	Clenbuterol	37148-27-9	Beta-Agonists	A1e	RF-00000478-VET	minimum required	MMPR, MRL	EURL_MMPR_guid...	1-(4-
5/14/2024	Brombuterol	Brombuterol-D9	Brombuterol	41937-02-4	Beta-Agonists	A1e	RF-00000455-VET	minimum required	MMPR	EURL_MMPR_guid...	1-(4-
5/14/2024	Isoxsuprine	Alloerythro-Isoxsu...	Isoxsuprine	395-28-8	Beta-Agonists	A1e	RF-00000461-VET	minimum required	MMPR	EURL_MMPR_guid...	4-[1-
5/14/2024	Ractopamine	Ractopamine-D6	Ractopamine	97825-25-7	Beta-Agonists	A1e	RF-00000468-VET	minimum required	MMPR	EURL_MMPR_guid...	4-[3-
5/14/2024	Salbutamol	Salbutamol-D9	Salbutamol	18559-94-9	Beta-Agonists	A1e	RF-00000459-VET	minimum required	MMPR	EURL_MMPR_guid...	4-[2-
5/14/2024	Zilpaterol	Zilpaterol-13C3	Zilpaterol	119520-05-7	Beta-Agonists	A1e	RF-00000493-VET	minimum required	MMPR	EURL_MMPR_guid...	(9R.1
5/14/2024	Chlorbrombuterol	Bromchlorbuterol-...	Chlorbrombuterol	37153-52-9	Beta-Agonists	A1e	RF-00000473-VET	recommended	MMPR	EURL_MMPR_guid...	1-(4-
5/14/2024	Cimaterol	Cimaterol-D7	Cimaterol	54239-37-1	Beta-Agonists	A1e	RF-00000481-VET	recommended	MMPR	EURL_MMPR_guid...	2-am
5/14/2024	Cimbuterol	Cimbuterol-D9	Cimbuterol	54239-39-3	Beta-Agonists	A1e	RF-00000482-VET	recommended	MMPR	EURL_MMPR_guid...	2-am

Privacy Policy

# Data Base for VMP Substances



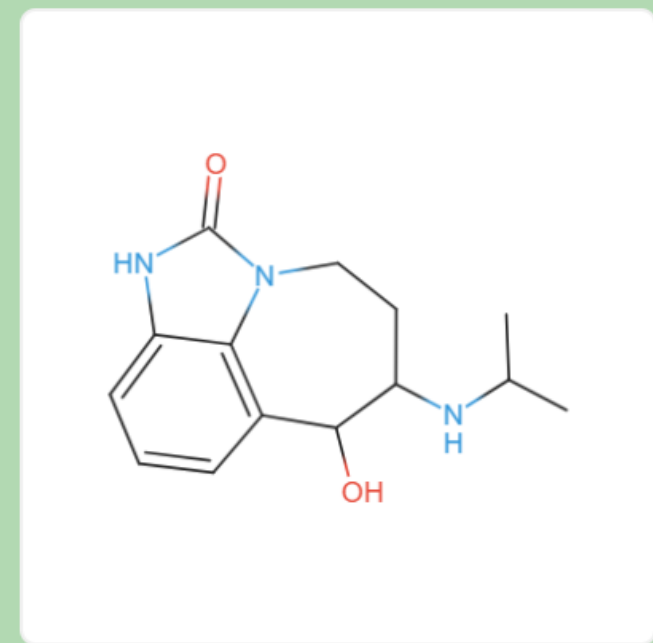
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## Information for Zilpaterol



<	Main information	Legal aspects	General chemical information	Analytical information (HRMS)	Analytical information (LRMS)	Standard information	Solubility and stability	Contact and remarks	>
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Pharmacologically Active Substance	Zilpaterol
Internal Standards	Zilpaterol-13C3
Marker Residue Definition	Zilpaterol
Main Compound	Zilpaterol
CAS Number	119520-05-7
Ionization mode	ESI (+)





# Validation Templates (ResVal)



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## Experiment 1

Instrument	WBA0321
Date	2-11-2021
Technician	
Project	Volledige validatie MVO152 (varkensnier)
Title method	MVO152
Compound	QCA
Internal standard	QCA-d4

Identifier (e.g. file names)	Sample name	Validation level	Concentration ug/kg	Confirmed X=Yes	Accuracy %
	202133446 (blanco E)	0	-0.04	-	-
	202133502 (blanco F)	0	-0.03	-	-
	202133596 (blanco G)	0	0.00	-	-
	202133629 (blanco H)	0	0.00	-	-
	202133630 (blanco I)	0	0.33	-	-
	202133649 (blanco J)	0	0.00	-	-
	202133742 (blanco K)	0	0.00	-	-
		0			
		0			
		0			
	202133446 (blanco E)	1	1.05	x	104.8
	202133502 (blanco F)	1	0.87	x	87.2
	202133596 (blanco G)	1	0.99	x	99.3
	202133629 (blanco H)	1	0.95	x	94.5
	202133630 (blanco I)	1	1.32	x	132.4
	202133649 (blanco J)	1	1.01	x	101.4
	202133742 (blanco K)	1	1.07	x	107.0
		1			
		1			
		1			
	202133446 (blanco E)	2	2.06	x	103.2
	202133502 (blanco F)	2	1.94	x	96.9
	202133596 (blanco G)	2	1.95	x	97.3
	202133629 (blanco H)	2	2.02	x	101.0
	202133630 (blanco I)	2	2.17	x	108.7
	202133649 (blanco J)	2	2.01	x	100.4
	202133742 (blanco K)	2	2.01	x	100.5
		2			
		2			
		2			
	202133446 (blanco E)	3	2.90	x	96.7
	202133502 (blanco F)	3	2.85	x	94.9
	202133596 (blanco G)	3	3.08	x	102.5
	202133629 (blanco H)	3	3.18	x	106.0
	202133630 (blanco I)	3	3.43	x	114.3
	202133649 (blanco J)	3	3.15	x	104.9
	202133742 (blanco K)	3	3.18	x	105.8
		3			
		3			
		3			

## ResVal (v. 3.0) Validation Report

Validation conform CD/2002/657, ISO17025 and ISO11843

**Calculate**

### 1. General Information

Instrument	TQS3		
Date (exp 1, 2, 3)	17-7-2017	24-7-2017	2-8-2017
Technician			
Project	1277352001	1277352001	1277352001
Title method	Zeranolen in bo	Zeranolen in bovine	Zeranolen in bovine hair
Compound	a-Zearalanol	a-Zearalanol	a-Zearalanol
Internal standard	a-Zearalanol-D	a-Zearalanol-D4	a-Zearalanol-D4

### 2. Validation Summary

	Full validation (Exp 1, 2, 3)
CC $\alpha$	0.11
CC $\beta$	0.23
CC $\alpha$ at MR(P)L or RC	1.06
CC $\beta$ at MR(P)L or RC	1.12
Accuracy	104.7%
Measurement of Uncertainty	12.9%
Specificity (conc. blancs < CC $\alpha$ )	Passed

### 3. Performance characteristics full validation, Exp 1-3

Level	0.5	1	1.5
Unit	$\mu\text{g}/\text{kg}$	$\mu\text{g}/\text{kg}$	$\mu\text{g}/\text{kg}$
Accuracy	103.1%	105.9%	105.0%
Relative st.dev. Reprod. (RSD $_n$ )	9.5%	3.5%	3.6%
Std. dev repeatability (s $_r$ )	0.022	0.035	0.042
Relative st.dev. Repeat. (RSD $_r$ ) repeatability	4.3%	3.3%	2.6%
St. dev BL-reproducibility (s $_n$ )	0.062	0.099	0.116
BL-reproducibility	0.049	0.037	0.057
Expanded M.U.	0.137	0.104	0.160
	0.098	0.074	0.114

# Validation Templates (Experimental Design Based Validation)



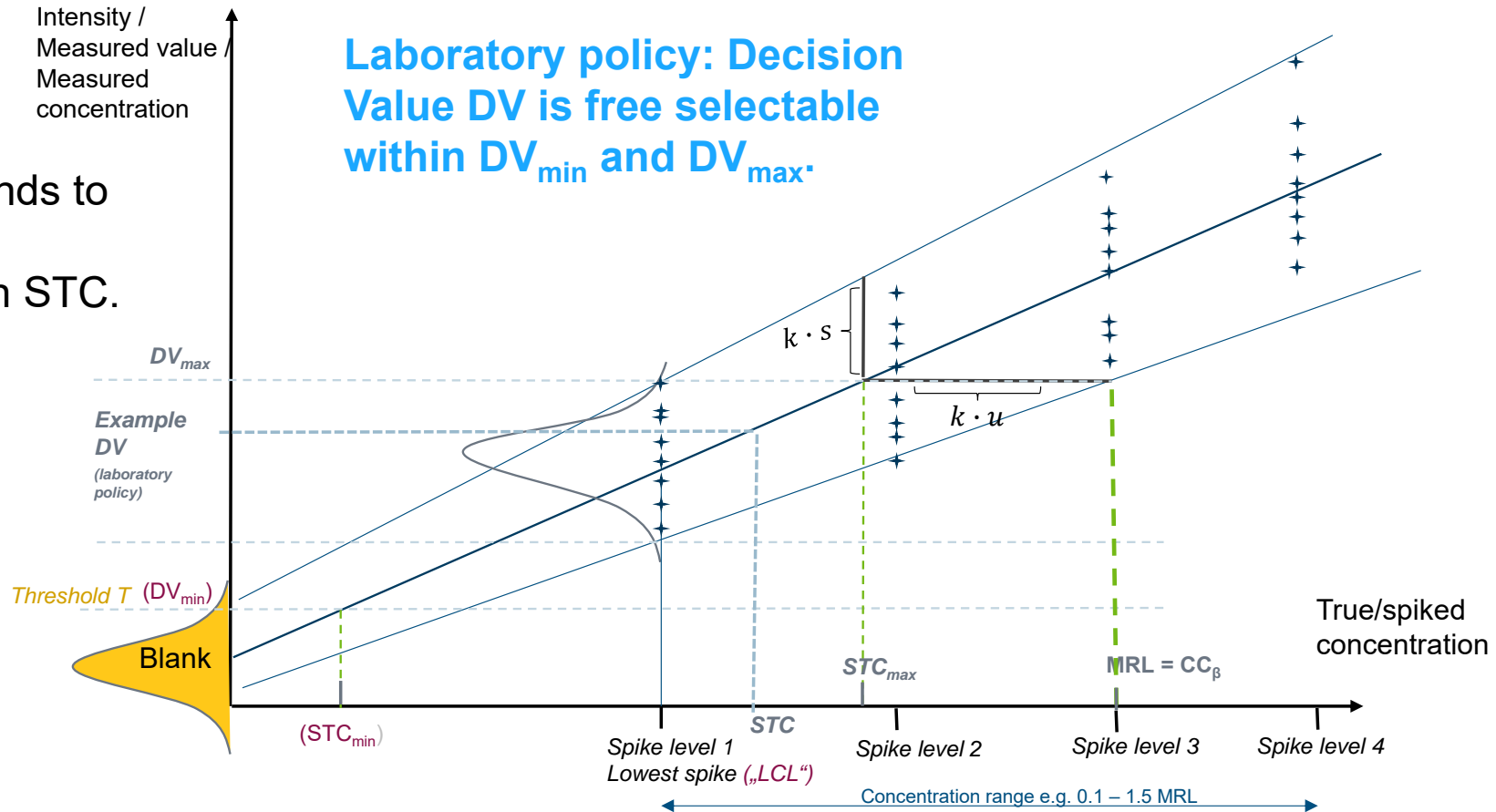
validation_template_COCC_008.xlsx - Excel						
Datei Start Einfügen Seitenlayout Formeln Daten Überprüfen Ansicht Hilfe ACROBAT						
A	B	C	D	E	F	
1	<b>Generic</b>	<b>Factor</b>				
	Run	I	II	III	IV	
2	Run 01	A	A	A	A	
3	Run 02	A	A	B	A	
4	Run 03	A	B	A	B	
5	Run 04	A	B	B	B	
6	Run 05	B	A	A	B	
7	Run 06	B	A	B	B	
8	Run 07	B	B	A	A	
9	Run 08	B	B	B	A	
10	<b>Specific</b>	<b>Factor</b>				
	Run	agricultural producer operator	HPLC column lot	storage of extract		
11	Sample					
12	eggblank01	Run 01	organic	routine	batch 1 (old)	without
13	eggblank02	Run 02	organic	routine	batch 2 (new)	without
14	eggblank03	Run 03	organic	occasional	batch 1 (old)	2-3 d at -20 °C
15	eggblank04	Run 04	organic	occasional	batch 2 (new)	2-3 d at -20 °C
16	eggblank05	Run 05	conventional	routine	batch 1 (old)	2-3 d at -20 °C
17	eggblank06	Run 06	conventional	routine	batch 2 (new)	2-3 d at -20 °C
18	eggblank07	Run 07	conventional	occasional	batch 1 (old)	without
19	eggblank08	Run 08	conventional	occasional	batch 2 (new)	without
20	<b>Randomised</b>	<b>Factor</b>				
	Run	agricultural producer operator	HPLC column lot	storage of extract		
21	Sample					
22	eggblank04	Run 04	organic	occasional	batch 2 (new)	2-3 d at -20 °C
23	eggblank02	Run 02	organic	routine	batch 2 (new)	without
24	eggblank07	Run 07	conventional	occasional	batch 1 (old)	without
25	eggblank08	Run 08	conventional	occasional	batch 2 (new)	without
26	eggblank03	Run 03	organic	occasional	batch 1 (old)	2-3 d at -20 °C
27	eggblank06	Run 06	conventional	routine	batch 2 (new)	2-3 d at -20 °C
28	eggblank01	Run 01	organic	routine	batch 1 (old)	without
29	eggblank05	Run 05	conventional	routine	batch 1 (old)	2-3 d at -20 °C

validation_template_COCC_008.xlsx - Excel							
Datei Start Einfügen Seitenlayout Formeln Daten Überprüfen Ansicht Hilfe ACROBAT							
A	B	C	D	E	F	G	
1	<b>Analyte</b>	<b>Concentration Level</b>					
		CL01	CL02	CL03	CL04	CL05	CL06
2	amprolium	0,200	0,500	1,000	2,000	3,000	4,000
3	arprinocid	0,200	0,500	1,000	2,000	3,000	4,000
4	buquinolate	0,200	0,500	1,000	2,000	3,000	4,000
5	canidazole	2,000	5,000	10,000	20,000	30,000	40,000
6	clazuril	0,200	0,500	1,000	2,000	3,000	4,000
7	clopidol, meticlorpindol, coyden	0,200	0,500	1,000	2,000	3,000	4,000
8	cyromazine	0,200	0,500	1,000	2,000	3,000	4,000
9	decoquinat	2,000	5,000	10,000	20,000	30,000	40,000
10	diaveridine	0,200	0,500	1,000	2,000	3,000	4,000
11	dichloroisoevernic acid	2,000	5,000	10,000	20,000	30,000	40,000
12	diclazuril	2,000	5,000	10,000	20,000	30,000	40,000
13	diflubenzuron	0,200	0,500	1,000	2,000	3,000	4,000
14	dimetridazole	0,200	0,500	1,000	2,000	3,000	4,000
15	dinitolimide, zoalene	2,000	5,000	10,000	20,000	30,000	40,000
16	dinitrocarbanilide, nicarbazin	30,000	75,000	150,000	300,000	450,000	600,000
17	ethopabat	0,200	0,500	1,000	2,000	3,000	4,000
18	fluazuron	0,200	0,500	1,000	2,000	3,000	4,000
19	fluralaner	0,200	0,500	1,000	2,000	3,000	4,000
20	halofuginon	0,600	1,500	3,000	6,000	9,000	12,000
21	HMMNI	0,200	0,500	1,000	2,000	3,000	4,000

# Revised definition of $CC\beta$

(quantitative approach- cf screening guidance)

DV corresponds to a true/spiked concentration STC.



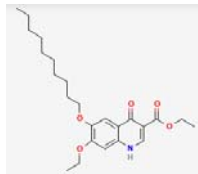
# Revised reports – Inclusion of CC $\beta$ requirements



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## Design-Parameters

Total-Number-of-Measurements: 56  
 Number-of-Measurements-Confirmed: 55  
 Samples: 8  
 Number-of-Outlier-Measurements: 0  
 Unit: µg



Decoquinatone  
ML of 20 ppb

Data before 20/07/2018 excluded from the validation.

## Decision-Value, Screening-Target-Concentration and CC $\beta$

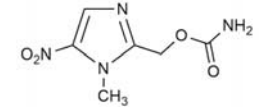
Level-of-interest	Matrix	DV	→ STC	CC $\beta$	$\beta$ -error-at-LOI
µg	µg	µg	µg	µg	[%]
20.000	µg	14.739	14.490	16.819	0.05

## Repeatability, In-house-Reproducibility and Recovery

Concentration	s <sub>r</sub> <sup>[2]</sup>	Rel.·s <sub>r</sub>	s <sub>wR</sub> <sup>[3]</sup>	Rel.·s <sub>wR</sub>	Recovery
µg	µg	[%]	µg	[%]	[%]
2.000	0.203	10.2	0.607	30.3	116.1
3.500	0.298	8.5	0.634	18.1	109.0
5.000	0.403	8.1	0.659	13.2	106.1
7.500	0.588	7.8	0.731	9.7	103.9
10.000	0.777	7.8	0.858	8.6	102.8
15.000	1.162	7.7	1.179	7.9	101.6
16.819	1.303	7.7	1.306	7.8	101.4
20.000	1.550	7.8	1.560	7.8	101.1

## Design-Parameters

Total-Number-of-Measurements: 48  
 Number-of-Measurements-Confirmed: 42  
 Samples: 8  
 Number-of-Outlier-Measurements: 0  
 Unit: µg



Ronidazole  
MMPR of 1 ppb

## Decision-Value, Screening-Target-Concentration and CC $\beta$

Level-of-interest	Matrix	DV	→ STC	CC $\beta$	$\beta$ -error-at-LOI
µg	µg	µg	µg	µg	[%]
0.000	µg	0.063	0.052	0.107	0.05

## Repeatability, In-house-Reproducibility and Recovery

Concentration	s <sub>r</sub> <sup>[2]</sup>	Rel.·s <sub>r</sub>	s <sub>wR</sub> <sup>[3]</sup>	Rel.·s <sub>wR</sub>	Recovery
µg	µg	[%]	µg	[%]	[%]
0.050	0.013	25.3	0.018	36.7	121.6
0.075	0.014	19.0	0.022	29.4	110.5
0.100	0.016	15.6	0.025	25.5	104.9
0.107	0.016	14.8	0.026	24.7	103.7
0.150	0.018	11.9	0.032	21.5	99.3

## Standard Addition – a Tool for „Special Cases“



....taking into account the specific properties of a sample  
e.g. correction of matrix effects



Basis : availability of a principally suitable (validated) method

### Potential applications might be :

- unique or exotic matrix (e. g. crocodile muscle, reindeer urine)
- lack of blank matrix (e. g. with endogenous hormones)
- Not fully identified matrix (e. g. fish species)
- analyte concentration(s) significantly outside the validated concentration range are expected

# Standard Addition - example



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## Template “MSA”

concentration outside the validation range (MRL 65 ng/g)

Concentration range adaption

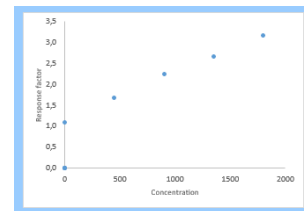
Check of RT criteria

Check of ion ratio criteria

Calculation of a “worst case”  $CC\alpha$

Data evaluation form multi-level standard addition for MRL substances							
Analysis date:		Always fill in C10, C11 and L34					
Analyte:	Meloxicam						
Lab journal / page:							
Matrix:	kidney						
MRL:	65,00						
Unit:	ug/kg						
<b>Sample 1</b>							
matrix	kidney						
Sample number	B-A250370						
Addition (ug/kg)	RT	Product ion 1	Product ion 2	RT IS	IS Area	Addition (ug/kg)	Relativ
0	10,19	1057500	843067	10,18	959167	0,0	1,00
450	10,19	1684000	1321000	10,18	1004000	450,0	1,00
900,0	10,19	2275000	1743000	10,19	1014000	900,0	1,00
1350,0	10,19	2253000	1724000	10,18	844100	1350,0	1,00
1800,0	10,19	2961333	2327000	10,18	935933	1800,0	1,00
						average	900,0
<b>Acceptance criteria of the sample:</b>							
Description	Result	Criterion	Accepted				
Linearity	0,998	> 0,990	YES				
Max. Δ ion ratio MLSA aliquots	1,7%	=< 40%	YES				
Max. Δ rel. RT MLSA aliquots	0,1%	=< 1,0%	YES				
<b>Result:</b>							
Δ ion ratio sample aliquot	3,2%	=< 40%	YES				
Δ rel. RT sample aliquot	0,0%	=< 1,0%	YES				
$s_x = s(xe)$	67,15						
RSD calculated result (%)	6,6%	< 11,0%	YES	→ $CC\alpha_{max} = 91,7$			
Calculated concentration (ug/kg):		1010,29	Confirmatory result:		NON COMPLIANT		
		=   b/a					

	Result
$y = ax + b$	
Slope	0,00114
y intercept	1,148
correlation	0,998



# Training Projects

## Training programme on methods



Training on a method for antivirals in chicken muscle at WFSR

# Training Projects



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## Training programmes on techniques



Training on the use of HRMS Techniques at ANSES

## HRMS – EURL/NRL working group



- Complexity is **not addressed in CIR (EU) 2021/808**
  - Need of interpretation of the requirements of CIR (EU) 2021/808
- **Discussion concerning confirmation** criteria when HRMS is used:
  - Are confirmation criteria for LC-MS/MS (e.g. N° IP) also sufficient for HRMS methods ?
  - Should the same number of identification points (IPs) be applied to HRMS?
  - Are additional criteria required due to the complexity of the HRMS data?
- Need for **harmonised guidance** on the interpretation of HRMS results

# Training programme on method validation

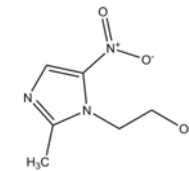
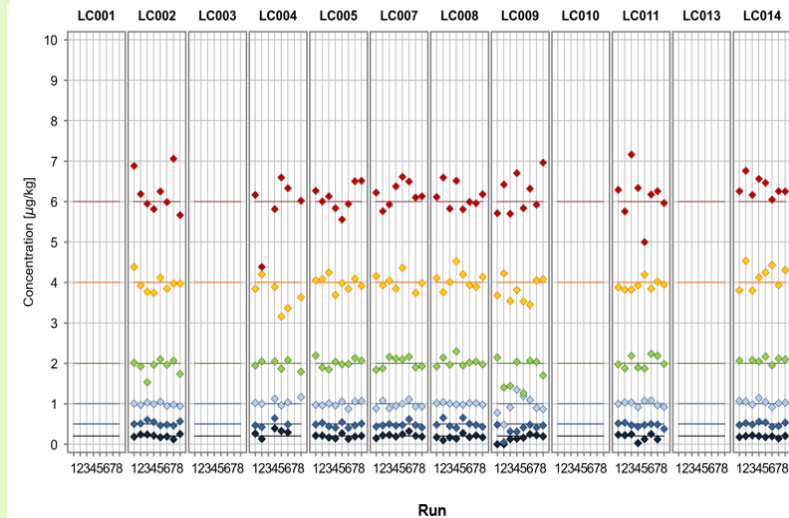


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- **Interlaboratory validation studies based on experimental design based validation plans**
- joint studies enhance **harmonization**
- **Robust method performance data.**
- Criteria-based approaches enable lab-specific validation
- 3 completed studies so far
  - NSAIDs in milk
  - $\beta$ -agonists in liver
  - coccidiostats in egg

**1 ongoing study (MULT A and B substances in milk - (presentation tomorrow)**

Example: coccidiostats in egg



**Molecular structure:** C<sub>6</sub>H<sub>9</sub>N<sub>3</sub>O<sub>3</sub>

**MW:** 171.156 g/mol

Lab specific CC $\alpha$  (MMPR, 1 µg/kg)

- IS : Metronidazole-<sup>13</sup>C<sub>2</sub><sup>15</sup>N<sub>2</sub>
- Rel reprod. s.d = 11.4 % (at MMPR of 1 ppb)

Analyte	LCL [µg/kg]	alpha	Laboratory												min	max
			LC001	LC002	LC003	LC004	LC005	LC007	LC008	LC009	LC010	LC011	LC013	LC014		
Metronidazole	0.2	1%		0.38		0.61	0.36	0.37	0.40	0.69		0.45		0.29	0.29	0.69

# Harmonisation / Interpretation Questions



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Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin (Text with EEA relevance)

OJ L 15, 20.1.2010, p. 1–72 (BG, ES, CS, DA, DE, ET, EL, EN, FR, IT, LV, LT, HU, MT, NL, PL, PT, RO, SK, SL, FI, SV)

► This document has been published in a special edition(s) (HR)

● In force: This act has been changed. Current consolidated version: 08/04/2024

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Home > Veterinary regulatory overview > Research and development (veterinary medicines) > Maximum residue limits (MRL)

## Maximum residue limits (MRL)

The **maximum residue limit (MRL)** is the maximum allowed concentration of a residue in a food product obtained from an animal that has received a veterinary medicine or that has been exposed to a biocidal product for use in animal husbandry.

Veterinary Maximum residue limit

Page contents

Also on this topic

Assessment criteria and extrapolation

Post assessment

Publication of information on MRLs

Biological substances not requiring an MRL evaluation

The European Medicines Agency's (EMA) **Committee for Veterinary Medicinal Products (CVMP)** is responsible for recommending MRLs, which, when adopted by the European Commission, become legally binding food safety standards. EMA provides guidance on establishing MRLs and submitting an application.

The European Union (EU) requires by law that **foodstuffs** such as meat, milk or eggs must not contain residue levels of veterinary medicines or biocidal products that might represent a hazard to the health of the consumer. [Regulation \(EC\) No 470/2009](#) lays down the rules and procedures for the establishment of MRLs.

Before a veterinary medicine intended for food-producing animals is authorised in the EU, the **Committee for Veterinary Medicinal Products (CVMP)** evaluates the **safety of its pharmacologically active substances** and their residues and recommends MRLs. The Agency has published [scientific guidance relevant to the establishment of MRLs for veterinary medicines](#).

EMA uses **human dietary exposure assessments** to establish MRLs of pharmacologically active substances of veterinary medicines.

## Frequent room for interpretation

### “No MRL required”

- no health concerns
- no residues present if correctly applied

## Residue definitions

- „Sum of .... „
- „expressed as ...

<https://www.ema.europa.eu/en/veterinary-regulatory-overview/research-development-veterinary-medicines/maximum-residue-limits-mrl>

# Harmonisation / Interpretation Questions



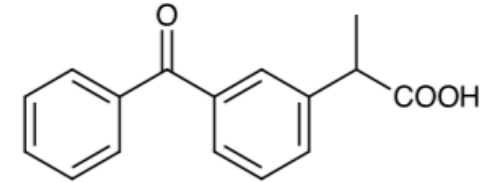
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## Ketoprofen

2022

Pharmacologically active Substance	Marker residue	Animal Species	MRL	Target Tissues	Other Provisions (according to Article 14(7) of Regulation (EC) No 470/2009)	Therapeutic Classification
Ketoprofen	NOT APPLICABLE	Bovine, porcine, Equidae	No MRL required	NOT APPLICABLE	NO ENTRY	NO ENTRY

8 November 2024  
EMA/CVMP/495258/2024  
Veterinary Medicines Division



2023

Ketoprofen	NOT APPLICABLE	Bovine, Porcine, Equidae	No MRL required	NOT APPLICABLE	NO ENTRY	NO ENTI
	Ketoprofen	Poultry	10 µg/kg 30 µg/kg 10 µg/kg 10 µg/kg	Muscle Skin and fat in natural proportion Liver Kidney	Not for use in animals from which eggs are produced for human consumption	NO ENTI

[MRL summary opinion<sup>1</sup>](#)

### Ketoprofen

All ruminants, porcine and Equidae

On 7 November 2024 the Committee for Veterinary Medicinal Products adopted an opinion<sup>2</sup> recommending the modification of the entry for ketoprofen in table 1 of the Annex to Regulation (EU) No 37/2010 of 22 December 2009. Maximum residue limits for ketoprofen in bovine and porcine are recommended. Furthermore, with reference to Article 5 of Regulation (EC) No. 470/2009 and in line with the criteria laid down in Commission Regulation (EU) 2017/880, the Committee agreed that the proposed maximum residue limits could be extrapolated to all ruminants and Equidae. Therefore, the amendment of the entry for ketoprofen in table 1 of the Annex to Regulation (EU) No 37/2010 of 22 December 2009, is recommended as follows:

2025

Further discussion ongoing....

Usually : for changes studies are required

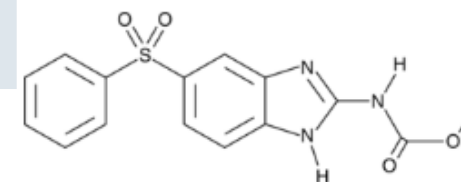
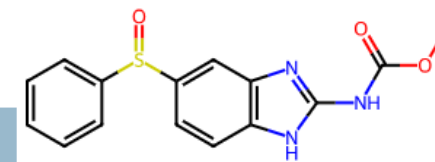
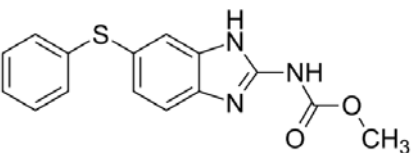
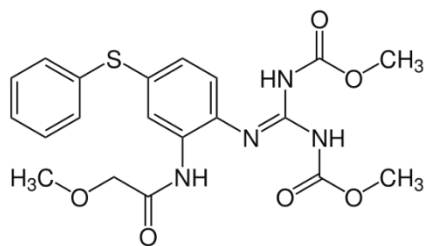
Pharmacologically active substance	Marker residue	Animal species	MRLs	Target tissues	Other provisions	Therapeutic classification
Ketoprofen	Ketoprofen	All ruminants, porcine, Equidae	50 µg/kg 20 µg/kg 20 µg/kg 50 µg/kg 20 µg/kg	Muscle Fat Liver Kidney Milk	For porcine species the fat MRL relates to 'skin and fat in natural proportions'	NO ENTRY
		Poultry	10 µg/kg 30 µg/kg 10 µg/kg 10 µg/kg	Muscle Skin and fat in natural proportion Liver Kidney	Not for use in animals from which eggs are produced for human consumption	NO ENTRY

# Harmonisation / Interpretation Questions



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„Sum of .... „  
„expressed as ...



Residue	Marker Residue	Abbreviation	EURL status	MRL (milk) / (µg/kg)	MRL (other) / (µg/kg)
Febantel	Sum of extractable residues which may be oxidised to oxfendazole sulfone	FEBAN	Minimum required	10	50 (muscle)
Fenbendazole		FEBZ			50 (fat)
Oxfendazole		OFEB			500 (liver)
Oxfendazole sulfone		O2FEB			50 (kidney) 1300 (eggs)

Febantel is absorbed by the intestines at a rate of 40%.

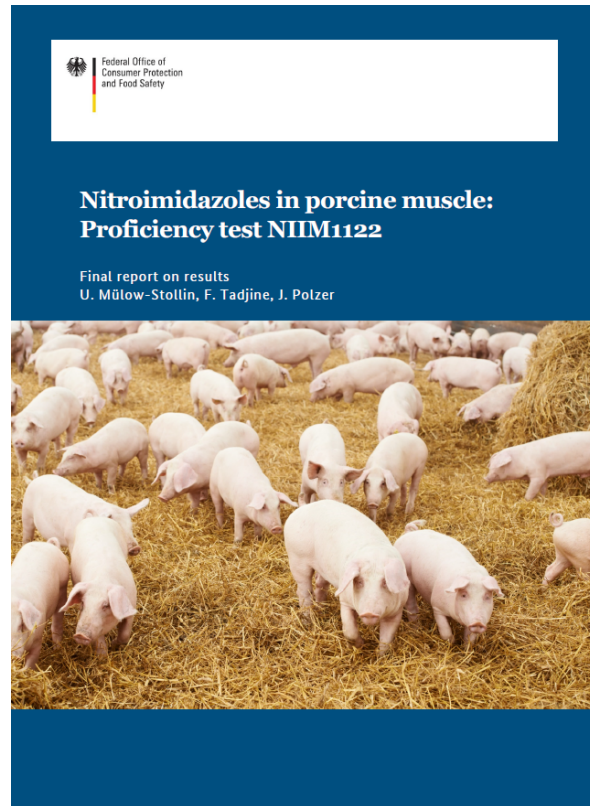
- converted into the active metabolites fenbendazole and oxfendazole.
- plasma half-life varies between 24 hours and 3 days (depending on the species)

Often single Methods are required - alternative: analysis of the single substances  
How to calculate the „sum“ ?

# Worldwide Traceability to SI



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## Linking the NRL Network with the National Metrology Institutes (NMI) Network

Version 1.1

CCQM K180 Draft A Report

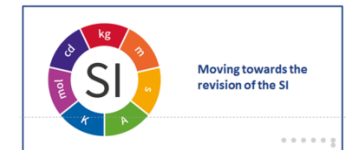
2024-04-16

CCQM-K180  
Polar analyte in high protein food matrix -  
metronidazole in porcine muscle

Key Comparison  
Track A

Draft A Report  
16.04.2024

U. Mütow-Stollin, J. Polzer  
Federal Office of Consumer Protection and Food Safety (BVL)  
EU Reference Laboratory for Residues (EURL)  
Diedersdorfer Weg 1 • 12277 Berlin • Germany  
P. O. Box 11 02 60 • 10832 Berlin • Germany



<https://www.bipm.org/kcdb/>

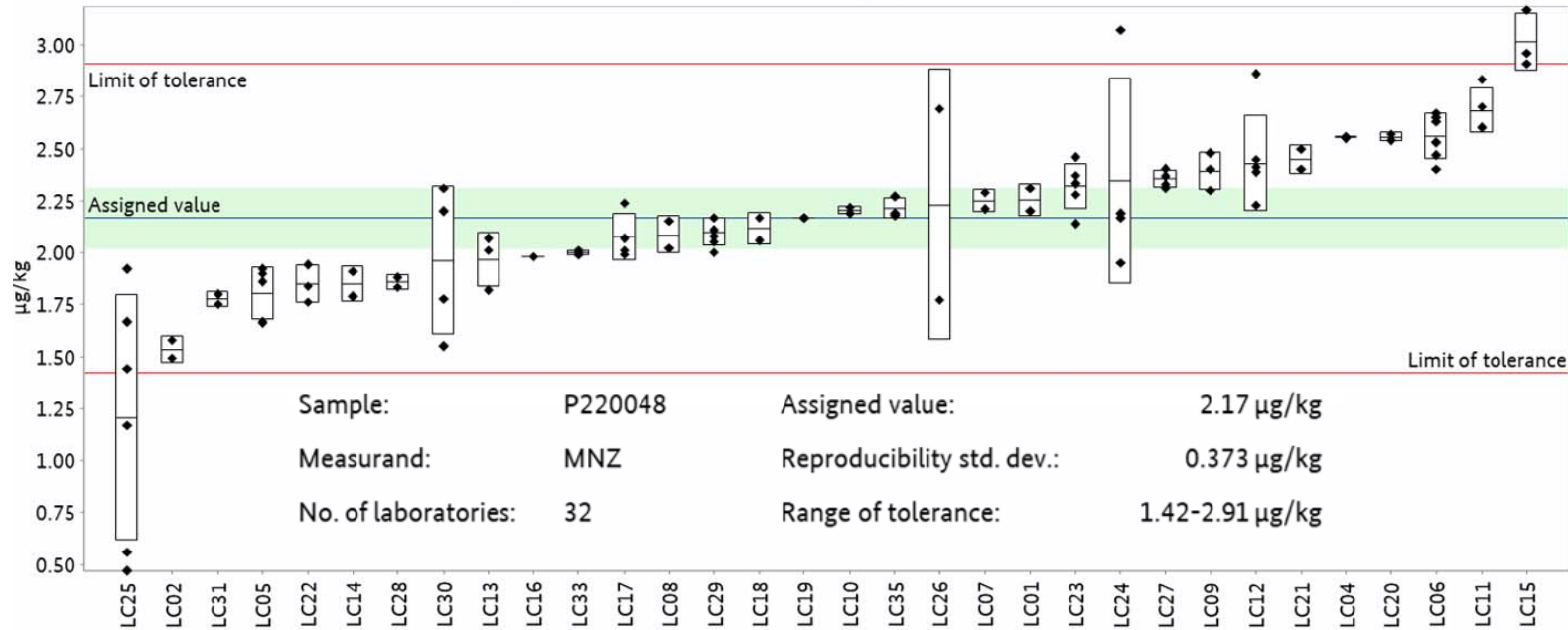
- „average performance“ / fit for purpose
- Routine methods / multi matrix / multi analyte

- very high performance on single spots

# PT Results / Key Comparison (preliminary)



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## NRL Network results

## NMI results (metrological traceable !)

Sample	Measurand	$x_{pt}$ /(µg/kg)	$\sigma_r$ /(µg/kg)	$\sigma_r$ /(%)	$\sigma_R$ /(µg/kg)	$\sigma_R$ /(%)	$u(x_{pt})$ /(µg/kg)	$u(x_{pt})$ /(%)	Number results	Number labs
NRLs	MNZ	2,17	0,098	4,5	0,373	17,2	0,082	3,8	103	32
OAWG	(Hampel)	2,18 *					0,034	1,6	15	15

# Metrology Network

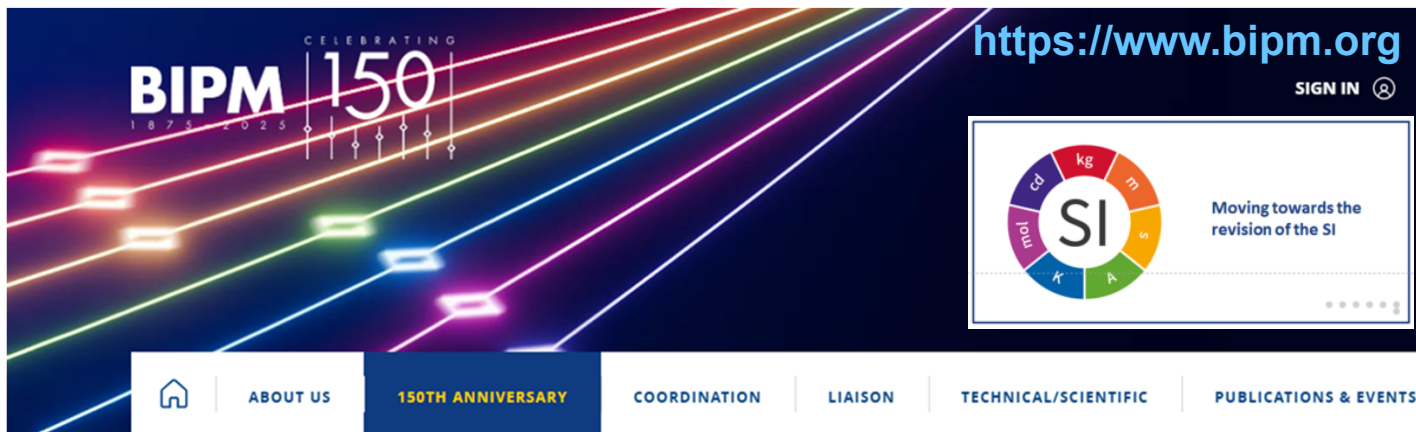


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## Collaboration with the OAWG of the CCQM at the BIPM

- **Benefits for the European NRL network**
- Provision of traceability by reference materials
- **Worldwide** accepted
- Pure substances with metrological traceability

150 years of meter convention !



**Thank you for your commitment !**

Views and opinions expressed are however those of the authors only and do not necessarily reflect those of the European Union or of the European Health and Digital Executive Agency (HADEA). Neither the European Union nor HADEA can be held responsible for them.

Contact :

<https://eurl-residues.eu/>

...and our EURL teams for their contributions !