



The document Version 2.0 of June 2022 and Version 2.1 of January 2025 have not been adopted by the European Commission. Any views expressed related to the interpretation of EU law may therefore not be regarded as stating an official position of the Commission. Only the Court of Justice of the European Union is competent to authoritatively interpret Union law.

Version 2.0 of the guidance document was endorsed by the Standing Committee on Plants, Animals, Food and Feed, section Novel Food and Toxicological Safety of the Food Chain at the meeting on 22 June 2022.

In Version 2.1 the only the MMPR for 17-beta oestradiol in bovine meat was lowered to 0.1 microgram per kilogram.

EURL GUIDANCE ON MINIMUM METHOD PERFORMANCE REQUIREMENTS (MMPRs) FOR SPECIFIC PHARMACOLOGICALLY ACTIVE SUBSTANCES IN SPECIFIC ANIMAL MATRICES

The purpose of this technical guidance is to improve and harmonize the performance of analytical methods used for the analysis of residues of unauthorised or prohibited pharmacologically active substances and for authorised pharmacologically active substances in matrices or species for which no use is authorised, taking into account state of the art analytical methods. For authorised pharmacologically active substances¹, for which no MRL has been set in a specific matrix or species, for those matrices/species the MMPR is 1/4th of the cascade MRL, established under Regulation (EU) 2018/470 for the concerned substance. The MMPR requirement '1/4th of the cascade MRL' requires in principle a spike level of down to 0.1 times the cascade MRL (which is in line with Commission Implementing Regulation (EU) 2021/808), where analytically feasible. This guidance applies to national residue control plans established in accordance with Council Directive 96/23/EC² and to all other official controls carried out on residues of pharmacologically active substances in live food-producing animals, their body parts and fluids, excrements, tissues, products of animal origin, animal by- products, and drinking water.

For specific prohibited³ or unauthorised pharmacologically active substances⁴, reference points for

¹ Substances included in Table 1 of the Annex to Regulation (EU) No 37/2010 or pharmacologically active substances that are authorised as a feed additive under Regulation (EC) No 1831/2003.

² Council Directive 96/23/EC remains applicable for the national residue control plans until 14 December 2022. For the period thereafter, new legislation is under preparation.

³ Substances within the scope of Directive 96/22/EC and substances included in Table 2 of the Annex to Regulation (EU) No 37/2010.

⁴ Pharmacologically active substances, which are not included in Table 1 of the Annex to Regulation (EU) No 37/2010 or substances that are not authorised as a feed additive under Regulation (EC) No 1831/2003, with the exception of substances essential for the treatment of equidae and substances bringing added clinical benefit compared to other treatment options available for equidae, as laid down in Regulation (EC) No 1950/2006.

action (RPAs) in food have been set under Regulation (EU) 2019/1871. Food of animal origin, containing residues of a pharmacologically active substance in a concentration at or above the reference point for action, shall be considered not to comply with Union legislation and shall not enter the food chain. By consequence, the RPAs also define the minimum method performance requirements (MMPRs) for these substances in food. However, when laboratories are able to reliably identify these substances at lower concentrations, also these concentrations shall lead to follow-up investigations for verifying whether an illegal treatment took place (Art. 6 of Regulation (EU) 2019/1871). For substances for which RPAs are established in food, this document defines the MMPRs in food and non-food matrices.

For prohibited or unauthorised pharmacologically active substances, for which no RPA has been set in food, this document specifies MMPRs for specific substances in specific food and non-food matrices.

Laboratories should ensure that the CC β for screening methods or the CC α for confirmatory methods⁵ is lower than the MMPR.

It needs to be emphasized that this document is a technical guidance for analytical methods in residues control. The MMPRs should by no means be considered as enforcement limits. They represent the minimum concentrations that official laboratories should be able to reliably identify. In case certain laboratories can identify lower concentrations in accordance with the method requirements established in Commission Implementing Regulation (EU) 2021/808, competent authorities should also enforce lower concentrations of residues of prohibited or unauthorised pharmacologically active substances. The enforcement should be similar to that in case of RPAs.

For practical reasons $\mu g/kg$ and $\mu g/l$ have been replaced by ppb in all tables. The analytes/matrices in bold are considered important.

For further technical assistance on how to improve analytical methods in order to reach the MMPRs the EURL responsible for the substance should be consulted.

⁵ As defined in Commission Implementing Regulation (EU) 2021/808.

EURL Name and Substance Groups	Address
Common EURL Portal	https://eurl-residues.eu
ANSES EURL	
Antibacterial substances, including sulphonamides and quinolones Dyes Carbadox and olaquindox Chloramphenicol Dapsone Nitrofurans	ANSES - Laboratoire de Fougères La Haute Marche – Javené – BP 90203 F-35302 Fougères, France Phone: +33(0)2 99 17 27 47 Director: Dr. Eric Verdon email: <u>eurl-vmpr-fougeres@anses.fr</u> <u>eric.verdon@anses.fr</u> <u>https://eurl-veterinaryresidues.anses.fr</u>
BVL-EURL	
Beta-agonists Nitroimidazoles Anthelmintics Anticoccidials Non-steroidal anti-inflammatory drugs (NSAIDs)	Bundesamt für Verbraucherschutz und Lebensmittelsicherheit Diedersdorfer Weg 1 12277 Berlin, Germany Phone: + 49(0)30 18445-8210 Fax: + 49(0)30 18445-8099 Director: Dr. Joachim Polzer email: <u>eurlvetdrug@bvl.bund.de</u> <u>https://www.bvl.bund.de/EN/Tasks/09_Labo</u> <u>ratories/01_Tasks/02_reference_laboratories/</u> 01_reference_laboratories_EURL/reference_ <u>laboratories_EU_node.html</u> password protected webpage, also in English: <u>https://fis-vl.bvl.bund.de/share/page/</u>
WFSR-EURL	
Stilbenes, stilbene derivatives and their salts and esters Antithyroid agents Steroids Resorcylic acid lactones (RALs) including zeranol Sedatives Mycotoxins	Wageningen Food Safety ResearchP.O. Box 2306700 AE Wageningen, The NetherlandsPhone: + 31(0)317 480256Fax: + 31(0)317 417717Director: Drs. Saskia Sterkemail: eurl.growthpromoters@wur.nlSaskia.sterk@wur.nlhttps://www.wur.nl/en/Research-Results/Research-Institutes/food-safety-research/Reference-Iaboratory/European-Union-Reference-Laboratory-I/EURL-growth-promoters.htm

1. A1 Stilbenes⁶⁶ (EURL WFSR Wageningen)

For the purpose of control the matrices of choice are urine followed by liver. Muscle has been included for the control of imports and for imported aquaculture products but it is not the matrix of choice for routine plans as the concentrations of residues are very low in muscle.

Substances	Matrix	MMPR*
Diethylstilbestrol (DES)		0.5 ppb for DES
Dienestrol (DE)	Urine	1 ppb for DE,
Hexestrol (HEX)		HEX, BENZ
Benzestrol (BENZ)	Liver	1ppb (for all substances)
	Meat (including fish)	1 ppb (for all substances)

* $CC\beta$ for screening methods or $CC\alpha$ for confirmatory methods should be lower than the value expressed in this column.

2. A2 Thyrostats (EURL WFSR Wageningen)

For the purpose of control the matrices of choice are urine and thyroid gland. Muscle has been included for the control of imports and for imported aquaculture products but it is not the matrix of choice for routine plans as the concentrations of residues are very low in muscle.

It should be noted that low concentrations of thiouracil (maximum 30 ppb) have been detected in animals fed with a diet containing cruciferous plants.

Substances	Matrix	MMPR*
Thiouracil	Urine Thyroid	10 ppb for all ^{&}
Methylthiouracil Propylthiouracil Tapazole Benzylthiouracil Mercaptobenzimidazol		

**CCβ* for screening methods or *CCα* for confirmatory methods should be lower than the value expressed in this column. [&]Low concentrations of thiouracil have been detected in bovine animals fed with cruciferous plants, however there is scientific evidence showing that levels above 30 ppb in urine have a low chance of being linked to natural origin due to this contamination. There are however cases where 30 ppb is exceeded for thiouracil and no exogenous source could be found. See Discrimination between the exogenous and endogenous origin of thiouracil in farm animals, the final chapter. Marco H. Blokland, Frederike E. van Tricht, Maria J. Groot, Leendert A. Van Ginkel & Saskia S. Sterk, Food Additives and contaminants Part A, 2021, Vol. 38, No 12, 2077-2090. For the latest strategies consult EURL Reflection Paper.

⁶ Classification according to Directive 96/23/EC remains applicable until 14 December 2022. For the period thereafter, new legislation in which a new classification is proposed, is under preparation.

3. A3 Steroids (EURL WFSR Wageningen)

For control purposes matrices of choice are urine followed by liver.

For 17ß-oestradiol, testosterone and esters of oestrogens, androgens and progestagens serum and for gestagens such as MPA kidney fat is the matrix of choice, as indicated in the table. The matrix hair can be used when controlling esters of oestradiol, testosterone, nortestosterone, boldenone and other steroid esters. Muscle has been included for control purposes of imports and for aquaculture products. For A3 steroids not all steroids are mentioned by name in this guidance paper. Generally, 0.5 ppb for the marker of the steroid in urine is an acceptable MMPR.

Substances	Marker residue- metabolite ^{\$}	Matrix	MMPR*
Boldenone [#] 17β-boldenone		Urine	1 ppb
	glucuronide (young	Liver	2 ppb
	bovine, <6 months)	Muscle	1 ppb
	17α-boldenone (bovine, sheep, goat, horse)	Urine	0.5 ppb
	sneep, goat, norse)	Liver	2 ppb
		Muscle	1 ppb as β-boldenone
176-19-	17α-19-	Urine	0.5 ppb
Nortestosterone ^{##}	Nortestosterone ^{###}	Liver	2 ppb
(nandrolone)	(epi-nandrolone)	Muscle	1ppb
Ethinylestradiol		Urine	0.5 ppb
·		Liver	2 ppb
		Muscle	1 ppb
17B-oestradiol	17β-oestradiol	Plasma/Serum	0.1 ppb
		Muscle	0.1 ppb
17β-oestradiol ester		Hair	20 ppb
		Plasma/Serum	0.1 ppb
			Male < 6 months: 10 ppb
17β-testosterone	17β-testosterone	Serum	Male 6 - 18months: 30 ppb
			Female < 18 months: 0.5 ppb
17β -testosterone este	er	Hair	10 ppb
		Serum	0.1 ppb
Methyltestosterone		Urine	0.5 ppb
Methylboldenone		Liver	2 ppb
		Muscle	1ppb
Chlorotestosterone	17α-clostebol	Urine	0.5 ppb
	Chlorandrostenedione	Liver	2 ppb
	(CLAD)	Muscle	1 ppb
17ß-trenbolone	17α-trenbolone (urine)		0.5 ppb
	17β-trenbolone	Liver	2 ppb
	(muscle)	Muscle	1 ppb
		Hair	10 ppb (ester)
Stanozolol	16B-hydroxystanozo	Urine	0.5 ppb
	lol	Liver	2 ppb
		Muscle(stanozolol	1 ppb
		Hair (stanozolol)	10 ppb

Dexamethasone		Urine	0.5 ppb	
		Liver, Muscle	MRL when there has been authorised treatment	
Megestrol	Megestrol (acetate)	Kidney fat	5 ppb	
		Muscle	1.0 ppb	
Melengestrol	Melengestrol	Kidney fat	5 ppb	
	(acetate)	Muscle	1.0 ppb	
Chlormadinone	Chlormadinone	Kidney fat	2 ppb	
	(acetate)	Muscle	1 ppb	
Medroxy-	Medroxy-progesterone	Kidney fat	1 ppb	
progesterone	(acetate)	Muscle	1.0 ppb	

* $CC\beta$ for screening methods or $CC\alpha$ for confirmatory methods should be lower than the value expressed in this column. [#]Boldenone as described in expert group paper of 2003, reference: Presence and metabolism of the anabolic steroid boldenone in various animal species (A review. July 2004, Food Additives and Contaminants 21(6):515-25).

[§]Porcine animals do not metabolise into α -isomers. For porcine animals the administered steroid is the marker.

^{##}17 β -19-nortestosterone occurs naturally in non-castrated pigs and horses. For the latest strategies consult EURL Reflection Paper.

^{###}17a-19-nortestosterone occurs naturally in pregnant cows and newborn calves. For the latest strategies consult EURL *Reflection Paper*.

Reflection paper EURL WFSR: <u>https://www.wur.nl/en/Research-Results/Research-Institutes/food-safety-</u> research/Reference-laboratory/European-Union-Reference-Laboratory/EURL-growth-promoters/Library-EURL-GP.htm

4. A4 Resorcylic acid lactones and derivates (EURL WFSR Wageningen)

For the purpose of control matrices of choice are urine followed by liver. Muscle has been included for control purposes of imports and for imported aquaculture products.

Substances	Marker residue- metabolite	Matrix	MMPR*
		Urine	1 ppb
Zeranol**	Taleranol	Liver	2 ppb
		Muscle	1 ppb
Zearalenone		Urine	2 ppb
Learaienone		Liver	2 ppb
		Urine	2 ppb
α-zearalenol		Liver	2 ppb
0 =====1		Urine	2 ppb
β-zearalenol		Liver	2 ppb

 $*CC\beta$ for screening methods or $CC\alpha$ for confirmatory methods should be lower than the value expressed in this column.

**In case both zeranol and zearalenone are present, the presence of zeranol is considered as the result of mycotoxin contamination. Screening can be done on zeranol and its marker metabolites taleranol. When one of these compounds is detected a full resorcylic acid lactone (RAL) profile is needed to decide on noncompliance. For the latest strategies consult EURL Reflection Paper.

5. A5 Beta-agonists (EURL BVL Berlin)

For control purposes the matrices of choice are urine and liver and especially retina since here higher concentrations of residues can be found for a longer time period. The analysis of complete eyes is the second choice compared to retina which is the first choice. Hair is also a recommendable matrix however the risk of external contamination has to be considered. When taking hair it is always recommended to sample also urine at the same time from the same animal. Muscle has been included for control purposes of imports but concentrations in muscle are significantly lower than in previously mentioned matrices.

Substances	Matrix	MMPR*
Clenbuterol:	Urine	0.1 ppb
MRL (for bovine and equidae**:	Liver	
$0.1 \mu g/kg$ in muscle	Lung	
$0.05 \mu g/kg$ in milk (only bovine)	Muscle	
$0.5 \mu g/kg$ in liver and kidney	Kidney	
Brombuterol,	Faeces	
Bromchlorbuterol	Plasma	
Cimaterol	Drinking water	
Cimbuterol	Retina	1 ppb
Clenpenterol	Hair (Screening)	
Clenproperol		
Hydroxymethylclenbuterol		
Mabuterol		
Mapenterol		
Tulobuterol		
	Urine	0.5 ppb
Carbuterol	Liver	
Clencyclohexerol	Lung	
Isoxsuprine	Muscle	
Ractopamine	Kidney	
Ritodrin	Faeces	
Salbutamol	Plasma	
Terbutaline	Drinking water	
Zilpaterol	Retina	5 ppb
	Hair (Screening)	
	Urine	1 ppb
Fenoterol,	Liver	
Salmeterol	Lung	
	Muscle	
	Kidney	
	Faeces	
	Plasma	
	Drinking water	
	Retina	5 ppb
	Hair (Screening)	

* $CC\beta$ for screening methods or $CC\alpha$ for confirmatory methods should be lower than the value expressed in this column. **According to Council Directive 96/22/EC beta-agonists may be authorised for very exceptional and restrictive therapeutic treatments.

6. A6 (EURL ANSES Fougeres, BVL Berlin and WFSR Wageningen)

For nitroimidazoles the matrices of choice are eggs, plasma/serum and retina, followed by - depending on the species - muscle. Then Milk can also be chosen if relevant. For aquaculture products muscle is the relevant matrix, furthermore crustacean and fish eggs.

Substances	Marker residue- metabolite	Matrix	MMPR*
Nitroimidazoles: Ronidazol Dimetridazol Metronidazol + other 5- nitroimidazoles	Parent drugs + Hydroxy- metabolites	Poultry: Plasma, Serum, Retina**, Eggs Pigs (and other species): Plasma, Serum, Muscle, Retina** Aquaculture products: Muscle Milk	1 ppb
muonmuazores		(Drinking water) Gut matrix /casings	1 ppb
Chloramphenicol		Meat, milk, eggs, aquaculture products, urine	0.15 ppb (RPA)
		Gut matrix / casings	0.15 ppb (RPA)
Nitrofurans	Metabolites AMOZ, AHD, SEM, AOZ, DNSH	Poultry Meat, Aquaculture products, Muscle/meat, Milk, Eggs	0.5 ppb (RPA)
		Gut matrix /casings	0.5 ppb (RPA)
Dapsone		Muscle/meat Milk	5 ppb
Chlorpromazine		Kidney	5 ppb

* $CC\beta$ for screening methods or $CC\alpha$ for confirmatory methods should be lower than the value expressed in this column. **For retina it is not possible yet to give a recommended concentration since it is not defined so far to which part of the eye (or the whole eye) the concentration should refer.

7. B2d Sedatives (EURL WFSR Wageningen)

Matrix of choice is kidney.

Substances	Matrix	MMPR*
Carazolol Acepromazine Propiopromazine Haloperidol Azaperon/Azaperol	Kidney	5 ppb

* $CC\beta$ for screening methods or $CC\alpha$ for confirmatory methods should be lower than the value expressed in this column.

8. B2e NSAIDs (EURL BVL Berlin)

For control purposes matrices of choice are muscle and milk, followed by kidney, liver and plasma.

Substances	Matrix	MMPR*
Phenylbutazone Oxyphenbutazone	Mugala	5 ppb
Ibuprofen Naproxen Mefenamic acid Niflumic acid Flufenamic acid	Muscle Milk Kidney Liver Plasma	10 ppb

*CCβ for screening methods or CCa for confirmatory methods should be lower than the value expressed in this column.

9. Other substances (EURL ANSES)

Substances	Marker residues	Matrix	MMPR*
Malachite green	Malachite green and Leucomalachite green	Muscle fish	Sum: 0.5 ppb (RPA)
Crystal violetCrystal violet and Leucocrystal(Gentian violet)violet (Leucogentian violet)		Muscle fish	Sum: 0.5 ppb
Brilliant green	Brilliant green and Leucobrilliant green**	Muscle fish	Sum: 0.5 ppb
Carbadox	QCA (quinoxaline- 2-carboxylic acid) and/or DCBX (Desoxycarbadox)	Muscle, liver	5 ppb
Olaquindox	MQCA (3-methylquinoxaline-2- carboxylic acid)	Muscle, liver	5 ppb

* $CC\beta$ for screening methods or $CC\alpha$ for confirmatory methods should be lower than the value expressed in this column. ** Control of this substance is not mandatory until certified reference standard is available.

Group	Substances to be included	MMPR*
A6	Chloramphenicol	0.15 ppb (RPA)
	Nitroimidazoles	1 ppb
	Nitrofurans	0.5 ppb (RPA)
Bl**	Tetracyclines	10 ppb
	Sulfonamides	10 ppb
	Streptomycin	50 ppb
	Macrolides:	
	Erythromycin	20 ppb
	Tylosin	10 ppb

10. Honey (EURL ANSES Fougeres for Antimicrobials and BVL Berlin for Nitroimidazoles)

* $CC\beta$ for screening methods or $CC\alpha$ for confirmatory methods should be lower than the value expressed in this column. **MMPRs for B1 substances in honey are related to control in the absence of a signified cascade use in line with Regulation (EU) 2018/470.