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

1. A1 Stilbenes (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 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) Dienestrol (DE) Hexestrol (HEX) Benzestrol (BENZ)	Urine	0.5 ppb for DES 1 ppb for DE, HEX, BENZ
	Liver	1ppb (for all substances)
	Meat (including fish)	1 ppb (for all substances)

** CCbeta for screening methods or CCalpha 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 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 Methylthiouracil Propylthiouracil Tapazole Benzylthiouracil Mercaptobenzi-midazol	Urine Thyroid	10 ppb for all[&]

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[&] 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. Research into discrimination is on-going. For latest strategies consult EURL Reflection Paper.

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 gestagens serum and for progestagens 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 a acceptable MMPR.

Substances	**Marker residue-Metabolite$**	**Matrix**	**MMPR***
Boldenone#	17ß-boldenone glucuronide (young bovine)	Urine	1 ppb
		Liver	2 ppb
		Muscle	1 ppb
	17α -boldenone (bovine, sheep, goat, horse)	Urine	0.5 ppb
17ß-19-nortestosterone[1] (nandrolone)	17α-19-nortestosterone[2] (epi-nandrolone)	Urine	0.5 ppb
		Liver	2 ppb
		Muscle	1ppb
Ethinylestradiol		Urine	0.5 ppb
		Liver	2 ppb
		Muscle	1 ppb
17ß-Oestradiol	17β-Oestradiol	Serum	0.1 ppb
		Muscle	1 ppb
17b-oestradiol-ester		Hair Serum	20 ppb 0.1 ppb
17β-Testosterone	17β-Testosterone	Serum	Male < 6 months: 10 ppb Male 6 - 18months: 30 ppb Female < 18 months: 0.5 ppb
17β-Testosterone ester		Hair Serum	10 ppb 0.1 ppb
Methyltestosterone **Methylboldenone**		Urine	0.5 ppb
		Liver	2 ppb
		Muscle	1ppb
Chlorotestosterone	17alfa-=clostebol Chlorandrostenedione (CLAD)	Urine Liver Muscle	0.5 ppb 2 ppb 1 ppb
17ß-Trenbolone	17α-Trenbolone	Liver	0.5 ppb
		Muscle	2 ppb
		Muscle Hair	1 ppb 10 ppb (ester)
Stanozolol	16ß-Hydroxystanozolol	Urine	0.5 ppb
		Liver	2 ppb
		Muscle	1 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 (acetate)	Kidney fat	5 ppb
		Muscle	1.0 ppb
Chlormadinone	Chlormadinone (acetate)	Kidney fat	2 ppb
		Muscle	1 ppb
Medroxy-progesterone	**Medroxy-progesterone (acetate)**	**Kidney fat**	**1 ppb MRPL**
		Muscle	1.0 ppb

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#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 alfa isomers. For porcine animals the administered steroid is the marker.

[1]17β-19-Nortestosterone occurs naturally in non-castrated pigs and horses. For latest strategies consult EURL Reflection Paper

[2]17α-19-Nortestosterone occurs naturally in pregnant cows and newborn calves. For latest strategies consult EURL Reflection Paper

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 aquaculture products.

Substances	**Marker residue-metabolite**	**Matrix**	**MMPR***
Zeranol[1]	Taleranol	Urine	1 ppb
		Liver	2 ppb
		Muscle	1 ppb
Zearalanone		Urine	2 ppb
		Liver	2 ppb
Zearalenone		Urine	2 ppb
		Liver	2 ppb
Alfa-Zearalenol		Urine	2 ppb
		Liver	2 ppb
Beta-zearalenol		Urine	2 ppb
		Liver	2 ppb

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[1] 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 RAl profile is needed to decide on non compliance. For 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. 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. Faeces and plasma are second choice matrices; the analysis of complete eyes is the second choice compared to retina which is the first choice.
Muscle has been included for control purposes of imports and for aquaculture products but concentrations in muscle are significantly lower than in previously mentioned matrices.

Substances	**Matrix**	**MMPR***
Clenbuterol: *MRL (for bovine and equidae)**:* *0.1 µg/kg in muscle* *0.05 µg/kg in milk (only bovine)* *0.5 µg/kg in liver and kidney* **Brombuterol**, Chlorbrombuterol, Mabuterol, Mapenterol, Tulobuterol, Hydroxymethylclenbuterol, Clenpenterol, Clenproperol, Cimaterol, Cimbuterol	**Urine**	0.1 ppb
	Liver	0.1 ppb
	Retina	1 ppb
	Muscle Kidney, Faeces Plasma, Drinking water	0.1 ppb 0.1 ppb 0.1 ppb 0.1 ppb
	Hair (Screening)	1 ppb
Ractopamine, Clencyclohexerol **Isoxsuprine**, Ritodrin **Salbutamol**, Salmeterol, **Zilpaterol**, Fenoterol, Pirbuterol, Carbuterol, Terbutaline	**Urine**	0.5 ppb
	Liver	0.5 ppb
	Retina	3 ppb
	Muscle	0.5 ppb
	Kidney, Faeces	0.5 ppb
	Plasma, Drinking water	0.5 ppb
	Hair (Screening)	3 ppb
	Feed	50 ppb for all

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*** 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. Milk and honey can 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	Hydroxy-metabolites	**Poultry:** Plasma Serum Retina** Eggs **Pigs (and other species):** Plasma Serum Muscle Retina** **Aquaculture products:** muscle Milk (Drinking water)	1 ppb
		Feed	50 ppb
Chloramphenicol		**Meat, milk, eggs, aquaculture products, urine**	**0.15 ppb RPA**
Nitrofurans	**Metabolites AMOZ, AHD, SEM, AOZ, DNSH**	**Poultry Meat, Aquaculture products, Muscle/meat, Milk, Eggs**	**0.5 ppb RPA for all**
Dapsone		Muscle Meat Milk	5 ppb
Chlorpromazine		Kidney	5 ppb

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*** 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

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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 **Oxyphenbutazon**	**Muscle**, **milk** Kidney Liver Plasma	5 ppb
Ibuprofen Naproxen Mefenamic acid		10 ppb

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9. Others (EURL ANSES +)

Substances	Marker residue-metabolite	Matrix	MMPR*
Malachite green	**Leucomalachite green**	**Muscle fish**	**Sum: 1ppb RPA**
Crystal Violet *(Gentian Violet)*	**Leucocrystal violet *(Leucogentian violet)***	**Muscle fish**	**Sum: 1 ppb**
Brilliant Green	**Leucobrilliant green**	**Muscle fish**	**Sum: 1 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

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

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	20 ppb
	Macrolides: Erythromycin Tylosin	 20 ppb 10 ppb

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** MMPRs for B1 substances in Honey are related to control in the absence of a signified Cascade use in line with Reg 2018/470. They have to be controlled at $1/10^{th}$ to the lowest MRL in other species accord. To Reg 2018/470.