

CRL GUIDANCE PAPER (7 December 2007)

CRLs VIEW ON STATE OF THE ART ANALYTICAL METHODS FOR NATIONAL RESIDUE CONTROL PLANS

The following is the Community Reference Laboratories' (CRLs) view on state of the art analytical methods for national residue control plans established in accordance with Council Directive 96/23/EC. The purpose of this technical guidance is to improve and harmonise the performance of analytical methods used for those substances for which maximum residue limits (MRLs) have not been established according to Council Regulation (EC) No 2377/90. Thus substances with MRLs are generally not listed in this guidance paper.

These substances without MRLs are in particular substances partly or entirely prohibited for use in food producing animals according to Council Directive 96/22/EC and Council Regulation (EEC) No 2377/90. Minimum required performance limits (MRPLs) established according to Commission Decision 2002/657/EC have been added for completeness and are marked in bold.

It needs to be emphasised that this document is to serve as technical guidance for analytical methods in residue control. The recommended concentrations in this document have no legal force. MRPLs, on the other hand, serve according to Commission Decision 2005/34/EC as reference points for action irrespective of the matrix tested.

For practical reasons $\mu\text{g}/\text{kg}$ and $\mu\text{g}/\text{l}$ have been replaced by ppb in all tables.

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

CRL Name and Groups	Address
BVL-CRL Beta-agonists Anthelmintics Anticoccidials including nitroimidazoles Non-steroidal anti-inflammatory drugs (NSAIDs)	Bundesamt für Verbraucherschutz und Lebensmittelsicherheit Diedersdorfer Weg 1 D-12277 Berlin, Germany Phone: + 49(0)3018-412-2302 Fax: + 49(0)3018-412-2300 http://www.bvl.bund.de/cln_007/nn_491400/DE/01_Lebensmittel/04_Lebensmittelanalytik/01_nrl_crl/nrl_crl_node.html_nnn=tr ue password protected webpage, also in English: http://fis-vl.bund.de/Public/irc/fis-vl/Home/main?index Director: Dr. Petra Gowik crlvetdrug@bvl.bund.de
RIVM-CRL Stilbenes, stilbene derivatives and their salts and esters Antithyroid agents Steroids Resorcylic acid lactones (RALs) including zeranol Sedatives Mycotoxins	EU CRL for residues RIVM – National Institute for Public Health and the Environment P.O. Box 1 NL-3720 BA Bilthoven, The Netherlands Phone: + 31-30-2742746 / 2742613 Fax: + 31-30-2744403 http://www.rivm.nl/residues Director: Dr. Leendert A. van Ginkel leen.van.ginkel@rivm.nl

AFSSA-LERMVD-CRL Antibacterial substances, including sulphonamides and quinolones Dyes Carbadox and olaquinox Chloramphenicol Dapsone Nitrofurans	Laboratoire d'études et de recherches sur les médicaments vétérinaires et les désinfectants AFSSA-Site de Fougères BP 90203 F-35302 Fougères Phone: + 33 (0)2 99 94 78 78 Fax: + 33 (0)2 99 94 78 80 http://crl.fougères.afssa.fr Director: Dr. Pascal Sanders p.sanders@fougères.afssa.fr
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1. A1 Stilbenes (CRL responsible RIVM-NL)

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	Recommended concentration*
Diethylstilbestrol (DES) Dienestrol (DE) Hexestrol (HEX)	Urine	1 ppb for DES 2 ppb for DE 2 ppb for HEX
	Liver	2ppb (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 (CRL responsible RIVM-NL)

For the purpose of control the matrices of choice are urine and thyroid gland.

It should be noted that low concentrations of thiouracil (maximum 10 ppb) have been detected in animals fed with diet containing cruciferous plants.

Substances	Matrix	Recommended concentration*
Thiouracil Methylthiouracil Propylthiouracil Tapazole	Urine Thyroid	10 ppb for all ^{&}

* *CCbeta for screening methods or CCalpha 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 10 ppb in urine cannot be linked to natural origin due to this contamination.*

3. A3 steroids (CRL responsible RIVM-NL)

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

For 17 β -oestradiol serum and for progestagens kidney fat is the matrix of choice, as indicated in the table. Muscle has been included for control purposes of imports and for aquaculture products.

Substances	Marker residue-metabolite	Matrix	Recommended concentration*
Boldenone	17 β -boldenone conjugate	Urine	1 ppb
		Liver	2 ppb
		Muscle	1 ppb
17 β -19-nortestosterone ¹ (nandrolone)	17 α -19-nortestosterone ² (epi-nandrolone)	Urine	1 ppb
		Liver	2 ppb
		Muscle	1ppb
Ethinylestradiol		Urine	1 ppb
		Liver	2 ppb
		Muscle	1 ppb
17 β -Oestradiol	17 β -Oestradiol	Serum	0.1 ppb
		Muscle	1 ppb
17 β -Testosterone	17 β -Testosterone	Serum	Male < 6 months: 10 ppb Male 6 - 18months: 30 ppb Female < 18 months: 0.5 ppb
Methyltestosterone		Urine	2 ppb
		Liver	2 ppb
		Muscle	1ppb
17 β -Trenbolone	17 α -Trenbolone	Urine	2 ppb
		Liver	2 ppb
		Muscle	1 ppb
Stanozolol	16 β -Hydroxystanozolol	Urine	2 ppb
		Liver	2 ppb
		Muscle	1 ppb
Dexamethasone		Urine	2 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	5 ppb
		Muscle	0.5 ppb
Medroxy-progesterone	Medroxy-progesterone (acetate)	Kidney fat	1 ppb MRPL
		Muscle	1.0 ppb

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

¹17 β -19-Nortestosterone occurs naturally in non-castrated pigs and horses.

²17 α -19-Nortestosterone occurs naturally in pregnant cows and newborn calves.

4. A4 Resorcylic acid lactones and derivates (CRL responsible RIVM-NL)

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	Recommended concentration*
Zeranol ¹	Taleranol	Urine	2 ppb
		Liver	2 ppb
		Muscle	1 ppb
Zearalanone		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.

5. A5 Beta-agonists (CRL responsible 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	Recommended concentration*
Clenbuterol: <i>MRL (for bovine and equidae)**:</i> <i>0.1 µg/kg in muscle</i> <i>0.05 µg/kg in milk (only bovine)</i> <i>0.5 µg/kg in liver and kidney</i> Brombuterol, Chlorbrombuterol, Mabuterol, Mapenterol, Tulobuterol, Hydroxymethylclenbuterol	Urine	0.2 ppb
	Liver	0.2 ppb
	Retina	2 ppb
	Muscle	0.1 ppb
	Kidney,	0.2 ppb
	Faeces	0.2 ppb
	Plasma, Drinking water	0.2 ppb
	Hair	2 ppb
Clenpenterol, Clenproperol, Cimaterol, Cimbuterol, Isoxsuprine, Ritodrin	Urine	0.5 ppb
	Liver	0.5 ppb
	Retina	5 ppb
	Muscle	0.5 ppb
	Kidney, Faeces	0.5 ppb
	Plasma, Drinking water	0.5 ppb
	Hair	5 ppb
Ractopamine, Clencyclohexerol	Urine	1 ppb

	Liver	1 ppb
	Retina	10 ppb
	Muscle	1 ppb
	Kidney, Faeces	1 ppb
	Plasma, Drinking water	1 ppb
	Hair	10 ppb
Salbutamol, Salmeterol, Zilpaterol, Fenoterol	Urine	1 ppb
	Liver	5 ppb
	Retina	10 ppb
	Muscle	5 ppb
	Kidney, Faeces	5 ppb
	Plasma, Drinking water	5 ppb
Terbutaline	Hair	10 ppb
	Urine	3 ppb
	Liver	10 ppb
	Retina	10 ppb
	Muscle	10 ppb
	Kidney, Faeces	10 ppb
Orciprenaline (Metaproterenol = orciprenaline)	Plasma, Drinking water	10 ppb
	Hair	10 ppb
	Urine	10 ppb
	Liver	10 ppb
	Retina	10 ppb
	Muscle	10 ppb
Feed	Kidney, Faeces	10 ppb
	Plasma, Drinking water	10 ppb
		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: Annex IV substances (CRL responsible Berlin and Fougères-FR)

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	Recommended concentration*
Nitroimidazoles: Ronidazol Dimetridazol Metronidazol	Hydroxy-metabolites	Poultry: Plasma Serum Retina** Eggs Pigs (and other species): Plasma Serum Muscle Retina** Aquaculture products: muscle Milk (Honey) (Drinking water)	3 ppb
		Feed	50 ppb
Chloramphenicol		Meat, milk, eggs, aquaculture products, urine	0.3 ppb MRPL
Nitrofurans	Metabolites AMOZ, AHD, SEM, AOZ	Poultry Meat, Aquaculture products, Muscle/meat, Milk, Eggs	1 ppb MRPL for all
Dapsone		Muscle Meat Milk	5 ppb
Chlorpromazine		Kidney	10 ppb

* CCbeta for screening methods or CCalpha 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 (CRL responsible RIVM-NL)

Matrix of choice is kidney.

Substances	Matrix	Recommended concentration*
Acepromazine Propiopromazine Haloperidol	Kidney	50 ppb

* CCbeta for screening methods or CCalpha for confirmatory methods should be lower than the value expressed in this column

8. B2e NSAIDs (CRL responsible Berlin)

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

Substances	Matrix	Recommended concentration *
Phenylbutazone Oxyphenbutazone	Muscle, milk Kidney	5 ppb
Ibuprofen Naproxen Mefenamic acid	Liver Plasma	10 ppb
Diclofenac (not authorised for milk-producing animals)	Milk	5 ppb

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9. Others (CRL responsible Fougères, France)

Substances	Marker residue-metabolite	Matrix	Recommended concentration*
Malachite green	Leucomalachite green	Muscle fish	Sum: 2 ppb MRPL
Carbadox	QCA (quinoxaline-2-carboxylic acid)	Muscle, liver	10 ppb
Olaquinox	MQCA (3 methylquinoxaline-2-carboxylic acid)	Muscle, liver	10 ppb

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10. Honey (CRL responsible Fougères, France)

Group	Substances to be included	Recommended concentration*
A6	Chloramphenicol	0.3 ppb MRPL
	Nitrofurans	1 ppb MRPL
B1	Tetracyclines	20 ppb
	Sulfonamides	50 ppb
	Streptomycin	40 ppb
	Macrolides: Erythromycin Tylosin	20 ppb

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