EUROPEAN UNION REFERENCE LABORATORIES IN THE FIELD OF VETERINARY PUBLIC HEALTH WITHIN THE EUROPEAN UNION

EURL for residues

RIKILT Wageningen UR

at Wageningen, NL

Work programme

January 1st, 2015 – December 31st, 2015

Status 25th August 2014

WORK PROGRAMME FOR THE EUROPEAN UNION REFERENCE LABORATORY FOR RESIDUES, RIKILT, Wageningen, the Netherlands

HORMONAL GROWTH PROMOTING COMPOUNDS, SEDATIVES AND MYCOTOXINS

January 2015 – December 2015

LEGAL FUNCTIONS AND DUTIES

The functions and duties of the Reference Laboratory are described in Article 32 of Regulation (EC) No 882/2004 of the European Parliament and of the Council of 29 April 2004 (Official Journal of the European Union L 165, 30.04.2005, pp 1-141, corrected and republished in Official Journal of the European Union L 191, 28.05.2005, pp 1-52.

1. OBJECTIVES FOR THE PERIOD JANUARY 2015 – DECEMBER 2015

The EURL workprogramme is divided in 4 parts, A-D. For the individual subjects it is shown under which DG SANCO Operational Objective they fall. (Annex to Commission implementing decision establishing the work programme for the year 2015 on financial contribution to the European Union reference laboratories).

EURL workprogramme part	Operational objectives
A: General Tasks	4. Sound and efficient management of EU-RL funding cycle
B: Development and validation of analytical methods *Article 32, paragraph 1(c)*	1. Ensure development and use of high quality analytical methods across the EU-RL framework
C: Quality Assurance and Quality control including the organisation and implementation of proficiency tests *Article 32, paragraphs 1 (a)(d)(e)(f)*	2. Maintain appropriate level of proficiency testing ensuring efficiency of control analysis methods
D: Technical and scientific support to NRLs and third countries	3. Ensure availability of scientific and technical assistance provided by the EU-RL

2. WORK PROGRAMME FOR THE PERIOD JANUARY 2015 – DECEMBER 2015

A. General Tasks (Operational objective 4)

1) Meeting 4 EURLs, EURLs for residues management

Participation in annual co-ordination meeting and general EU-RL-management activities.

2) Technical and scientific support to the Commission

Upon request, technical assistance will be given to the European Commission and its Offices and its related institutes like the Joint Research Centre (JRC), the European Food Safety Authority (EFSA) and the European Medicines Agency (EMA).

3) Compilation of annual report and cost-statement

Annual reports and cost statements with respect to the 2014 contract period will be prepared before 1st of April, 2015.

4) Co-operation with international organisation

Specific: EC/EU-RL related co-operation with International Bodies (e.g. AOAC international, Eurachem, Codex, CVMP, TAIEX, EMA, EFSA, JRCs, IRMM, FVO and IAEA) on method validation, analytical methodology, reference materials and performance quality criteria (communication, co-ordination, and harmonisation).

5) Documentation and information services

Developments with respect to analytical methodology, (EU) legislation and the results of relevant scientific studies are constantly monitored. In addition, information on the use of new compounds or alternative approaches to improve the growth of livestock will be collected and used as input for future studies. Communication about issues of interest for NRLs will be through the annual workshop and the EU-RL website.

Specific. This EU-RL-website is maintained. The EU-RL website will be maintained with continued efforts to further implement its use within the EU-NRL/RFL network.

The database with EURL literature inclusive scientific reports, will be maintained as a source of information for EURLs and NRLs .

6) An evaluation of the draft Annual National Residue Plans of 2015 will be produced. A list of matrix/method combinations which was prepared by the EU-RLs (Guidance paper of December 2007), has been distributed as a reference that remains the basis for further evaluations. When necessary, specific suggestions for improvement will be included in the report. In 2015 the plans for both bovine and porcine animals will be evaluated.

7) Extension and promoting use of EU-RL web forum for information exchange.

8) The Reflection paper with respect to the (semi)-natural occurrence of group A compounds prepared for discussion with the NRLs and the Commission in 2014 has generated research questions and control strategy approaches. The objective of this review was to provide both the NRLs and the Commission with tools for evaluating results of the NRPs and to provide general guidelines for enforcement. In 2014 four working-groups were established with an important role in initiating new research and evaluating new (published and unpublished) scientific information. In 2015 and an extension of the reflection paper with regard to Bovine Somatotropine will be prepared. The revision of the document, scheduled for 2016, will also include pro-hormones

Specific products related to A:

Topic	Product	Planned for
1	Management information at RIKILT and meeting minutes prepared by the Commission (4)	Ongoing, meeting to be set by the Commission
2	Advises (reports, e-mails or letters) (3,4)	Ongoing on an Ad Hoc basis
3	Annual report and cost statement (4)	1st of April 2015
4	Co-operation with international organisations (3)	Ongoing on an Ad Hoc basis
5	Documentation and Information Services, general aspects (4)	Ongoing on an Ad Hoc basis
6	Evaluations of ANPs (2015) for bovine and porcine animals (3)	June 2015
7	Forum on the EU-RL website will be maintained and used for information exchange and questions and answers (3,4)	Ongoing
8	Extension of the Reflection paper for bovine somatotropine and pro-hormones, additional chapters. (3)	September 2015

B: Development and validation of analytical methodology (Article 32, paragraph 1c)(1)

Development and validation of state of the art analytical methods is one of the major tasks of the EU-RL. New analytes, or metabolites of compounds, will have to be included on a regular basis and new technologies will have to be implemented. Based on the results of research activities within the EU-RL-NRL network methods will have to be re-evaluated on specific aspects. Adequately validated methods for all analyte: matrix combinations included in the list of RPA-values will be maintained

and made available on request. Regular updates are foreseen. The annual workshops will be used to actively discuss the priority setting for this part of the work programme. Based on the current 'state-of-the-art" of analytical methods, the current priorities for the 2015 work programme are.

Specific

9**) Maintenance or extension of existing analytical methods**, inclusive the validation status. It is foreseen that updated procedures of existing analytical methods for the following analyte matrix combinations will become available in 2014, to be validated in 2015. The individual studies are prioritised. Validation studies with lower priorities 2015 possibly will be performed in 2016..

1. Validation of SOP A0920 Trenbolone in urine for edible tissues of bovine and porcine species.
2. Validation of SOP A1112 for RAls in edible tissues and bile.
3. Validation of SERMs method for urine.
4. Validation of A1118 for thyroid gland and edible tissues of bovine and porcine animals
5. Validation of method secretagogues, GHrelines, in serum with LC-MS/MS.
6. Validation of IGF-1 quantitative confirmatory method.

10) **New analytical methods**:

Development of an analytical method for confirmation of Boldenone and Nortestosterone in respectively bovine and porcine urine using GC-c-IRMS.

11) Development of a tool for identification of injection sites. Knowledge on recognition of injection sites in slaughterhouses is not in all Member States available. RIKILT has a lot of knowledge and documentation including pictures of injection sites. To instruct Member States on this subject in 2013 an expert system was built where information can be found on detection of illegal growth promoters in cattle. The focus was on changes that can be observed in living animals and in the carcass, especially injection sites. In 2014 additional inforamiton on morphological and histological changes in the target tissues was, suitable for inclusion in the database, was selected. This work will be continued in 2015. This will be differentiated for anabolic steroids, corticosteroids, thyreostatic agents and bST.

12) Studies to detect abuse of (semi-)natural hormones. Based on the methods and models developed within the EU-RL, which were presented during EuroResidue VII (May 2012, The Netherlands), selected populations of samples were analysed for their steroid profiles (precursors, physiological active compounds and their metabolites). For the models to be implemented effectively, it is necessary to (1) improve the quality of the reference datasets of well described and untreated animals and (2) the development of a confirmatory method on the basis of GC-c-IRMS.

In 2014 RIKILT this strategy is implemented in the Dutch Annual residue Control Plan. The GC-c-IRMS methods developed for confirmation of testosterone and estradiol will be used to confirm exogenous administration in the cases screening analysis turns out suspect.

Based on the EURL reflection paper, priorities for research were set. Specifically for the EURL this includes:

- Estradiol in poultry liver. Levels of this compounds can vary in poultry liver. A survey will be conducted with poultry liver of untreated animals of different ages to establish the normal range of alfa- and beta-oestradiol in this matrix. With the results a recommended concentration in poultry liver will be proposed.

- Elimination of recombinant somatotropine from existing animal experiments in milk will be studied by analysing earlier collected samples with the developed confirmatory mass spectrometric method.

- In the reflection paper it was shown that the analysis of steroid esters in plasma could also be a relevant workflow to detect abuse of natural hormones. The steroid esters in plasma method will be implemented and validated and distributed amongst the NRLs.

13) Identification of new compounds. Identification of new and unknown compounds illegally used for growth promoting purposes. On the basis of sample materials received (biological samples, cocktails or animal feed) or information obtained through other sources, studies will be undertaken to identify individual compounds. When necessary, based on *in vitro* studies, the metabolism will be studied. Special attention will be given to the use of e.g. pro-hormones. This is a general ongoing activity. Investigation into the possibilities of using this technique for the synthesis of reference standards will be started.

- In 2015 focus will lay on recombinant somatotropine with a similar amino acid composition as the endogenous BST. Analysis and identification of preparation is planned.

Specific products related to B (1):

Topic	Product	Planned for
9	Maintenance and extension of methods,(1) 1. Validation of SOP A0920 Trenbolone in urine for edible tissues of bovine and porcine species. 2. Validation of SOP A1112 for RAls in edible tissues and bile. 3. Validation of SERMs method for	December 2015 December 2015 December 2015

	urine. 4. Validation of A1118 for thyroid gland and edible tissues of bovine and porcine animals. 5. Validation of method secretagogues, GHrelines, in serum with LC-MS/MS 6. Validation of IGF-1 quantitative confirmatory method	December 2015/2016 December 2015/2016 December 2015/2016
10	Development of an analytical method for confirmation of Boldenone and Nortestosterone in respectively bovine and porcine urine using GC-c-IRMS. (1)	December 2015
11	Extension of the expert system with histological and morphological information for different groups of forbidden growthpromoters (1)	
12	- Estradiol in poultry liver. A survey will be conducted with poultry liver of untreated animals of different ages to establish the normal range of alfa- and beta-oestradiol in this matrix. With the results a recommended concentration in poultry liver will be proposed. (1) - Elimination of recombinant somatotropine from existing animal experiments in milk will be studied by analysing earlier collected samples with the developed confirmatory mass spectrometric method. (1) - In the reflection paper it was shown that the analysis of steroid esters in plasma could also be a relevant workflow to detect abuse of natural hormones. The steroid esters in plasma method will be implemented and validated and distributed amongst the NRLs. (1)	December 2015 December 2015 June 2015

13	Identification of new compounds, inclusive studies on metabolism when relevant. (1) - Investigation into the possibilities of using this technique for the synthesis of reference standards will be started. - In 2015 focus will lay on recombinant somatotropine with a similar amino acid composition as the endogenous BST. Analysis and identification of preparation is planned	Ongoing activity, progress report December 2015 December 2015

C: Quality Assurance and Quality Control. (2)

14) Maintenance of in-house QA/QC activities in consequence of the ISO 17025 accreditation of all analytical work done within the EU-RL (no costs included).

15) Organisation of two proficiency tests. Topics to be determined during annual workshops. Proficiency tests are organized on a regular basis, on average 3 tests per period of 2 years. Priorities are set on an annual basis, after consultation of the NRLs, amongst others during the workshops. As a rule, the proficiency tests are based on incurred materials, obtained during a controlled animal experiment. It is then objective to prepare a preliminary report within 2 months after the results have been received, a full report within 6 months.

16) Production of incurred sample material.

An animal study in preparation of future proficiency tests are scheduled for 2015. Priorities will be set during the 2014 annual workshop.

Specific products related to C:

Topic	Product	Planned for
14	Annual re-accreditation (4)	April 2015
15	Proficiency test Zeranol A4 in bovine urine (2): Full NRL participation Research Study steroid esters in plasma. Limited NRL participation expected Proficiency test A3 in bovine urine	February 2015. June 2015 December 2015

	(blind) (2). Full NRL participation.	
16	Technical report animal study treatment with natural hormones and synthetic hormones (2)	Following animal study

D: Technical and scientific support to Member States and the Commission, inclusive arbitration and training activities. (3)

17) Analytical support and training. Analytical support, both by means of advise or training, will be given to NRLs upon their request. Organisation of an additional training for NRLs on analyses of growthpromoters. This training will be organised if a minimum number of 5 participants is reached.

18) Missions to NRLs and dissemination of scientific information. Missions will be undertaken to specific NRLs on the basis of their individual needs, e.g. in order to discuss and evaluate the results of a proficiency test. Analytical support. The choice for 2015 will be based on the current progress in the NRLs in the newer EU-Member States, and in consultation with the other EU-RLs for Residues.

19) Provision of standard substances including storage, administration, documentation and shipment. *Annex V, Chapter 2, section 1 (j).* When necessary and possible, selected compounds will be purchased or (custom) synthesised.

20) Analyses of official samples. *S*amples submitted by EU Member states in case of dispute between Member States or in case of analytical problems within a responsible NRL will be analysed.

21) Organisation of annual workshop on residue analysis. The topic will be selected on the basis of a consultation of the NRLs during the 2014 workshop.

Specific products related to D (3)

Topic	Product	Planned for
17	Training documentation and/or report	On an Ad Hoc basis
18	Visit report	December 2015
19	Provision of selected reference compounds	Annual overview
20	Analyses reports	On an Ad Hoc basis
21	Workshop proceedings	September 2015