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, 2014 – December 31st, 2014

Status 29th August 2013

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

HORMONAL GROWTH PROMOTING COMPOUNDS, SEDATIVES AND MYCOTOXINS

January 2014 – December 2014

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 2014 – DECEMBER 2014

A: General Tasks

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

C: Quality Assurance and Quality control including the organisation and implementation of proficiency tests *Article 32, paragraphs 1 (a)(d)(e)(f)*

D: Technical and scientific support to NRLs and third countries

2. WORK PROGRAMME FOR THE PERIOD JANUARY 2014 – DECEMBER 2014

A. General Tasks

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 2013 contract period will be prepared before 1st of April, 2014.

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 by the EU-RL-documentation services. The EU-RL website will be maintained with continued efforts to further implement its use within the EU-NRL/RFL network.

6) An evaluation of the draft Annual National Residue Plans of 2014 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 2014 not only for the species bovine but also for porcine the evaluation will be made.

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

8) The review with respect to the (semi)-natural occurrence of group A compounds prepared for discussion with the NRLs and the Commission in 2013 will generate research questions and control strategy approaches. The objective of this review is to provide both the NRLs and the Commission with tools for evaluating results of the NRPs and to provide general guidelines for enforcement. The draft report will be rewritten in a review on semi-natural hormones and submitted for publication.

Specific products related to A:

Topic	Product	Planned for
1	Management information at RIKILT and meeting minutes prepared by the Commission	Ongoing, meeting to be set by the Commission
2	Advises (reports, e-mails or letters)	Ongoing on an Ad Hoc basis
3	Annual report and cost statement	1st of April 2014
4	Co-operation with international organisations	Ongoing on an Ad Hoc basis

5	Documentation and Information Services, general aspects	Ongoing on an Ad Hoc basis
6	Evaluations of ANPs (2014) for bovine and porcine animals	June 2014
7	Forum on the EU-RL website will be maintained and used for information exchange and questions and answers	Ongoing
8	Submission of review article to peer reviewed journal based on EURL Review (semi) natural occurrence group hormonal growth promoters from 2013.	September 2014

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

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 2014 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.

IGF-1, development of quantitative confirmatory method.

Validation of multi-hormone method, SOP A1160 for serum and milk matrix

Method development for secretagogues, GHrelines, in serum with LC-MS/MS

Validation of biomarker for oestradiol treatment

10) **New analytical methods**:

Development of an analytical method for Selective Estrogen Receptor Modulators (SERMs) in urine.

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 it is planned to expand this system with data on morphological and histological changes in the target tissues. 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 will continue analysing reference samples with the methods developed. Moreover, 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.

Sample preparation for IRMS analyses needs to be very selective. Immunoaffinity clean-up as pretretament before IRMS analyses will be investigated together with other research groups.

Depending on the outcome of the EURL reflection paper priorities for research will be defined and activities incorporated where possible.

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. A protocol for *in-vitro* metabolism studies is prepared. This will be compared with *in vivo* studies. The protocol will cover phase 1 and phase 2 metabolism. Investigation into the possibilities of using this technique for the synthesis of reference standards will be started.

Specific products related to B:

Topic	Product	Planned for
9	Maintenance and extension of methods, a. IGF-1, development of quantitative confirmatory method b. Validation of multi-hormone method, SOP A1160 for serum and milk matrix	December 2014 December 2014

	c. Method development for secretagogues, GHrelines, in serum with LC-MS/MS d. Validation of biomarker for estradiol treatment	December 2014 November 2014
10	Methods for SERMs in urine	December 2014
11	Extension of the expert system with histological and morphological information for different groups of forbidden growthpromoters	December 2014
12	Confirmatory analyses for testosterone and estradiol using IRMS Development of specific immunoaffinity based sample preparation for IRMs analyses Research priorities depending on outcome EURL reflection paper to be discussed with NRLs during annual workshop in November 2013	On going Progress report December 2014 To be determined
13	Identification of new compounds, inclusive studies on metabolism when relevant. Protocol in vitro metabolism for phase 1 and phase 2 metabolites	Ongoing activity, progress report December 2014 December 2014

C: Quality Assurance and Quality Control.

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 2014. Priorities will be set during the 2012 and 2013 annual workshop.

Specific products related to C:

Topic	Product	Planned for
14	Annual re-accreditation	April 2014
15	Proficiency test Diethylstilbestrol A1 in bovine urine Proficiency test aflatoxine M1 in raw milk in cooperation with IRMM.	March 2014 Report A1 steroids, summer 2014 August 2014, report December 2014
16	Technical report animal study treatment with natural hormones and synthetic hormones	Following animal study

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

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 2014 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 2013 workshop.

Specific products related to D:

Topic	Product	Planned for
17	Training documentation and/or report	On an Ad Hoc basis
18	Visit report	December 2014
19	Provision of selected reference compounds	Annual overview
20	Analyses reports	On an Ad Hoc basis
21	Workshop proceedings	December 2014