WORK PROGRAMME FOR THE EUROPEAN UNION REFERENCE LABORATORY FOR RESIDUE TESTING, 2015

Groups of substances: A5-B2a-B2b-B2e

I LEGAL FUNCTIONS AND DUTIES

The functions and duties of the European Union Reference Laboratories 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, 30.04.2004, pp. 1 – 141, corrected and republished in the Official Journal of the European Union L 191, 28.05.2004, pp. 1 - 52).

II WORK PROGRAMME FOR THE PERIOD JANUARY – DECEMBER 2015

ACTIVITIES

1. Meeting 4 EURLs

4 EURLs for residue management

As a consequence of the EURL evaluation, the Commission stated that EURLs with overlapping or similar responsibilities should agree upon their work more closely. The agreement with the Commission is also indispensible. For this reason at least one meeting of the 4 EURLs for residues and a representative of the European Commission is necessary per year.

Objective: Information management and coordination of work programmes (Contribution to operational objectives 1 and 3 of the Commission work programme)

Expected Output: internal documents

2. EU/EURL-related EU and internal bodies; co-operation with international organisations

Technical and scientific support will be provided to the Commission institutions DG SANCO, DG JRC (IRMM), EMA and EFSA.

The cooperation with international organisations is an ongoing task and will be intensified to the largest possible extent. At the moment the EURL is participating in ISO working groups for standardisation, in CEN working groups for standardisation, in the Codex Alimentarius Committees CCRVDF and CCMAS and in the CCQM working group OAWG of the CIPM.

Objective: Cooperation with external bodies (Contribution to operational objectives 1 and 3 of the Commission work programme)

Expected Output: working documents

3. Reports, cost estimate, documentation

Several reports will be issued, e.g. the report on proficiency test 2014, the evaluation of the NRCPs of the Member States, the technical and financial reports on EURL working period 2014, reports on the EURL performance (performance indicators) as well as the cost estimate and work programme for 2016. Other reports will be provided upon request.

Objective: Documentation of the EURLs work (Contribution to operational objective 4 of the Commission work programme)

Expected Output: reports as described above

4. Validation of a multi-residue method for antiparasitics by LC-MS/MS

The substance group of endoparasiticides comprises the groups of anthelmintics and anticoccidials (B2a/B2b). The NRLs keep expressing a lot of interest in the use of substance-group-comprehensive methods, but at present only separate validated multi-residue methods for the respective groups exist at the EURL Berlin. By implementing new technical developments and possibilities, a substance-group-comprehensive method was developed during the 2014 work period. This method was optimised for the included substances as a confirmatory method. The validation of the newly developed and optimised method will be performed and a method description will be provided.

Objective: validation of the method (Contribution to operational objective 1 of the Commission work programme)

Expected Output: validated method; validation report; method description

5. Re-validation of a method for nitroimidazoles in eggs

The validated method for the determination of nitroimidazoles in eggs is meanwhile several years old and needs to be revised and updated. Optimisation potential for the sample preparation is checked, the analyte list will be enhanced and lower decision limits should be achieved due to more sensitive instruments. An improved method will be the basis for the analysis of incurred samples as potential reference material (see point15).

Objective: re-validation of the method (Contribution to operational objective 1 of the Commission work programme)

Expected Output: validated method; validation report; lowered decision limits, method description

6. Re-validation of the methods for NSAIDs

The 3 methods for the determination of NSAIDs in plasma, muscle and milk are meanwhile several years old and the instrument used for the validation of the methods was replaced by a new and more sensitive one. The method will be revalidated accordingly, the analyte list will be revised and - if possible - lower decision limits shall be achieved for the non-MRL compounds.

Objective: re-validation of the method (Contribution to operational objective 1 of the Commission work programme)

Expected Output: validated methods; validation reports; method descriptions

7. Re-validation of the methods for beta-agonists and coccidiostats

The methods for the determination of beta-agonists and coccidiostats were validated on an instrument which proved to be not sufficiently reliable. Hence the instrument will be substituted by the end of 2014. Accordingly, the methods for the different relevant matrices will be revalidated, the analyte list will be reviewed and enhanced if required; lower decision limits should be achieved for the non-MRL compounds. In a first step, the methods for beta agonists in liver and urine as well as the method for coccidiostats in eggs will be revalidated.

Objective: re-validation of the methods (Contribution to operational objective 1 of the Commission work programme)

Expected Output: validated methods; validation report; lowered decision limits; method descriptions

8. Pre-tests for the development of a multi-method for basic and acidic NSAIDs

Following requests from NRLs for the development of a joint multi-method for basic and acidic NSAIDs, the feasibility of the development of such a method is checked in pre-tests. The results of the pre-tests are used to decide whether a new method may, in addition to offering a more efficient residue control due to an increased number of analytes, allow to maintain the performance characteristics of the separate methods. The model matrix is milk.

Objective: Pre-tests of a multi-method (Contribution to operational objective 1 of the Commission work programme)

Expected Output: Decision whether or not to develop a joint multi-method

9. Investigation of fundamental questions:

a) Influence of matrix components on signal intensity of different veterinary drugs by LC-MS/MS

b) Use of calibration curve data as a QA tool for the improvement of the reliability of measurement results

a) In the course of the establishment of the LC-MSn technique, which has meanwhile become the most frequently applied technique in the field of residue analysis, the problem of matrix influences on the intensity of the signal is observed more and more often. The phenomenon is difficult to describe, and its causes have still not been entirely understood. The results of the studies carried out in 2014 showed that it looked promising to use two approaches for the estimation of potential matrix effects: a post-column infusion approach and the fortification of extracts of blank samples after the last step of the sample preparation procedure. These approaches shall be checked as part of selected validation studies in 2015.

b) Commission Decision 2002/657/EC requires a calibration curve for each analytical series. In most cases the information from these calibrations is used only within the respective analytical series, but not, e. g. in the form of control charts, in order to implement preventive measures before questionable results are produced. Based on the evaluation of available validation data, the validity of the respective data evaluations will be checked and suggestions for the implementation in routine control will be given.

Objective: Evaluation of fundamental questions of reliability of analytical results (Contribution to operational objectives 1 and 3 of the Commission work programme)

Expected Output: summary of results; recommendations for QA measures

10. Testing and evaluation of appropriate procedures for the development of a draft guideline for purity testing

Accreditation bodies require the traceability of measurements to SI units, hence also the knowledge of the purity of standard substances. This knowledge is a prerequisite for reliable testing as well as for a correct estimation of the measurement uncertainty. Experience showed that the values indicated on the bottles or certificates of commercial providers are not always correct. Thus the EURL Berlin decided to start a project on purity testing of selected standard substances. Criteria for the selection were: particularly important substances, substances often used but for which no purity is given, or substances for which irregularities have been observed. For purity testing new types of instruments were to be purchased and established, like HCN analyser and Karl-Fischer-titration. Recently a TGA (coupled to GC/MS) and an ELSD coupled to a QTOF-MS were put into operation. In addition classical chromatographic techniques were applied for the characterisation of organic impurities. The purity figures are and will be spread among the relevant NRLs and routine laboratories together with the respective standard substances to support their QA systems and to enhance the reliability of measurements.

Based on the experiences from the 2013 and 2014 work plans on this topic, possible general approaches on how to do these highly labour-intensive purity studies systematically and efficiently, are developed and tested. In 2016 the approaches shall lead to a draft guideline for purity testing as a basis for discussions with the EURLs and NRLs.

Objective: Testing and evaluation of appropriate procedures for purity testing (Contribution to operational objectives 1 and 3 of the Commission work programme)

Expected Output: summary of possible procedures; report(s) on purity

11. Stability studies for all substance groups

The stability testing of analytes in solution and in matrix is required by CD 2002/657/EC. It was agreed that it is not necessary for each individual laboratory to carry out these investigations themselves, but that they can use stability data provided by the EURLs. Therefore and for the production of proficiency test material and in-house reference material as well as for the EURL's own needs, stability studies are and will be carried out for all analytes we are responsible for in several incurred matrices and in solutions.

Objective: Testing of analyte stability (Contribution to operational objectives 1 and 2 of the Commission work programme)

Expected Output: after the respective time period (in general after one year) a report on the detected stability of the analyte/matrix sample is issued

12. Research and identification of unknown compounds

It is an ongoing task to investigate possible new veterinary drugs, their metabolisation or degradation products as well as adequate internal – preferably isotopically labelled – standards.

Objective: Research and identification of new compounds (Contribution to operational objective 1 of the Commission work programme)

Expected Output: Cooperation with synthesis laboratories, synthesis of new standards and/or literature reviews on new substances

13. Proficiency tests on NSAIDs in milk and beta-agonists in urine

A proficiency test on NSAIDs in milk will be organised depending on the availability of appropriate material with sufficient concentration levels. It is planned to produce matrix samples (see point 16) with different analytes spread over 3 to 4 samples (including a blank sample).

A second proficiency test on beta-agonists in urine will be organised depending on the availability of appropriate material with sufficient concentration levels. It is planned to produce matrix samples with different analytes spread over 3 to 4 samples (including a blank sample).

Objective: Provision of proficiency tests for NRLs (Contribution to operational objective 2 of the Commission work programme)

Expected Output: short reports on proficiency tests, assessment of the performance of the NRLs, assignment of values to the reference materials

14. Participation in PTs by commercial providers

In order to document our proficiency not only in the framework of our own proficiency tests and in order to fulfil the requirements of EA and of the German accreditation body, it is necessary to participate in commercially offered PTs, as well. Furthermore, this way, PT providers can be checked for quality. Participation depends on the selection of PTs offered by commercial providers. So far the programmes for 2015 have been published only in part so that we cannot state yet in how many and in which PTs we will participate.

Objective: Independent QA control by participation in external PTs (Contribution to operational objective 1 of the Commission work programme)

Expected Output: certificates by the providers

15. Production of incurred "raw" sample material – animal study with laying hens

Hens will be treated with nitroimidazoles to produce residues in egg (exclusively production, animal treatment, egg collection, pre-testing, storage). The material is the basis for the production

of new reference materials in order to substitute the RM from 2006, which shows a beginning degradation.

Furthermore, based on the results of the animal studies with turkeys in 2013, feather samples will be collected in order to check the potential of this matrix for residue control.

Objective: Production of incurred material for QA purposes (Contribution to operational objective 1 and 2 of the Commission work programme)

Expected Output: pre-tested incurred egg material for proficiency tests and for scientific purposes; pre-tested incurred feather material

16. Production of reference materials from "raw" incurred sample material

The production covers the following steps: dilution of the material if necessary, homogenisation of the material, aliquotation and packaging of test portions; tests on homogeneity and stability (short-term and mid-term). The following materials will be produced and characterised:

Cows were treated with beta-agonists to produce incurred sample materials, primarily in the matrices urine and liver, but also in muscle, lung and gut. The material is the basis for the production of new reference materials and will substitute the old RMs, which were distributed to the NRLs and RFLs for QA-purposes and are meanwhile out of stock. In 2015 the production will start with urine as priority matrix for the production of reference materials.

Cows were also treated with NSAIDs to produce incurred milk samples. The material is the basis for the production of new reference materials in an appropriate concentration range covering the most important analytes.

The material produced in point 15 will be used to generate a new reference material for nitroimidazoles in egg, since the old material shows beginning analyte degradation.

Objective: Production of Reference Material (Contribution to operational objective 2 of the Commission work programme)

Expected Output: reference materials for beta-agonists in urine, NSAIDs in milk and nitroimidazoles in eggs as support for NRLs/RFLs and for scientific purposes

17. Technical, scientific support and training

Technical and scientific support and training will be provided on request to NRLs and official routine laboratories as well as to official laboratories of Third Countries. The support via internet (FIS-VL), where all relevant information is available on validated methods, standard substances, reference materials, reports and many more, will be continued. E-mail and telephone support will be provided.

Objective: Technical, scientific support and training of NRLs and third countries (Contribution to operational objective 1 of the Commission work programme)

Expected Output: provision of reference materials and of information on analytical methods; scientific support via e-mail or telephone; training courses

18. Follow-up of PT

Follow-up measures will be carried out if necessary in compliance with the Commission draft "Protocol for management of underperformance […]" guideline of 2007. An overview of the performances per laboratory and MS in the past few years was establish in 2013/2014 and will be continued in 2015.

Objective: Management of underperformance in PTs (Contribution to operational objective 2 of the Commission work programme)

Expected Output: certificates on successful participation; questionnaire of the EURL sent to the participants asking the failing laboratories what kind of support they need (substances, materials, methods, training); provision of additional PT test material on request; diagrams on the trend and development of the performance of the NRLs; report to COM on underperformance (if applicable)

19. Provision of standard substances incl. procuring, storage, administration, documentation, shipment, QA measures

Small amounts of standard substances will be provided to official laboratories on request.

Objective: Technical support of NRLs and third countries (Contribution to operational objectives 1 and 3 of the Commission work programme)

Expected Output: provision of standard substances and corresponding certificates and material safety data sheets; annually updated substance lists and lists of suppliers

20. Analysis of official samples

Official samples will be analysed on request in case of disputes between MS.

Objective: Technical support of COMM, NRLs and third countries (Contribution to operational objective 1 of the Commission work programme)

Expected Output: measurement reports and definite results

(Contribution to operational objective 1 of the Commission work programme)

21. Visit to NRL

In general one NRL per year is visited after consultation with the Commission on necessity. Scientific information and technical support in the form of methods, SOPs etc. and/or a specific training (practical or theoretical) will be provided, and specific problems like QA, QC, validation, legislation etc. will be discussed.

Objective: Visit of a NRL (Contribution to operational objective 1 of the Commission work programme)

Expected Output: support of the respective NRL, report on the visit

22. Organisation and performance of a workshop

An EURL-workshop will be organised. The following subjects are possible:

- Validation of multi-residue/multi-substance-group methods
- Purity testing of standards
- Influence of bound residues
- Ideas of NRLs (collected during an NRL opinion poll in 2014, a survey conducted at the end of the 2014 workshop and a query at the beginning of 2015)

The evaluation of the 2014 PT as well as the forthcoming 2015 PT will be treated and further specific questions will be discussed depending on the needs of the participants.

Objective: Organisation and performance of a workshop (Contribution to operational objectives 1, 2 and 3 of the Commission work programme)

Expected Output: several days' workshop

It is understood that the above-mentioned objectives are not exclusive of other work of more immediate priority which may arise during the reference period in question.