WORK PROGRAMME FOR THE EUROPEAN UNION REFERENCE LABORATORY FOR RESIDUE TESTING, 2014

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 PLAN FOR THE PERIOD JANUARY - DECEMBER 2014

Activities

1. **Meeting 4 EURLs**

   4 EURLs for residues management

   As a consequence from 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.

   Output: internal documents

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

   Technical and scientific support will be provided to the Commission institutions DG SANCO (e. g. evaluation of the NRCPs of the MS), 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.

   Output: working documents

3. **Reports, cost estimate, documentation**

   Several reports will be issued, e.g. the report on proficiency test 2013, the evaluation of the NRCPs of the Member States, the technical and financial reports on EURL working period 2013 as well as the cost estimate and work plan for 2015. Other reports will be provided upon request.

   Output: reports as described above

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

   The substance group of endoparasiticides comprises the groups of anthelmintics as well as of benzimidazoles. At present separate multi-residue methods for the respective groups exist at the EURL Berlin. Thanks to new technical developments and possibilities, a tendency towards substance-group-comprehensive methods can be observed. In contrast to the multi-residue screening method for anthelmintics, anticoccidials, nitroimidazoles and NSAIDs, which has been developed and validated at the EURL Berlin in the last few years (cf. point 5), this method will be optimised for the included substances as confirmatory method. NRLs keep expressing a lot of interest for the use of

substance-group-comprehensive methods.

Output: development of the method is started, and finalised until 31 Dec 2014, a short description will be available

5. **Validation of a multi-group-multi-residue method (finalisation)**

At the EURL Berlin the development of a multi-substance-group method for screening purposes was started in 2009. The substance groups B2a, B2b and B2e, for which we are responsible, were included. In the meantime a new LC-TOF instrument could be purchased, which is generally more sensitive and more powerful, e. g. regarding software and data generation. Moreover a new instrument allowing a smoother and faster evaporation of extracts was installed. This is very important with regard to the great number of unpredictable reactions that may occur when a solution of 250 substances is evaporated. So far around 250 substances have been included in the database of the instrument. A generic sample preparation method is also in place. In 2013 the validation of the complete analytical system (sample preparation and LC-TOF measurement) according to CD 2002/657/EC was started. This process has to be carried out consecutively substance group by substance group. In 2014 it will be finalised. As an outcome we expect the finally validated method to perform well as targeted or semi-targeted screening method for approximately 200 of the 250 tested substances.

Output: validated multi-substance-group method; validation report

6. **Short validation of a method extension (adaptation of a method for NSAIDs in muscle to other matrices or species)**

In 2013 we started to develop procedures for validations in case of method extensions. Different suggestions have been collected. These suggestions are now to be checked for their statistical and practical applicability using the example of the EURL's NSAID method, which needs to be extended.

Output: validated method; validation report; verification of the suggestions gathered in 2013

7. **Investigation of fundamental questions:**
a) influence of matrix components on signal intensity of different veterinary drugs by LC-MS/MS
b) enzymatic hydrolysis of different incurred materials in stock

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 has been observed increasingly. The phenomenon is difficult to describe, and its causes have still not been entirely understood. It might become apparent, for example, in unpredictable signal amplifications or degradations. So far only few publications have dealt with this topic, by picking out important, but singular matrix components and systematically investigating their influence. Since matrix interferences can – and often do – have a considerable influence on the measurements, which may lead to significantly different results depending on the employed method, instrument and the examined tissue, we want to take the investigations mentioned above as a starting point to examine matrix influences more profoundly in a systematic manner. The aim is to be able to give advice in future on how to deal with matrix suppressions, so that results can be produced that are comparable not only within one laboratory, but also between different laboratories.

b) Numerous substances are present in the animal’s body in a metabolised form, mostly protein-bound or as glucuronide. It is not known for all substances to which extent they are present in a bound form in the tissue to be examined, and thus escape detection. For this reason the EURL Berlin intents to carry out investigations of incurred materials. For this purpose, materials from former animal studies are to be used, so that no new animal studies have to be performed and the studies can be carried out without causing harm to any animals.

Output: reports on results

8. **Purity testing for selected substances**

Accreditation bodies require 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 are: especially important substances, substances often used but for which no purity is provided, or substances for which irregularities have been observed. For purity testing new types of instruments have to be purchased and established like HCN analyser, Karl-Fischer-titration etc. The purity figures 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.

Purity studies are highly labour-intensive. They require numerous analyses with a wide range of different analytical techniques. For this reason only a limited number of substances (approx. 1 – 2) can be examined per year. The studies will be continued in 2014. Routinely new lots of deuterated banned substances are examined for the presence of the unmarked substance. Furthermore, substances which do not have any certificate or only one that is not clear or not meaningful, are investigated. A prerequisite for this is the availability of a sufficient quantity of standard substance, which entails considerable costs.

Output: report(s) on purity

9. **Stability studies for all substance groups**

The stability testing of analytes in solution and in matrix is required by CD 2002/657. It was agreed that it is not necessary for each individual laboratory to carry out these investigations separately, 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.

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

10. **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.

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

Proficiency test on antiparasitics in milk

11. A proficiency test on antiparasitics in milk will be organised depending on the availability of appropriate material with sufficient concentration levels. It is planned to produce matrices with different analytes spread over 4 to 5 samples (including a blank sample).

Output: report on proficiency test, assessment of the performance of the NRLs

Participation in PTs by commercial providers

12. In order to document our proficiency not only in the framework of our own proficiency tests, 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 2014 have not yet been published so that we cannot state yet in how many and in which PTs we will participate.

Output: certificates by the providers

Production of incurred sample material

13. Hens will be treated with fenbendazole to produce residues in egg (exclusively production, animal treatment, egg collection, storage). It will be investigated whether metabolised residues occur. Furthermore cows will be treated with selected antiparasitics for the production of material for the 2014 proficiency test.

Output: incurred material for the proficiency test and for scientific purposes; report on results of the fenbendazole study for distribution to NRLs

14. **Technical, scientific support and training**

Technical and scientific support and training will be provided on request to NRLs and official routine labs 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.

Output: reference materials, analytical methods, scientific support via e-mail or telephone, training courses

15. **Follow-up of PT**

Follow-up measures will be carried out if necessary in compliance with the Commission draft guidelines of 2007. An overview of the performances per lab and MS in the past few years will be produced.

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), diagrams on the trend and development of the performance of the NRLs

16. **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.

Output: provision of standard substances which are, in some cases, not available on the commercial market

17. **Analysis of official samples**

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

Output: measurement reports and definite results

18. **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 will be provided and discussions on specific problems like QA, QC, validation, legislation etc will be led.

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

19. **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
- Extended validation
- First results on matrix effects
- Ideas of NRLs (collected at the beginning of 2014 and from the survey conducted at the end of the 2013 workshop)

The evaluation of the 2013 PT as well as the forthcoming 2014 PT will be treated and further specific questions will be discussed depending on the needs of the participants. For this purpose a questionnaire will be distributed beforehand.

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.