WORK PROGRAMMES
OF
EUROPEAN UNION
REFERENCE LABORATORIES
2011
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VETERINARY PUBLIC HEALTH
(Residues of Veterinary Medicinal Products in Food of Animal Origin)

1. Berlin  (Beta-agonists, coccidiostats, anthelmintics, NSAIDs)  p. 2
2. Wageningen (Hormonal growth promoters, sedatives, mycotoxins) p. 7
3. Fougères  (Antibiotics, forbidden substances, dyes)  p. 16
4. Rome  (Chemical Elements)  p. 22
WORK PROGRAMME FOR THE
EUROPEAN UNION REFERENCE LABORATORY
FOR RESIDUE TESTING, 2011


I. LEGAL FUNCTIONS AND DUTIES


1. OBJECTIVES FOR THE PERIOD JANUARY - DECEMBER 2011

A General tasks (~ 13 %)
B Development and validation of analytical methods (~ 37 %)
   Article 32, paragraph 1(c)
C Quality assurance and quality control including the development of incurred test material and the organisation of a proficiency test (~ 18 %)
   Article 32, paragraph 1(b)
D Technical and scientific support to Member States, the Commission, including arbitration and training activities (~ 32 %)
   Article 32, paragraphs 1(a)(d)(e)(f)
2. **WORKING PLAN FOR THE PERIOD JANUARY - DECEMBER 2011**

A **General Tasks**

**sub items**

1. **Meeting 4 EU-RLs**
   
   EC-4 EURL for residues management

2. **EC/EURL related EC and International Bodies; Co-operation with international organisations**
   
   Technical and scientific support will be provided to the Commission institutions DG SANCO (e.g. the evaluation of the NRCPs of the MS), DG JRC and EFSA.

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

3. **Reports, cost estimate, documentation**
   
   Several reports will be issued, e.g. the workshop report, the report on proficiency test 2010, the technical and financial reports on EURL working period 2010, the interim report 2011 as well as the cost estimate and work plan 2012, the evaluation of the NRCPs of the Member States. Other reports will be provided upon request.

B **Development and Validation of Analytical Methods**

**sub items**

1. **Validation of multi-residue method for anticoccidials in cattle / pig muscle / liver and in milk**
   
   A multi-residue method for anticoccidials in muscle and liver of cattle and pig was developed and optimised at the EURL Berlin in 2010. It has to be validated in order to become officially applicable.

2. **Validation of NSAID method in milk by lab-comprehensive validation approach**
   
   The first study on a new statistical approach for the validation of methods taking into account the lab standard deviation in addition to other uncertainty components will be organised and performed. Discussion at the EURL workshop in May 2010 showed a great interest in such a study and extension of in-house
validation among the NRL.

3. **Optimisation of the method for diclofenac in milk to be able to control MRL of 0.1 µg/L**
   In 2009 a MRL in milk of 0.1 µg/L was established. The EURL reported to COM that this level will be difficult to achieve for routine laboratories although not impossible. Therefore the EURL will start the development and validation of an appropriate sample preparation and detection procedure.

4. **Check of a commercial method for acid NSAIDs in plasma**
   Interesting sounding new applications which are commercially available will be checked for their proficiency level. The applications include the use of new cartridges and/or new kind of sample preparation techniques which will be checked for their applicability in residue control.

5. **Development of multi-screening methods**
   More and more often, multi-analyte / multi-substance-group methods are requested for the screening of sample material. Therefore the development of a LC-MS / TOF method started in 2009. Due to the complexity of this project it is planned as multi-annual task. Until now approx. 350 substances are included in the database. In 2011 further substances will be included. Furthermore adequate sample preparation procedures will be investigated and checked for their possibilities to extract as many substances as possible.

6. **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 upon 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.

7. **Research and identification of unknown compounds**
   It is and ongoing task to investigate possible new veterinary drugs, their metabolisation or degradation products as well as adequate internal – preferably isotopically labelled – standards.
C Quality assurance and quality control including the development of incurred test material and the organisation of a proficiency test

sub items

2. **Proficiency test on nitroimidazoles**

A proficiency test on nitroimidazoles in plasma will be organised depending on the availability of appropriate material with sufficient concentration levels.

3. **Participation in PTs by commercial providers**

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 choice of PTs offered by commercial providers.

4. **Production of incurred sample material**

In the last years in addition to clenbuterol isoxuprin was found as a non-complaint within the NRCP. Therefore it seems to be reasonable to include this compound within the animal study on beta-agonists in cattle hair.

D Technical and scientific support to Member States, the Commission, including arbitration and training activities

sub items

1. **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) will be continued where all relevant information is available on validated methods, standard substances, reference materials, reports and many more. Email and telephone support will be provided.
2. **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 last years’ performances per lab and MS will be produced.

3. **Provision of standard substances incl. procuring, storage, administration, documentation, shipment**

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

4. **Analysis of official samples**

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

5. **Visit to NRLs**

In general one NRL will be visited per year after consultation with the Commission on necessity. Scientific information and technical support in form of methods, SOPs etc will be provided and discussions on specific problems like QA, QC, validation, legislation etc will be led.

6. **Organisation and performance of a workshop**

A workshop will be organised. The following subjects are possible:

- TOF, screening techniques,
- validation criteria for TOF,
- methodical aspects

The evaluation of the 2010 PT and forthcoming 2011 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.

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.
Hormonal growth promoting compounds, sedatives and mycotoxins

LEGAL FUNCTIONS AND DUTIES


1. OBJECTIVES FOR THE PERIOD JANUARY 2011 – DECEMBER 2011

A: General Tasks

B: Development and validation 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
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 Agency for the Evaluation of Medicinal Products (EMEA).

3) Compilation of annual report and cost-statement

Annual reports and cost statements with respect to the 2010 contract period will be prepared before 1 April, 2011. This activity will be conducted in close cooperation with RIVM, Bilthoven.

4) Co-operation with international organisation

Specific: EC/EURL related co-operation with International Bodies (e.g. AOACi, Eurachem, Codex, CVMP, TAIEX, EMEA, EFSA, JRCs, IRMMand 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 EURL-documentation services. The EURL website will be maintained with continued efforts to further implement its use within the EU-NRL/RFL network.

An evaluation of the Annual National Plans of 2010 and results National Plans 2009 will be produced. A list of matrix/method combinations which was prepared by the EURls (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.

Specific products related to A:
<table>
<thead>
<tr>
<th>Topic</th>
<th>Product</th>
<th>Planned for</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Management information at RIKILT and meeting minutes prepared by the Commission</td>
<td>Ongoing, meeting to be set by the Commission</td>
</tr>
<tr>
<td>2</td>
<td>Advises (reports, e-mails or letters)</td>
<td>Ongoing on an Ad Hoc basis</td>
</tr>
<tr>
<td>3</td>
<td>Annual report and cost statement</td>
<td>1 April 2011</td>
</tr>
<tr>
<td>4</td>
<td>Co-operation</td>
<td>Ongoing on an Ad Hoc basis</td>
</tr>
<tr>
<td>5</td>
<td>Documentation and Information Services</td>
<td>Ongoing on an Ad Hoc basis</td>
</tr>
<tr>
<td></td>
<td>Evaluations of ANPs (2010) and results reported (2009)</td>
<td>March 2011</td>
</tr>
<tr>
<td></td>
<td>Forum on the EU-RL website will be made available and will be used for information exchange and questions and answers</td>
<td>May 2011</td>
</tr>
</tbody>
</table>

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

Development and validation of state of the art analytical methods is one of the major tasks of the EURL. 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 EURL-NRL network and methods will have to be re-evaluated on specific aspects. Adequately validated methods for all analyte: matrix combinations included in the list of RLA-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 2011 work programme are.

**Specific**

6) **Maintenance of analytical methods**, inclusive additional validation in case of extension of the scope. In spite of the wide range of analytical methods currently validated, there will be a continued need for further extension and improvement.

Extension and improvement of the methods for natural hormones in serum with GC-MS (SOP 492 and SOP 544). Inclusion of several additional metabolites and revalidation of this method.
Extension of the method for steroids (A3) with new markers for exogenous Nortestosterone, 1-testosterone and methyltestosterone abuse with GC-MS/MS. Validation of this extended method.

Validation of LC-MS/MS method for steroids (A3) with new markers and validation of this method.

After inclusion of these new marker analytes, an update of the CRL guidance paper is foreseen.

7) Method development for a new category of substances with an androgenic and/or estrogenic effect. The selective androgen receptor modulators (SARMs) and the selective estrogen receptor modulators (SERMs) are new compounds which are being developed by pharmaceutical industry. The molecules do not have the same structure as the steroid skeleton. However, these substances bind to the androgen or estrogen receptor and exert an hormonal and potential grow promoting effect. These SARMs and SERMs can be (mis)used as growth promoting agents. An internet survey learns that a lot of products are being advertised with SARM and/or SERM activity. In human doping research and analysis these compounds are already placed on the forbidden list. RIKILT can detect these compound in a bioassay based on the hormonal effect but at the moment the EURL does not have confirmatory methods of analysis. Based on a literature review a confirmatory method of analysis will be developed and validated.

8) Development of generic (non-targeted) approaches for the screening and confirmation of anabolic compounds. Over the past years, numerous targeted analytical methods have been developed with the objective to detect and confirm the presence of specific residues in biological samples. Currently, NRLs have a wide choice when selecting appropriate analytical methods for their Annual Residue Plan, based e.g. on the compounds listed in the EURL guidance paper of December 2007. Though highly suitable for their purpose, these methods all have in common that they are targeted, meaning that there always has to be a pré-determined specific list of compounds. During the previous years the EURL has worked on new approaches, using advanced Mass Spectrometric techniques (MS) based on Time of Flight (ToF) MS. These so-called fast scanning techniques enable us to collect far more data than previously, opening possibilities for non-targeted analyses. Proof of principle was published by us during the EuroResidue VI conference (May 2008, The Netherlands). Non-targeted analyses for anabolic compounds was the topic of the 2008 mini-symposium during the annual EURL/NRL workshop in October 2008. The objective for 2009 was to further develop this approach, to set up a working group to further discuss, harmonize and validate this approach. Part of the discussions focused on the integration of instrumental techniques with generic approaches based on bio-recognition (response) approaches as they were developed e.g. within the BIOCOP project. This work was previously undertaken as ToF method development. Based on the results obtained in 2010 it is foreseen that the work will continue in 2011 with a focus on evaluation of the LC-ToF-MS method for EURL guidance paper compounds. This evaluation will include a detailed comparison of analytical parameters like the detectable levels and applicability in comparison with the
available targeted methods. The objective is to define the added value of non-targeted analyses in residue control and to direct future development of the non-targeted approach. Also, a research study within the EURL-NRL network will be organised (also see item 13).

9) Studies to detect abuse of natural hormones. Based on the methods developed within the EURL, which were presented during EuroResidue VI (May 2008, The Netherlands), selected populations of samples were analysed for their steroid profiles (precursors, physiological active compounds and their metabolites). Already in 2008 this approach proved to be useful in identifying treated animals in practical cases where a good correlation was found with the results of hair analyses. This work was continued in 2009 with the further extension of the database of compounds. Previously collected data are of limited interest because most of the metabolites were not included. Moreover, conjugated steroids were not measured before. This work will continue of close cooperation with a group of laboratories, partly also involved in a UK (HFL) study sponsored by DEFRA. The objective for 2009 was to develop a set of decision criteria for the discrimination of treated and non-treated animals. For 2010 this approach was validated based on animal experimental work and a research study within the Netherlands. For 2011 the approach will be validated with samples coming from different, all, Member States to test the robustness of the model.

Next to this general approach, specific studies will continue focussing on making the detection of steroid-esters in hair more generic, continued evaluation of the practicability of C12/C13 measurements and the detection of Somatotropin.

Prednisolone is a corticosteroid similar to Cortisol, which is a natural compound. More and more reports are received about the possible change of endogenous cortisol into prednisolon. Studies into the natural occurrence of prednisolone will continue.

10 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.
Specific products related to B:

<table>
<thead>
<tr>
<th>Topic</th>
<th>Product</th>
<th>Planned for</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Maintenance and extension of methods,</td>
<td>December 2011</td>
</tr>
<tr>
<td></td>
<td>a. Revised SOP for Testosterone, Estradiol and Progesterone and metabolites in serum, inclusive a validation file</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. SOP update for steroids (A3) with different markers in urine with GC-MS/MS (inclusive validation file)</td>
<td>December 2011</td>
</tr>
<tr>
<td></td>
<td>c. SOP update for steroids (A3) with different markers in urine with LC-MS/MS (inclusive validation file)</td>
<td>December 2011</td>
</tr>
<tr>
<td>7</td>
<td>Analytical confirmatory method for SARMs and SERMs in urine</td>
<td>December 2011</td>
</tr>
<tr>
<td>8</td>
<td>Report on “Development of generic (non-targeted) approaches method. Evaluation of this approach for EURL priority compounds”</td>
<td>December 2011</td>
</tr>
<tr>
<td>9</td>
<td>Report on the following studies</td>
<td>December 2011</td>
</tr>
<tr>
<td></td>
<td>Studies to detect abuse of natural hormones?</td>
<td>December 2011</td>
</tr>
<tr>
<td></td>
<td>Addition of the results of analyses of samples obtained from member state to the model to test the robustness and applicability of the hypothesis for natural hormone detection.</td>
<td>December 2011</td>
</tr>
</tbody>
</table>
PM activities within EU framework projects, e.g. BIOCOP and MONIQA

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

11) 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). Accreditation of Proficiency tests EURL.

12) Establishment of a protocol for follow up after proficiency test. MS with low scores are contacted with a newly developed protocol to help them with their analysis of the PT study which did not perform so well.

13) Organisation of proficiency tests for Clortestosterone-acetate (metabolite of) in bovine urine. 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. For 2011 a research study on natural hormones (multi residue) is foreseen in order to validate decision models developed in 2009.

14) Production of incurred sample material.

An animal studies in preparation of future proficiency tests are scheduled for 2011. Priorities will be set during the 2010 annual workshop.

Specific products related to C:

<table>
<thead>
<tr>
<th>Topic</th>
<th>Product</th>
<th>Planned for</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Annual re-accreditation</td>
<td>February 2011</td>
</tr>
<tr>
<td>12</td>
<td>Protocol follow up Proficiency tests</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Proficiency study Chlortestosterone acetate Research study for validation natural hormones strategy</td>
<td>Preliminary reports are prepared within 2 months after conclusion of the proficiency tests. Full reports within</td>
</tr>
<tr>
<td></td>
<td>Technical report animal study treatment with natural hormones</td>
<td>6 months</td>
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<tr>
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<td>----------</td>
</tr>
<tr>
<td>14</td>
<td>Following animal study</td>
<td></td>
</tr>
</tbody>
</table>

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

Analytical support and training. Analytical support, both by means of advice or training, will be given to NRLs upon their request.

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 2011 will be based on the current progress in the NRLs in the newer EU-Member States.

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.

Analyses of official samples. Samples 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.

Organisation of annual workshop on residue analysis. The topic will be selected on the basis of a consultation of the NRLs during the 2010 workshop.
Specific products related to D:

<table>
<thead>
<tr>
<th>Topic</th>
<th>Product</th>
<th>Planned for</th>
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</thead>
<tbody>
<tr>
<td>15</td>
<td>Training documentation and/or report</td>
<td>On an Ad Hoc basis</td>
</tr>
<tr>
<td>16</td>
<td>Visit report</td>
<td>December 2011</td>
</tr>
<tr>
<td>17</td>
<td>Ongoing</td>
<td>Annual overview</td>
</tr>
<tr>
<td>18</td>
<td>Ongoing written reports</td>
<td>On an Ad Hoc basis</td>
</tr>
<tr>
<td>19</td>
<td>Workshop proceedings</td>
<td>December 2011 / January 2012</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2011 workshop)</td>
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</tbody>
</table>
WORK PROGRAMME OF THE EUROPEAN UNION REFERENCE LABORATORY AT THE FRENCH AGENCY FOR FOOD, ENVIRONMENTAL AND OCCUPATIONAL HEALTH SAFETY

Antimicrobials and dyes
Group of substances: B1, A6, B2f, B3e

Laboratoire de Fougères

P. SANDERS
Head of EU-RL

&

E. VERDON
Deputy Head of EU-RL

LEGAL FUNCTIONS AND DUTIES

OBJECTIVES FOR THE PERIOD JANUARY - DECEMBER 2011

General tasks  
*Article 32, paragraph 1 (e)*

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

Quality assurance and quality control including the organisation and implementation of proficiency tests  
*Article 32, paragraph 1 (b, c)*

Technical and scientific support to NRLs and third countries  
*Article 32, paragraph 1(a, d, e, f)*

WORKING PLAN FOR THE PERIOD JANUARY - DECEMBER 2011

A. General Tasks - *Article 32, paragraph 1 (e)*

1. Meeting 4 EURLs, EURLs residues management,  
2. Technical and scientific support to the Commission,  
3. Compilation of annual report and cost estimate,  
4. Co-operation with international organisations,  
5. Documentation services, inter change of information via the website.

B. Development and Validation of Analytical Methods - *Article 32, paragraph 1 (a, c)*

6. Development and Confirmatory method for antimicrobials in different matrices (muscle, milk, eggs, honey …).  
6.1 Non-targeted analysis of antibiotic residues in meat and in milk – Physico-chemical part (continued task 2009/2011)

Research and development on non-targeted monitoring of antibiotic residues by physico-chemical methods is now getting possible thanks to enhancement of new high resolutive technologies such as time-of-flight mass spectrometric instruments (ToF, Q-ToF) and/or even newer high resolutive mass spectrometric instruments such as FT-Orbitrap MS. The EU-RL from ANSES-Laboratory of Fougeres completed in 2008 the acquisition of such a technology, the LC-LTQ-FT-Orbitrap-MS, and started to investigate in this area of research. During the 2009-2011 period, it is particularly proposed to get a better knowledge of the characteristics of the full-scan monitoring of about 50-100 antibiotic residues in meat and afterwards in milk with the objective to be in position to disseminate a methodology for exact mass and molecular identification of each antimicrobial compound in biological samples. The final aim of this study will be to implement
an analytical strategy able to evaluate on a non-targeted mode of acquisition any relevant unspecified molecular signals by means of high resolution exact mass measurements (30,000 < Resolution < 100,000) whatever the biological matrix of concern it is. Specific examples will be investigated (beta-lactam metabolites, ...).

6.2 Multi-antimicrobial family method by LC-MS/MS (2010-2011)

Following the validation of the 1st step development of the method regarding the selective identifying screening in meat and in milk for about 60 antimicrobials as completed in the 2007-2008 period, the method was disseminated to NRLs end-2007 and also submitted to publication in an international peer-reviewed journal in 2009. Now the project was started again in 2010 considering a new LC-MS/MS equipment acquired at the end of 2009. An extension of the method to other antimicrobials was proposed in 2010. An evaluation of another matrix of interest for the network of NRLs (Honey) is also considered with a development scheduled over a 2-year period during the 2010/2011 programmes. Discussion about collaboration with FERA-YORK on this topic is on-going.

6.3 Confirmatory method for tetracyclines in meat and in milk matrix (new task)

As a follow-up of the multi-antimicrobial screening method by LC-MS/MS, a new confirmatory method for tetracyclines including accurate quantification for all the 4 analytes (oxytetracycline, chlortetracycline, tetracycline and their 4-epimers and doxycycline) will be validated and proposed to the network of NRLs.

6.4 Study of the Stability of Antimicrobials in specific Analytical Conditions (new task)

As a follow-up of the multi-antimicrobial screening method by LC-MS/MS will be started a stability study in stock standard solutions and in spiked milk and meat samples for the set of antimicrobials as they are routinely prepared for residue testing. This study will complement the validation of the method in meat and in milk. First results of this study will be presented during the next EU-RL workshop.

7. Study of screening tests (methods and kits).

7.1 A continuous evaluation of the performance of different screening kits for antimicrobial residue testing (either microbiological or immunological) proposed by manufacturers to be applied on different matrices will be investigated.
C. Quality Assurance and Quality Control - Article 32, paragraph 1 (b, c)

8. Organisation of proficiency tests (characterisation of the material, packaging, evaluation, report)

According to our agreement with the network of NRLs, the EU-RL will proceed in 2011 to the organisation of a large Proficiency Testing Study dedicated to the evaluation of the overall strategies for monitoring antimicrobial substances in milk products.

8.a Antimicrobials

The antimicrobials of choice should be made from representative compounds of the following families of antimicrobials, ie. penicillins, cephalosporins, tetracyclines, aminoglycosides, macrolides, sulfonamides, quinolones, amphenicols which are registered in Annex I of Directive 2377/90/EC. The matrix of choice will be cow raw milk or swine meat.

8.b Banned substances

The banned substance of choice shall be nitrofurans (NIFU) as a come back after the last 2008 PT for nitrofurans and after having proceeded to interlaboratory analysis of dyes (malachite green/ crystal violet) in 2009 and chloramphenicol in 2010. The matrix of choice might be if technically possible honey otherwise in aquaculture products and/or other meat tissues.

8.c Proficiency test in relation with coordinated monitoring programme

No coordinated monitoring programme for 2011 is defined by the Commission.

8.d State-of-the-art in EU for the monitoring of quinoxalines.

A questionnaire will be sent to establish a state-of-the-art in this field.

9 Production of incurred sample material

9.a According to the previous point, the different sampling materials will be produced by the EU-RL in accordance with the standards of testing material preparation (homogeneity and stability studies).

9.b A list of the EU-RL testing materials will be released and made available to the NRL-network

D. Technical and Scientific Support to NRLs in the Member States, the Commission and Third Countries - Article 32, paragraph 1 (a, d, e, f)

10. Analytical support and training

10.a Participation to SARAF training courses (June 2011, October 2011).
10.b Organisation of EU-RL-Fougeres training courses for scientists from Member States, Acceding Countries and/or Candidate Countries and from Third Countries, on request.

11. Missions to NRLs and Third Countries - diffusion of scientific information

11.a Projection of 3 visits to NRLs from the New Member States
11.b International missions for scientific information dissemination
11.c Follow-up and improvement of the 8-year-old EU-RL Website

12. Provisions of standard substances including storage, administration, documentation, shipment, etc

12.a Request for Standard substances
All the NRL requests considering standard substances will be investigated but according to the commercial availability or non-availability of the substances.

It is intended to establish an official document giving information on stability of various antimicrobials in various solvents or mixtures of solvents as generally prepared for stock standards solutions or spiking solutions. This document will gather all the available and relevant information collected from all the NRLs from the EU-RL/NRLs network.

13. Analysis of official samples

As a EU-RL, the ANSES-Fougeres will go on with analysing at a reference status some of the official samples coming from the NRLs and at their demand.

The specific requests rising from certain NRLs to analyze in their place a part or all of the confirmatory sets of samples coming from their National Monitoring Plan especially for confirmation of Group B1 compounds will not be accepted as this kind of workload is neither a priority in EU-RL activities nor a specific task requested by the Directive 96/23/EC.

14. Organisation of a workshop

A workshop for the attention of the network of NRLs in charge of antimicrobial residue control in food will be organized. The main subject will
be the advances in screening and confirmation of antimicrobials by LC-MS/MS methods.

15. Analysis of the National Residue Monitoring Plans of the 27 Member States

According to the request of the Commission, the EU-RL will consult on line the RESIDUE database dealing with proposed National Residue Monitoring Plans and their Year N-1 results. Existing tables will be loaded at the EU-RL location. Information will be extracted and analysed by a EU-RL scientist to check for the adequateness of methods/matrices/combinations proposed by each of the Member States and at the European level. The EU-RL will publish a report for the Commission before the end of March 2012.
WORK PROGRAMME OF THE
EUROPEAN UNION REFERENCE LABORATORY
FOR RESIDUE TESTING, 2011

at the Istituto Superiore di Sanità
(EU-RL CEFAO)
Viale Regina Elena 299
00161 Rome, Italy

Group of substances: chemical elements
LEGAL FUNCTIONS AND DUTIES

The functions and duties of the European Union Reference Laboratory (EU-RL CEFAO) are described in Article 32 of Regulation (EC) No 882/2004 of the European Parliament and of the Council of 29 April 2004 where the Laboratories were defined Community Reference Laboratories.

1. OBJECTIVES FOR THE PERIOD 01 JANUARY 2011 - 31 DECEMBER 2011

A. General tasks
   Article 32, paragraph 1 (e)

B. Development and validation of analytical methods
   Article 32, paragraph 1 (a, c)

C. Quality Assurance and Quality Control, including the organisation of proficiency tests and the development of test material.
   Article 32, paragraph 1 (b)

D. Technical and scientific support to NRLs and Third countries
   Article 32, paragraph 1 (a, d, e, f)

2. WORKING PLAN FOR THE PERIOD 01 JANUARY 2011 - 31 DECEMBER 2011

A. General Tasks - Article 32, paragraph 1 (e)

1. Meeting of all EU-RLs

The EU-RL CEFAO is willing to participate in any coordination meeting of the EU-RLs that may be organised.

2. Technical and scientific support to the Commission and co-operation with international organisations

Upon request, technical and scientific support will be provided to the European Commission and its related Institutes.

Contacts with the ISO/IDF Standing Committee on Analytical Methods for Additives and Contaminants (SCAMAC) will be established on the occasion of the "SUMMILK IDF World Dairy Summit 2011"(see 5.2).

3. Compilation of annual reports

The reports on the activities carried out for the relevant contract period will be regularly issued (e.g. final report 2010, interim report, report on PT 2011, financial reports, workshop report, report on NRLs visits).

4. Documentation services, interchange of information

The EU-RL CEFAO will provide any information and/or technical and scientific assistance requested by the EU NRLs and Official Laboratories of Third Countries. In
the EU-RL CEFAO website, the EU-legislation, the list of the Official Methods, the NRLs Control Charts and new relevant documents will be updated. In the Restricted Area the NRLs can report their PT results, gain access to the reports of the PTs, have information on the annual Workshop, and, finally consult the Handbook of Analytical Methods of the NRLs. As for this last document, the reviewed analytical methods and/or new methods adopted by NRLs are yearly updated. The EU-RL CEFAO will request NRLs to provide this information.

B. Development and Validation of Analytical Methods - Article 32, paragraph 1 (a, c)

5. Analytical methods
5.1 Maintenance of analytical methods

This is an ongoing activity that can also include the updating/revision of accredited methods; it also comprises the additional validation necessary for the use of the “flexible scope”.

5.2 Development of analytical methods

Details of the “ISO/TS 6733 IDF/RM133 "Milk and Milk products-Determination of lead content-Graphite furnace atomic absorption spectrometric method” will be developed in order to improve the performance of the method and to facilitate its application. Modifications could be proposed.

The reason of this work is also supported by the considerations in Annex A on the interlaboratory trials of ISO/TS where it is reported that the results of the study are not satisfying. The results will be submitted to the Committee of the "SUMMILK IDF World Dairy Summit 2011" Congress. They will be illustrated and discussed in the analytical section “Methods and Sampling”. Besides, a comparison with an EU-RL CEFAO analytical method based on ICP-MS will be presented for the same matrices.

This work, dealing with the ICP-MS and ETA-AAS for the principles of measurement, and with dry-ashing and microwave digestion for the sample treatment, includes all situations present in the NRLs laboratories.

The outcome will be provided to the NRLs and a method related to the “cheese matrix” will be proposed to the NRLs in a future interlaboratory trial.

The ongoing study on arsenic speciation will be continued focusing on the separation and quantification of the inorganic arsenic fraction. Since it turned out that most studies reported in literature are based on samples in freeze-dried state, whereas few are those using fresh samples, the work will be focused on fresh samples. Furthermore, the freeze-dried process is an expensive and time consuming process not used by the NRLs on a routine basis. Instead, a method based on fresh material would be more easily transferred to the NRLs and this is in fact the final aim of this work. Pursuing this last objective, the analytical techniques experimented for the quantification will be those routinely used by the NRLs.
C. Quality Assurance and Quality Control, including the organisation and implementation of proficiency tests - Article 32, paragraph 1 (b)

6. Maintenance of the QA/QC system

The activities as accredited laboratory and accredited PT provider will be regularly run.

In order to monitor and document the QC, the EU-RL CEFAO will apply for some commercial PTs, besides the ones carried out within its own organisation.

7. Proficiency test

Since the 3rd round on frozen fish of the 14th PT started in November 2010, the evaluation of the results will be carried out in 2011; the relevant reports will also be issued.

The 15th PT will be constituted of only two rounds, since the previous one consisted of 3 rounds, according to the foreseen alternating sequence. The analytes will be arsenic, cadmium, lead and mercury. A liver sample will be used in the 1st round, being this matrix considered in most NRCPs of the MS. A meat sample is foreseen for the 2nd round. As for the materials, the liver will be in a frozen state in order to propose a state similar to that of the incurred samples. Furthermore, standard solutions at unknown concentration of Arsenic are planned in this round in order to continue the improving processes of the Laboratories performance on the total element analysis; the exercise will also turn out to be useful for the future speciation work (see 5.2).

The meat sample instead will be in a freeze-dried state in order to have the possibility to supply the NRLs with a surplus of test items.

As for the preparation, samples will be prepared in the EU-RL CEFAO laboratory and the elements concentration will be adjusted pursuing specific objectives. The lyophilisation and the sterilization of the meat will be subcontracted to qualified suppliers.

The performance of the participants will be assessed by the z-scores approach fixing the $\sigma_p$ at a value suitable to the performance of the NRLs but, in order to allow a comparison with the performances obtained in commercial programmes, the scores using the $\sigma_{Horwitz}$ will be supplied as well.

The NRLs will be requested to use their methods as routinely applied. The participants are also recommended to give details of their sample preparation and measurement parameters in a questionnaire especially designed for this purpose.

Where applicable, the NRLs were asked to state the “acceptance of the sample” as indicated in the CR (EC) 333/2007 (point D.2.1).

As usual, a “Preliminary Report”, containing a summary statistics, the results and the z-scores, will be published in the Restricted Area of the website, approximately
within 40 days from the deadline of the round. The “Final report” including several issues (e.g. rationale of the round, appropriate statistics, homogeneity and stability data, comments) will be sent to the participants in paper form and will replace the preliminary Report in the website. NRLs will be informed of the issuing of these reports via e-mail.

The Final report is also sent to the European Commission and also to the NRLs that did not participate in that round.

8. New Reference Materials for PTs

The previous activities led to obtain a procedure suitable for the production of a repined cheese with a sufficient homogeneity. To continue this work a commercial cheese at a concentration of interest will be searched and studied. This is a worthwhile ongoing activity producing materials and procedures useful in internal development of methods and future interlaboratory trials for the NRLs (see 5.2).

D. Technical and Scientific Support to NRLs and Third Countries - Article 32, section 1 (a, d, e, f)

9. Analytical support and training

In case the need arises to check a method or a particular step of the analytical procedure, the EU-RL CEFAO will analyze specific samples (incurred samples, digested solutions, etc.), upon request of NRLs. In addition, the analytical performance of the NRLs is monitored through the control charts of their participation in the PTs. Some control charts will be examined during the annual workshop and, when necessary, these charts will confidentially be discussed together with the interested parties.

The EU-RL CEFAO will perform official analyses if necessary.

Analytical support by means of advice or ad-hoc training courses will be given to the Official Laboratories of Candidates Member States and Third Countries when requested (e.g. in the framework of the TAIEX cooperation). The courses can be given at the EU-RL CEFAO laboratory or at the applicant State’s laboratory. A “Training Course on Arsenic, Cadmium, Lead and Mercury analyses in food of animal origin” for 3-4 Members of the Ministry of Agriculture, Livestock and Supply of Brazil, is foreseen at the EU-RL CEFAO in the first semester of the year 2011.

10. Provision of reference materials

In the framework of the round on meat a high number of test items will be produced so that the NRLs will receive not only the sample for the round but also several test items they can use as reference material for their own scopes (internal control charts, validation methods, etc).

The surplus of the reference materials produced for the previous PTS will be available for the NRLs upon request.
11. Visits to NRLs and international mission for scientific information

A visit to a NRL will be carried out to exchange information on their analytical techniques, problems of QA/QC, legislation etc. The full report on the visit will be sent to the Commission and to the relevant NRL as well.

The participation of the EU-RL CEFAO is foreseen at Eurachem, 7th Workshop, “Proficiency Testing in analytical chemistry, microbiology and laboratory medicine”, 3-6 October, Istanbul, Turkey and at the international congress "SUMMILK IDF World Dairy Summit 2011", 15-19 October, Parma, Italy

12. Organisation of the workshop

The EU-RL CEFAO will organise the usual annual workshop where the evaluation of the 15th PT, the general performance achieved by the NRLs and the analytical issues of interest for participants will be discussed. During this event NRLs will receive two questionnaires where they are asked to anonymously give their opinion on the workshop itself and on the EU-RL CEFAO activities