2WORK PROGRAMMES
FOR
COMMUNITY REFERENCE LABORATORIES
2003
**********

VETERINARY PUBLIC HEALTH
(Residues)

1. Berlin (Group of substances: A5, B2a, B2b and B2e)
2. Fougeres (Group of substances: A6, B1 and B3e)
3. Bilthoven (Group of substances: A1, A2, A3, A4, B2d and B3d)
4. Rome (Group of substances: B2c, B3a, B3b and B3c)
WORK PROGRAMME FOR THE
COMMUNITY REFERENCE LABORATORY
FOR RESIDUE TESTING, 2003

BERLIN


I. LEGAL FUNCTIONS AND DUTIES


1. OBJECTIVES FOR THE PERIOD JANUARY - DECEMBER 2003

1.1. General tasks

1.2. Development and validation of analytical methods

1.3. Production of incurred sample material

1.4. Quality Assurance and quality control including organisation and implementation of proficiency tests

1.5. Organisation of a Workshop

1.6. Technical and Scientific Support to NRLs and Third Countries

2. WORKING PLAN FOR THE PERIOD JANUARY - DECEMBER 2003

2.1. General tasks

1. Research and identification of unknown compounds, Annex V, chapter 2, section 1 (a, j)

2. Analysis of official samples, Annex V, chapter 2, section 1 (h)

3. Meeting 4 CRLs, Annex V, chapter 2, section 1 (j)

4. Visit to NRLs, Annex V, chapter 2, section 1 (b)

5. Co-operation with internat. organisat., Annex V, chapter 2, section 1 (j)

6. 1. Maintenance QS Annex V, chapter 2, section 1 (a-l) and Decision 98/179/EEC, No 1.2

7. Techn. and scientific support, Annex V, chapter 2, section 1 (j)

8. Compilation of annual report and cost estimate Annex V, chapter 2, section 1 (h)
2.2. **Development and validation of analytical methods and animal studies, Annex V, chapter 2, section 1 (a, c, d)**

9. Development of a multi-residue method for several anticoccidials in egg and muscle

10. Validation of the multi-residue method for several anticoccidials in egg and muscle

11. Validation of the method for avermectines in milk

12. Implementation of the LC-MSMS method for nicarbazin in poultry muscle**)

13. Development of a multi-residue method for acidic NSAIDs in liver and/or muscle

**) This method was developed at the Laboratory in Belfast within a fifth framework project "Poultry-check". A joint workshop is planned to be organised by the CRL Berlin. Travel costs and daily allowances will be financed by the project's budget. The workshop will be held at the BgVV facilities.

2.3. **Production of incurred sample material, Annex V, chapter 2, section 1 (a, b, g)**

14. Two different treatments

2.4. **Quality Assurance and quality control, Annex V, chapter 2, section 1 (a, b, c, g)**

15. Maintenance of equipment, documentation, audits, management

16. Proficiency test: characterisation of the material, packaging, evaluation, report

2.5. **Organisation of a Workshop, Annex V, chapter 2, section 1 (i, e)**

17. One workshop on coccidiostats will be performed for Member States

2.6. **Technical and Scientific Support to NRLs and Third Countries**

*Annex V, chapter 2, section 1 (d, f, h, l)*

18. Analytical support and training

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

20. Workshop for Candidate Countries, excl. practical work

It is understood that the above-mentioned objectives are not exclusive to other work of more immediate priority which may arise during the reference period in question.
WORK PROGRAMME OF THE COMMUNITY REFERENCE LABORATORY AT THE AGENCE FRANCAISE DE SECURITE SANITAIRE DES ALIMENTS (AFSSA)

Laboratoire d'études et de recherches sur les médicaments vétérinaires et les désinfectants

Programme for the contract period: January 2003 – December 2003

P. SANDERS
3. **LEGAL FUNCTIONS AND DUTIES**


4. **OBJECTIVES FOR THE PERIOD JANUARY 2003 – DECEMBER 2003**

   4.1. **General tasks**

   4.2. **Development and validation of analytical methods**

   4.3. **Production of incurred sample material**

   4.4. **Quality Assurance and quality control including organization and implementation of proficiency tests**

   4.5. **Technical and Scientific Support to NRLs and Third Countries**

5. **WORKING PLAN FOR THE PERIOD JANUARY 2003 – DECEMBER 2003**

   5.1. **General tasks**

   1. Research and identification of unknown compounds  
   2. Analysis of official samples  
   3. Meeting 4 CRLs  
   4. Visit of NRLs  
   5. Co-operation with international. Organisation  
   6. Maintenance QS  
   7. Techn. and scientific support
5.2. **Development and validation of analytical methods and animal studies** *Annex V, chapter 2, section 1 (a, c, d)*

- Cefalosporines (milk) or Quinolones (milk)

A multi analyte method for each family (Cefalosporines and Quinolones) based on liquid chromatography and UV detection will be developed to quantified these compounds in milk at the MRL levels. The development for cefalosporines is on going. The steps of the development are the optimization of chromatographic conditions, the conception and development of extraction and the optimization of the overall procedure before validation. The time needed for the development of one method is estimated from 6 months to one year and is function of the problems observed during the different steps.

- Carbadox – Olaquindox (Muscle, Liver, Feeds)

Carbadox and olaquindox are banned substances in EU. They are used as growth promoters in the past. The development of a method based on LC/SM-SM is on-going to detect and confirm the presence of these compounds or their metabolites in muscle, liver and feeds (parental compounds). The work planned is to validate the methods before the training courses.

- Biospecific interaction analysis and detection of residues

The laboratory collaborate on the development of a system of detection of residue by biospecific interaction (BIACORE). The performance of the system will be analyzed in comparison with other detection system (ELISA Kits) by measure of the affinity and specificity of the binding of different antibodies for aminoglycosides.

- Comparative study of ELISA Kits (antibacterial substances)

A comparative study of ELISA Kits used to detect aminoglycosides is planned. This comparison is necessary to give independent information about the performance of these tests to NRLs and is a first step before the organization of proficiency test on the detection of antibacterial residues with these kits.

5.3. **Production of incurred sample material** *Annex V, chapter 2, section 1 (a, b, g)*

- Incurred sample material of different species and substances will be produced in order to support the development and validation of test methods and for use in proficiency testing and distribution studies.
  - Treatment and slaughter of animals
  - Determination of residue concentrations
  - Packaging and shipment of samples
- Nitrofurans metabolites – Muscle
- Carbadox – Olaquindox - Muscle, Liver
- Macrolides – Muscle – Species not determined
- Aminoglycosides – Milk  (laboratory incurred)

The 4 proficiency test are planned during 2003 according CRL/NRL meeting held at Fougères, the 17 and 18 September 2002.

5.4. **Quality Assurance and quality control** *Annex V, chapter 2, section 1 (a, b, c, g)*

- Adaptation of the QA/QC system to ISO 17025
- Proficiency test : nitrofurans metabolites - Confirmation
- Proficiency test : Carbadox/Olaquindox - Confirmation
- Proficiency test : Macrolids – Confirmation
- Proficiency test : Aminoglycosides - Screening

5.5. **Technical and Scientific Support to NRLs and Third Countries** *Annex V, chapter 2, section 1 (d, f, h, l)*

- Analytical support to NRLs and other official laboratories (ongoing task)
- Promotion of exchange of information via the web-site
- Provision of standard substances to the NRLs in the Member States and to official laboratories in third countries (ongoing task)

The synthesis of different compounds (metabolites of carbadox, olaquindox, nitrofurans) is needed for control of banned substances. The laboratory will analyse the capacity of different partners to provide the CRL/NRL with these standards and evaluate the costs.

- Provision of training to scientists from the EU Member States and from third countries (ongoing task)
  - Training course Member states "Carbadox/olaquindox"
  - Training course Candidate countries “Antimicrobial residue"

- Promotion of exchange of information via the web-site
COMMUNITY REFERENCE LABORATORIES IN THE FIELD OF VETERINARY PUBLIC HEALTH WITHIN THE EUROPEAN UNION

CRL for residues RIVM-ARO at Bilthoven, NL

---------------------------------

Group of substances: A1, A2, A3, A4, B2d, B3d
WORK PROGRAMME FOR THE
COMMUNITY REFERENCE LABORATORY
FOR RESIDUE TESTING, RIVM, Bilthoven,

January 2003 – December 2003

I. LEGAL FUNCTIONS AND DUTIES


II. Objectives and indicative percentage of the total of activities for the period January 2003 – December 2003

A: General Tasks. Annex V, chapter 2, section 1 (c,d,f,i,k)
Indicative percentage of total of activities: 16%

B: Development and validation analytical methodology. Annex V, chapter 2, section 1(a,e,h,j,l)
Indicative percentage of total of activities: 46%

C: Quality Assurance and Quality control activities, inclusive the development of incurred test materials and the organisation of proficiency tests. Annex V, chapter 2, section 1 (b,e,g).
Indicative percentage of total of activities: 20%

D: Technical and scientific support to Member States and the Commission, inclusive arbitration and training activities. Annex V, chapter 2, section 1(c,e,f,h,i)
Indicative percentage of total of activities: 19%

III. Work programme for the period 2003

A. General Tasks

1) EC-4 CRL for residues management (co-ordination, co-operation and administration, inclusive the preparation of technical and financial reports) Annex V, chapter 2, section 1 (k)
   - Contribution to Joint 4 CRL Report 2001-2002

2) EC/CRL related EC and International Bodies (e.g. AOACi, Eurachem, Codex, CVMP, EMEA, EFSA, JRCs) performance quality criteria (communication, co-
ordination, co-operation and harmonisation) Annex V, chapter 2, section 1 (c and d). Explicit co-ordination of CCRVDF - EU/EC involvement.

Specific products scheduled:

- Publication of report “Worldwide regulations for mycotoxins in product of animal origin” (activity shared with FAO)

3) Documentation services Annex V, chapter 2, section 1 (f and i)
   - Further improvement of internet site "CRL for Residues": Bilthoven
   - Maintenance of database “CB\METHODS” with methods and contact points

B: Development and validation of analytical methodology

4) Identification of new and unknown compounds illegally used for growth promoting purposes. Annex V, chapter 2, section 1 (a,j)

5) Development and validation of analytical methods necessary for effective inspection and control Annex V, chapter 2, section 1 (e and l), focussing on improving methodology for relevant metabolites, the analyses of alternative matrices and the analyses of meat. "The matrices will be urine, feces and muscle tissue. Analytes of special interest are the metabolites of boldenone, methyltestosterone, methylboldenone, norethandrolone, normethandrolone and chlortestosterone."

Specific products scheduled:

- Publication of second edition of the technical manual: "Analytical modules for the isolation, detection, quantification and identification of steroids”.

- Publication of method validation report: "Analytical methods for the detection metabolites of androgenic anabolic steroids in urine”.

- Publication of method validation report: analytical methods for the detection of Zeranol, fusicarium toxins and related metabolites in biological matrices.”

- Publication of second interim report on analytical methods for detection, identification and quantification of peptide hormones.

6) Supportive research in the mandate of the CRL and the acquisition/participation in EC/CRL –related ECs DGs programmes Annex V, chapter 2, section 1 (a)

   - Analytical methods for the detection of illegal use of natural hormones by GC-IRMS.

   - PM Activities resulting form the 4CRL EOI ““FaFoRescontrol”(sixth framework program)
C: Quality Assurance and Quality control activities, inclusive the development of incurred test materials and the organisation of proficiency tests

7) Maintenance of in-house QA/QC activities in consequence of the ISO 17025 accreditation of all analytical work done within the CRL Annex V, chapter 2, section 1 (b)

8) Assistance with the implementation of Quality Assurance and Quality Control systems in NRLs Annex V, chapter 2, section 1 (b). Active participation in projects focussing on Candidate Member States.

Specific products scheduled:


9) Organisation of proficiency tests of methylboldenone and norethandrolone. Preparation of materials for proficiency test on chlortestosterone and nor-chlortestosterone. Annex V, chapter 2, section 1 (e and g).

Specific products scheduled:

- Publication of report: "Proficiency test Methyltestosterone and metabolites"

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

10) Analyses of samples submitted by EU Member states in case of dispute between Member States or in case of analytical problems within a responsible NRL Annex V, chapter 2, section 1 (h)

11) Providing the Commission Services, National Reference Laboratories, the European Food Safety Authority (EFSA), the European Agency for the Evaluation of Medicinal Products (EMEA) and Third Countries with technical and scientific assistance (j,f)

12) EC-CRL-NRLs for residues establishment of confirmatory methods for arbitration and minimum quality criteria (co-ordination, co-operation and harmonisation) Annex V, chapter 2, section 1 (c and e)

13) Organisation of annual workshop on residue analysis, tentatively entitled “MRPLs and validation procedures, setting criteria and procedures” Annex V, chapter 2, section 1 (i)
Work programme of the Community Reference Laboratory for Residues at the Istituto Superiore di Sanità of Rome (ISS-CRL) for the period 1 January – 31 December 2003

Group of substances: B2(c), B3(a), B3(b), B3(c)
I. Legal functions and duties.


II. Objectives and break-down of activities for the period 1 January – 31 December 2003.

A. General tasks (as mentioned in Annex V, Chapter 2, Section 1, items d, e, g, j, k and l).
   Anticipated break-down of all activities: 20%.

B. Development and validation of analytical methods (as mentioned in Annex V, Chapter 2, Section 1, items a).
   Anticipated break-down of all activities: 25%.

C. Quality assurance and quality control programmes, including the organization of proficiency tests (as mentioned in Annex V, Chapter 2, Section 1, items b, g).
   Anticipated break-down of all activities: 30%.

D. Technical and scientific support to the Commission, EU Member States and Third Countries (as mentioned in Annex V, Chapter 2, Section 1, items c, f, g, h, i, j and l).
   Anticipated break-down of all activities: 25%. 

General tasks.

A1. Management of administrative duties, coordination with the Commission services, cooperation among the four CRLs for residues, harmonization of approaches among the NRLs and preparation of technical and financial reports (as mentioned in Annex V, Chapter 2, Section 1, item k). Anticipated break-down of all activities: 5 %.

A2. Systematic revision and updating of the Handbooks of Analytical Methods for chemical elements, carbamates, pyrethroids, organophosphorus compounds, organochlorine compounds, polychlorobiphenyls, polychlorodibenzo-p-dioxins and polychlorodibenzofurans. All Handbooks on Analytical Methods for residues in use at the NRLs will be revised at intervals of six months. To this end, twice a year the NRLs are requested to submit to the ISS-CRL updated information on the analytical methods already in use as well as on new methods which meanwhile may have been adopted. This implies that the relevant Handbooks are thoroughly revised at intervals of six months to constantly monitor the capabilities of the NRLs and new editions thereof (both printed and electronic) are released at such intervals to the benefit of the NRLs, in particular to facilitate the mutual knowledge of their approaches and the harmonization of procedures and to receive inputs on possible modifications and improvements (Annex V, Chapter 2, Section 1, items d and e). Anticipated break-down of all activities: 5 %.

A3. Publication of technical reports and scientific papers. The results of the activities listed under item C2 above will be accomplished to make them available to the interested scientific community (Annex V, Chapter 2, Section 1, items g and j). Anticipated break-down of all activities: 5 %.

A4. Development of bilateral contacts with other organizations. Information of mutual interest will be exchanged between the ISS-CRL and the EC-JRC, the OECD, the EMEA and the Australian Residues Survey, also in view of possible joint projects (Annex V, Chapter 2, Section 1, item l). Anticipated break-down of all activities: 5 %.

B. Development and validation of analytical methods.

B1. Improvement of already existing analytical methods for trace elements and their chemical species in order to enhance detection power and reliability. In particular:

B1.1. Procedures will be developed for the identification and minimization of mass interferences by multiple ions in inductively coupled plasma quadrupole and magnetic sector mass spectrometry. Such interferences (e.g., those of ArCl on As...
and of ArC on Cr) can seriously impair the reliability of analyses (Annex V, Chapter 2, Section 1, item a).
Anticipated break-down of all activities: 6 %.

B1.2. A combined method for the speciation of As in fish and poultry (see below) based on inductively coupled plasma quadrupole mass spectrometry coupled to capillary electrophoresis will be developed and validated (Annex V, Chapter 2, Section 1, item a).
Anticipated break-down of all activities: 6 %.

B2. Refinement of extraction and purification procedures from a pork fat matrix will be eventually carried out on the basis of the results of the ongoing proficiency test. A gas chromatographic/mass spectrometric method for the simultaneous quantification of organophosphorus compounds will be also assessed (Annex V, Chapter 2, Section 1, item a).
Anticipated break-down of all activities: 13 %.

C. Quality assurance and quality control programmes, including the organization of proficiency tests.

C1. Support to the NRLs regarding the development and adoption of quality assurance schemes as dictated by the ISO 17025 and the OECD Principles of Good Laboratory Practice. Updated information on the implementation of the ISO 17025 criteria and of the OECD principles of Good Laboratory Practice will be regularly made available to the NRLs in order to further promote their adoption in the organization of the laboratory activities (Annex V, Chapter 2, Section 1, item b).
Anticipated break-down of all activities: 6 %.

C2. Organization and conduct of proficiency tests.

C2.1. As decided during the Workshop on the Seventh Proficiency Test on Trace Elements (As, Cd, Cr, Cu, Fe, Hg, Pb and Zn) in synthetic solution simulating the acid digestion of real meat samples, the next proficiency tests will again be conducted on a quarterly basis to better assess the performance of NRLs. These proficiency tests will also include a real matrix (tuna fish tissue) and will be organized in close cooperation with the EC-JRC-IRMM, where such material will be produced, preliminary characterized and stabilized. The outcome of such tests will be assessed by the ISS-CRL and each participant will receive a detailed provisional report which will allow all laboratories to interpret their own results as well as to identify any possible source of procedural errors. A final report summarizing the scope, expected advantages and actual benefits of the proficiency tests will be prepared and made available to the NRLs in the shortest possible time after completion of each stage of the exercise (Annex V, Chapter 2, Section 1, item g).
Anticipated break-down of all activities: 8%.
C2.2. As agreed during the First Workshop on the Proficiency Test on Organophosphorous Compounds Determinations in Matrices of Animal Origin held in Rome, April 2002, proficiency tests for the determination of these residues will be permanently conducted. To this end, a matrix simulating the fat extracted from meat will be prepared. The pork lard has been considered the best matrix for this purpose and therefore spiked sample of pork lard will be used to perform the next exercise. The selection of the actual compounds will be done on the basis of compounds explicitly mentioned in European Directives. The amount of active ingredients added will be calculated taking account of the average percentage of fat in meat. Two vials will be sent to each NRL. The first vial will contain a blank sample of pork lard and the second one about 10 g of a spiked sample. Each NRL will report in detail all experimental steps (clean-up and instrumental analysis) and the results will be discussed during the next Workshop to be held in 2003. On the basis of the results of the described test, a further proficiency test will be performed, at the end of 2003, for checking the stability of the spiked pork lard samples in order to propose this matrix as reference material (Annex V, Chapter 2, Section 1, item g).

Anticipated break-down of all activities: 8%.

C2.3. The ISS-CRL will also prepare a fortified homogeneous matrix, namely fish oil, to organize the first proficiency test on PCBs, PCDDs and PCDFs. The following contaminants will be considered: i) eighteen PCBs: T3CB-28, T4CB-52, P5CB-95, P5CB-99, P5CB-101, P5CB-105, P5CB-110, P5CB-118, H6CB-138, H6CB-146, H6CB-149, H6CB-151, H6CB-153, H7CB-170, H7CB-177, H7CB-180, H7CB-183 and H7CB-187; ii) seven PCDDs: 2,3,7,8-T4CDD, 1,2,3,7,8-P5CDD, 1,2,3,4,7,8-H6CDD, 1,2,3,6,7,8-H6CDD, 1,2,3,7,8,9-H6CDD, 1,2,3,4,6,7,8-H7CDD and O8CDD; iii) ten PCDFs: 2,3,7,8-P5CDF, 2,3,4,7,8-P5CDF, 1,2,3,4,7,8-H6CDF, 1,2,3,6,7,8-H6CDF, 1,2,3,7,8,9-H6CDF, 2,3,4,6,7,8-H6CDF, 1,2,3,4,6,7,8-H7CDF, 1,2,3,4,7,8,9-H7CDF and O8CDF. The outcome of this pilot proficiency test will be illustrated in a final report in order to highlight the state-of-the-art of the NRLs responsible for the three groups of contaminants mentioned above and to develop further action aimed at assisting the NRLs showing substantial inadequacies in performing the task and at harmonizing the experimental approach to this kind of analysis (Annex V, Chapter 2, Section 1, item g).

Anticipated break-down of all activities: 8%.

D. Technical and scientific support to the Commission, EU Member States and Third Countries.

D1. Training of technical personnel of the NRLs. Training of technical personnel of the NRLs will occur specifically in the framework of proficiency tests in connection with items C2 and C3 above. This will cover both EU Member States and, separately, also Accession Countries, if a decision in this sense is taken by the Commission (Annex V, Chapter 2, Section 1, item i, j).

Anticipated break-down of all activities: 4 %.
D2. Two Workshops will be organized to debate the capabilities of the NRLs in determining the contaminants mentioned under points C2.2 and C2.3 above, as detailed below.

D2.1. A Workshop will be held to discuss the results obtained by the NRLs for organophosphorus compounds in the frame of the second PT focused on these contaminants. In particular, the meeting will facilitate the mutual understanding of the NRLs as regards the approaches followed in carrying out the requested determinations, the identification of procedural errors and pitfalls and the planning of remedial action as needed to improve their performance in this specific field (Annex V, Chapter 2, Section 1, item g).
Anticipated break-down of all activities: 5 %.

D2.2. A Workshop will be held to examine the performance of the NRLs for PCBs, PCDDs and PCDFs in the frame of the pilot PT centered on these contaminants. In particular, the meeting will facilitate the mutual understanding of the NRLs as regards the approaches followed in carrying out the requested determinations, the identification of procedural errors and pitfalls and the planning of remedial action as needed to improve their performance in this specific field.
Anticipated break-down of all activities: 5 %.

D3. Assistance to Commission in the assessment of new analytical methods. In consideration of the fact that the Commission Decision 2002/657/EC has been recently issued and that it lays down performance criteria for the analytical methods to be used for certain substances and residues thereof in live animals and their products as prescribed by Council Directive 96/23/EC, the NRLs will be assisted in understanding and implementing the new criteria brought about by this legal provision (Annex V, Chapter 2, Section 1, item c).
Anticipated break-down of all activities: 2 %.

D4. Arbitration in the event of litigation. In the case of disputes involving EU Member States as well as non-EU countries, the ISS-CRL is ready to provide its assistance and arbitration within the field of its competence, in particular, to analyze controversial samples for the residues under its mandate in the relevant matrices. (Annex V, Chapter 2, Section 1, item h). Anticipated break-down of all activities: 3 %.

D5. Technical assistance to the NRLs as required by circumstances, including visits to the premises, facilities and laboratories at the appropriate locations. Whenever the need arises, technical advice will be provided to the NRLs upon request. The ISS-CRL will support the NRLs with technical information, in particular as regards the implementation of quality systems and possible critical aspects that can impair the reliability of experimental data produced by the laboratory (Annex V, Chapter 2, Section 1, item f). Anticipated break-down of all activities: 3 %.

D6. Assistance to Third Countries in the submission of plans to be presented to the EC upon formal request by such countries (Annex V, Chapter 2, Section 1, item l). Anticipated break-down of all activities: 3 %.