The duties and operating conditions of the CRL for residues are laid down in Annex V, Chapter 2 of Council Directive 96/23/EC.

GENERAL TASKS

1) Management of EC CRL for residues (co-ordination, co-operation and administration, inclusive the preparation of technical and financial reports) Annex V, chapter 2, section 1 (k)

The cost statement and summary report for the period 1 July 2001 – 30 June 2002 were prepared and submitted for review by the Commission. The laboratory was audited, both with respect to the workprogram and the financial aspects, by representatives of the Commission, on November 7th 2002. Areas of improvement and clarification were identified and specific questions of the Commission were answered.

2) 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)

On request of the Austrian NRL, dated 6 February 2002, a series of urine samples was analysed for the presence of 17alpha-Boldenone and 17beta-Boldenone. A formal report was issued on 11 March 2002.

3) Providing the Commission Services, National Reference Laboratories and Third Countries with technical and scientific assistance Annex V, chapter 2, section 1 (j,f).

On request of the Yugoslavian Ministry of Economy and Internal Trade, assistance was given to the analyses of samples of animal feed for the presence of a series of anabolic steroids. In addition, specific questions were answered, 32 from NRLs of Member States, 25 from NRLs from other countries. Related quantitative data are summarized in the annex.

The Commission was assisted with respect to the current problems associated with the detection of residues of 17alpha-boldenone and 17beta-boldenone in samples of urine obtained from cattle. A third position paper was prepared on 9 December 2002 (ref. 1520/2002 ARO-CRL) and contributions were made on 13 December 2002 to a draft proposal for discussion in the Standing Committee for the Food Chain and Animal Health prepared by the Commission in consultation with the NRL from Italy.

1 Official Journal of the European Communities (1996) L125, 10-31
Evaluation of the Annual residue plans of all EU Member States has started based on documentation submitted to the CRL by the Commission. A letter report to the Commission, summarizing the main conclusions with respect to residues of hormonal growth promoting compounds, will be prepared.

**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 (h)*

During this contract period no indications on the use of new compounds or preparations possibly containing such compounds were found.

5) Development and validation of analytical methods necessary for effective inspection and control *Annex V, chapter 2, section 1 (e and l)*, focusing on improving methodology for relevant metabolites, the analyses of alternative matrices and the analyses of meat.

Research was conducted on samples of urine, feces and muscle tissue. Urine studies focused on norethandrolone and methylboldenone and their metabolites. Analytical methods for urine were developed and validated. Target metabolites for residue testing programmes were selected. The results of this study on norethandrolone were used as input for a proficiency test. The metabolites identified for methylboldenone currently are not available as internal standard. This study therefore was postponed to 2003 and replaced by the study on norethandrolone.

To further study the possible natural occurrence of 17alpha-boldenone and 17beta-boldenone the procedure for analyzing feces samples was further improved and validated. Current explanations of the possible natural occurrence of both 17alpha-boldenone and 17beta-boldenone include their formation in feces.

To further improve the analytical possibilities for the detection and identification of corticosteroids, the use of Supercritical Fluid Extraction was studied. Results for the matrix liver are promising. Current analytical methods are in need of improvement.

The first edition of the technical manual: "Analytical modules for the isolation, detection, quantification and identification of steroids" became available. The publication of individual modules is preferred over full methods, provided the modules are such that they can be combined. However, to further validate the analytical modules based on Commission Decision 2002/657 and to include modules of special interest for the Candidate Member States, it was decided to schedule the second edition for printing during 2003 and not to distribute the complete first edition, but, on request, only the individual modules. Biannual updates are foreseen.

Publication of method validation report: "Analytical methods for the detection of anabolic compounds in muscle tissue". The validation studies were finalized and a report was written. This report will be combined with additional data on the natural hormones and the influence of enzymatic treatment of primary extracts and is scheduled for publication in 2003.

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 (l)*

Progress within the project “Analytical methods for the detection of illegal use of natural hormones by GC-IRMS” (Fifth framework project ISOTRACE) was limited due to technical problems with the equipment.

**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)*

The report “QA inventory of Mycotoxin analyses in National Reference Laboratories” became available as CRL report 389002 120

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.

On an individual basis RIVM staff was involved in advising and training of laboratory staff within NRLs of Candidate Member States. This activity is conducted in close cooperation with the Commission’s TAIEX project.

Also in close cooperation with TAIEX, and together with the CRL in Berlin, preparations were started for a workshop specific for NRLs from Candidate Member States. This workshop is tentatively planned for June 2003.

9) Organisation of proficiency tests of methyltestosterone and norethandrolone. Preparation of materials for a proficiency test for methylboldenone. *Annex V, chapter 2, section 1 (e and g).*

All proficiency tests are based on an animal experiment to obtain incurred materials and to perform, when necessary, a metabolism study. The three compounds included in the last animal experiment were methyltestosterone, methylboldenone and norethandrolone. Since the PT for methyltestosterone involved for most NRLs the analyses for new analytes, the metabolites not tested for previously, more time was needed. The sequence of PT was changed because one of the identified metabolites of methylboldenone is not available as reference standard. Efforts currently are being undertaken to obtain this standard to organize this PT in 2003. The experience over the years has taught that two PTs each year is not possible when the analyses requested go beyond the normal daily routine.

On 24 July 2002 a preliminary report (2002/0987 ARO) was send to the participants with the results a the proficiency test “corticosteroids in bovine urine and liver”. A full report was prepared and will be distributed among the participants early 2003.

The results of the proficiency test “Methyltestosterone and metabolites” were received from most of the participants. A preliminary report will be distributed early 2003. Results are available for review by the participants on the CRL Website.

The proficiency test “Norethandrolone and metabolites” was started with the distribution of the sample materials on 2 December 2002 (2002/1458 ARO).

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

10) EC/CRL related EC and International Bodies (e.g. AOACi, Eurachem, Codex, CVMP, EMEA, FVA, 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

Discussions were started with JRC in Geel with respect to the development of analytical (LC-based) methods for the analyses of estrogenic steroids. With this JRC also a Memorandum of Understanding is drafted to underpin closer cooperation.
11) EC-CRL-NRLs for residues establishment of reference methods and minimum quality criteria (coordination, co-operation and harmonisation) *Annex V, chapter 2, section 1 (c and e).*

With the publication of Commission Decision No. 2002/657/EC of 12 August 2002 the basis for introducing the new minimum quality criteria and the directly related Minimum Required Performance Limits was formalized. A small series of draft proposed MRPLs was discussed during the Annual workshop.

12) Documentation services *Annex V, chapter 2, section 1 (f and i)*

Official start of internet site "CRL for Residues": Bilthoven.

The CRL internet site became operational at the occasion of the 2003 workshop [http://www.rivm.nl/crl/residues]. Further improvement is ongoing.

13) Organisation of annual workshop on the analysis of natural or naturally occurring hormones *Annex V, chapter 2, section 1 (i)*

A workshop titled: “An update on the control for Natural Hormones” was organized from 14 – 18 October 2003. The outcome of this workshop will be included in an EU expert report on boldenone (Ed. Prof H.F. de Brabander). Proceedings of this workshop are in preparation (CRL document 389002 122).

13) An overview of the EU regulations with regard to veterinary drugs has been presented (by mediation of the Commission at Beijing, PR China).

14) By invitation of FAO/IAEA the CRL contributed as consultant to the drafting and training programs for veterinary drug residue analysis in so-called less developed countries.
Numerical data

### I. **Overview of CRL Actions**

**period:** 2002.07.01 – 2002.12.31 **contract year:** 10

<table>
<thead>
<tr>
<th>Action</th>
<th>EU member states</th>
<th>Other countries</th>
<th>Total</th>
</tr>
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<tr>
<td>number of questions answered / advice’s given</td>
<td>32</td>
<td>25</td>
<td>57</td>
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<tr>
<td>number of items sent</td>
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<td></td>
<td></td>
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<tr>
<td>Ampoules with reference standards (BRS)</td>
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<tr>
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<td>23</td>
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<tr>
<td>Reference sets of blank bovine, ovine and porcine urine</td>
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<td></td>
<td>10</td>
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<tr>
<td>Sets of incurred test samples (QA-sets)</td>
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<td>Leaflets on BRSEU/CRL</td>
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</table>
Comparison of planned and realized personnel capacity

A: General Tasks. *Annex V, chapter 2, section 1 (f,h,k,j)*

Indicative percentage of total of activities: 10%

Percentage of staff input: 14

B: Development and validation analytical methodology. *Annex V, chapter 2, section 1(e,h,l)*

Indicative percentage of total of activities: 40%

Percentage of staff input: 40

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%

Percentage of staff input: 19

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,i)*

Indicative percentage of total of activities: 30%

Percentage of staff input: 27