



**JOINT FAO/IAEA DIVISION  
OF NUCLEAR TECHNIQUES IN FOOD AND AGRICULTURE**



INTERNATIONAL ATOMIC ENERGY AGENCY  
FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

**Report on the**

**First Research Co-ordination Meeting**

**of the Co-ordinated Research Project :**

**“The Development of Strategies for the Effective  
Monitoring of Veterinary Drug Residues in Livestock  
and Livestock Products in Developing Countries”  
(D3.20.22)**

*2-6 September 2002*

*Vienna International Centre*

*Vienna, Austria*

**Animal Production and Health Sub-Programme  
Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture  
International Atomic Energy Agency**

The first Research Co-ordination Meeting (RCM) of the Co-ordinated Research Project (CRP) on ‘the development of strategies for the effective monitoring of veterinary drug residues in livestock and livestock products in developing countries’ was held in the Vienna International Centre from 2 to 6 September 2002. Twelve Research Contracts (RCs) and 3 Research Agreements (RAs) have been awarded under this CRP and all awardees, the Project Officer (Dr. Andrew Cannavan, IAEA) and a guest speaker from the Austrian Agency for Health and Food Safety (AAHFS) participated in the RCM.

The objective of the RCM was to plan the first phase of the CRP, initiation of the development and validation of methods. Specific objectives were to:

- Agree upon a small number of veterinary drugs upon which to focus the research;
- Agree upon analytical methodologies to be employed;
- Formulate individual work plans for each research contract holder within the framework of the overall work plan

The meeting was opened by Dr. Chris Rigney, Head of the Agency’s Agriculture and Biotechnology Laboratory at Seibersdorf. Dr. Rigney outlined the role of the FAO/IAEA Training and Reference Centre for Food and Pesticide Control (TRC). He emphasised the potentially enormous costs incurred by non-compliance with international regulations with regard to export of food products and stressed the importance of the promotion of good agricultural practices in any residues monitoring strategy, including rapid feedback of information to the producer. Dr. John Crowther, Technical Officer (TO) of the FAO/IAEA Joint Division presented an overview of IAEA support in agriculture and the mechanisms involved in planning and implementing a CRP. Dr. Harinder Makkar (TO) gave a synopsis of current CRPs in the field of animal nutrition and the future shift in emphasis towards the application of gene-based technologies. Dr. Andrew Cannavan, the Scientific Secretary of the meeting, reviewed the background and objectives of the CRP and the expected outputs from the RCM.

Each RA holder gave a presentation of 1 hour, including discussion. Dr. Chris Elliott (UK) gave an overview of the importance of measuring drug residues, which generated intense discussion. Prof. Heinrich Meyer (GFR) gave a presentation on the relevance and residue control of  $\beta$ -agonists and Dr. Håkan Johnsson (SWE) described the approach taken to residue monitoring in Sweden.

D.I. Thomas Kuhn, from the AAHFS laboratory at Mödling, gave a presentation on EU Commission Decision 2002/657/EC, which describes new performance criteria for analytical methods. The participants of the meeting expressed a great deal of interest in this presentation, since the legislation will have profound effects on developing countries that export livestock products to the EU. Dr. Iris Lange, from the RA group in Munich, outlined that group’s approach to the development of  $^{125}\text{I}$ -labeled RIA methods for estradiol and chloramphenicol.

Each RC holder presented an overview of residues monitoring from the perspective of their respective countries. Emphasis was placed on problems encountered and future requirements.

The participants visited the Austrian National Reference Laboratory for veterinary drug residues at Mödling and discussed the activities there with Mr. Kuhn and laboratory staff.

An overall framework for phase I of the CRP, focusing upon the compounds and analytical techniques of major importance to the majority of participants, was formulated. Each RC holder discussed and revised their individual work plan with the RA holders and the PO. The overall framework was then reviewed and a summary of the individual work plans presented. Conclusions and recommendations were drafted.

Mr. Ian Ferris gave a presentation on the TRC International Food Contaminant and Residue Information System (INFOCRIS). The meeting participants were invited to act as editors for the database.

A summary of the work plan for the 1st phase of the CRP and a list of participants at the RCM are annexed.

## Conclusions

1. Each RC holder has formulated a work plan that both meets the requirements of his/her country and is in accordance with the framework of the CRP.
2. Three compounds, or compound groups, were identified to be of common interest to the majority of participants:
  - Chloramphenicol (CAP)
  - Nitrofurans (NF)
  - $\beta$ -agonists
3. All three compounds/groups are included as “group A” drugs in EU legislation and are banned for use in food producing animals. CAP and NF are also either prohibited for extralabel use in food producing animals, or not registered for use in the USA. These compounds are not, therefore, subject to EU MRLs and have had no MRLs set by the Codex Committee for Residues of Veterinary Drugs in Food. However, because of their efficacy and/or low cost, CAP and NF are still used in many parts of the world. Of the  $\beta$ -agonists, ractopamine and zilpaterol have recently been licensed for use in food producing animals in the USA and SA, respectively. Other drugs in this group are widely abused as growth enhancing and repartitioning agents.
4. Since they are not subject to MRLs, the important criterion for analytical methods for each of the chosen compounds is the Minimum Required Performance Limit (MRPL).
5. The analytical methodologies of choice for screening are EIA, HPLC, RIA and CHARM II. The majority of participants were also interested in the application of biosensor technology in this field, but no RC holder currently has access to a biosensor instrument. The methods of choice for confirmation are HPLC and LC-MS-MS.
6. The compound of most interest to the majority of participants is CAP. ELISA is the method of choice to screen for CAP. Commercial ELISA kits are available for CAP, but are prohibitively expensive. In some instances, reagent stability has also caused problems.
7. Methods are available for the measurement of NF. However, NFs are quickly metabolised into stable, tissue bound metabolites, which contain the intact side-chain moiety of the parent drug. Methods are, therefore, required to measure the metabolites. Methods measuring the parent compounds are of limited value, but may be applied to the measurement of these substances in, for example, feedstuffs.
8. NF metabolites have been found to be unsuitable for analysis by immunoassay, since efforts to raise suitable antibodies have, for the most part, been unsuccessful. HPLC is the method of choice for screening for these compounds.
9. In many laboratories in the South American continent, RIA is the method of choice for screening.

## Recommendations

1. Analytical standard materials should be procured, where possible, from EU Community Reference Laboratories (CRLs). Standards should be procured by IAEA and distributed to participants by the PO.
2. Transport mechanisms must be identified for the supply of consumables and equipment for the CRP, especially for thermolabile reagents. Care must be exercised in choosing the best means of delivery, e.g. supply via UNDP office.
3. Two Technical Contracts should be awarded for:
  - production and distribution of immunogens and immunoassay reagents
  - development and transfer of <sup>125</sup>I-labeled RIA methodology
4. Guidelines should be produced for the validation of screening methods, since this subject is not well defined by existing EU legislation or Codex guidelines.
5. A report should be produced, in the form of a paper for publication in the scientific literature, on the implications for developing countries of the newly adopted EU legislation regarding the performance of analytical methods (Commission Decision 2002/657/EC).
6. A workshop should be organised on the interpretation and application of 2002/657/EC.
7. A list of useful links to databases and residues information should be prepared by the PO and distributed to the CRP participants.
8. A web site should be developed for the CRP.
9. Analytical methods developed should be able to achieve the sensitivity necessary to reach MRPLs for the relevant compounds.
10. An evaluation of existing EIA and CHARM II methods for CAP should be conducted.
11. New screening methods should be developed for:
  - CAP (ELISA and RIA)
  - NF metabolites (HPLC)
  - $\beta$ -agonists (multi-residue RIA)
12. A confirmatory LC-MS-MS method for CAP should be developed at the laboratory of the RC holder with LC-MS-MS capability. If successful, this institute should act as a confirmatory laboratory for the other participants.
13. Work on other compounds of specific interest to each participant should proceed in parallel with the major focus of this phase of the CRP.
14. All participants should remain in frequent contact with the PO and with each other.
15. The 2<sup>nd</sup> RCM should be held in September 2003 in South Africa, immediately before a FAO training course to be held at the same location.

## ANNEX I

### Summary of Work Plan for 1<sup>st</sup> Phase

- New ELISA and /or RIA methods will be developed for CAP. This will form the basis of the work plan for the first year for 9 participants. Participants from Sri Lanka (SRL), Indonesia (INS), Kenya (KEN) and Korea (ROK), in collaboration with the agreement holder in UK, will develop EIAs for CAP using various strategies based upon established practices. ROK will attempt to develop the EIA into a membrane-based format. The first working methods should be produced in the second half of the year. Participants from Thailand (THA), Malta (MAT), Barbados (BAR) and Cyprus (CYP) will evaluate currently available ELISA and/or CHARM II kits and, when the new methods are available, will verify and compare their performance.
- The participant from Turkey (TUR), in collaboration with the RA holder in Germany (GFR), will commence the development of a RIA for CAP.
- THA will commence method development for the confirmation of CAP by LC-MS-MS. If successful, this institute will act as a confirmatory laboratory for the other participants. If the instrument becomes available, THA, using reagents provided by UK, will also develop a CAP method using an optical biosensor.
- Participants from South Africa (SAF) and Namibia (NAM) will collaborate in the development of a HPLC method for the NF metabolites, using the existing method from THA as a starting point. The sensitivity of this method needs to be improved, and various derivatisation and detection strategies will be investigated. If a working method is produced, the technology will be transferred to the laboratories in THA, KEN and possibly others, for verification.
- The participant from Brazil (BRA) should develop a multi-residue RIA for  $\beta$ -agonists, based upon antibody supplied by the RA holder in the UK, which cross-reacts with approximately 10 compounds in this class. If successful, the method will be verified by TUR and GFR.

**ANNEX II**

**List of Participants at 1<sup>st</sup> RCM**

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