WORK PROGRAM

FOR THE
COMMUNITY REFERENCE LABORATORY
FOR PESTICIDE RESIDUES USING
SINGLE RESIDUE METHODS

Time: January-December 2009

LEGAL FUNCTIONS AND DUTIES

The functions and duties of the Reference Laboratory are described in Article 32 of the EC Regulation No 882/2004.

Contents:

A. General tasks

B. Development and validation of analytical methods

C. Quality assurance and quality control including the organisation and implementation of proficiency tests

D. Technical and scientific support to NRLs/ EU official labs and third country labs

A. General Tasks

A.1 CRL meetings for coordination, planning and evaluation of activities

Tasks: Missions will be carried out to participate at inter-CRL-meetings; aiming at planning, coordinating, evaluating or conducting CRL activities such as work programs, proficiency tests (PTs), method validations, internet portal design etc. Date and place of these meetings will be decided later. Meetings in presence of the CRL- and PT-advisory group will be organized by the CRL for fruits and vegetables (CRL-FV).

A.2 Technical and scientific support to the Commission and other CRL-related communication with the Commission

Tasks: The CRL-SRM (having a lot of experience in designing targeted, information-based sample testing schemes) could decisively contribute to the Commission's efforts to draft a meaningful coordinated monitoring plan. Other scientific opinions will be drafted by the CRL upon request by the Commission. Missions to meetings in Brussels or elsewhere will be carried out if requested by the Commission.

A.3 Compilation of financial and technical reports

Tasks: The annual technical and financial reports for 2008 will be drafted and submitted to the Commission report by the end of March 2009. Reports of other relevant activities will be drafted as required.

A.4 Preparation of work program and provisional budget for following year

Tasks: The work program for the year 2010 will be drafted and submitted to the Commission by the end of August 2009

A.5 Co-operation with international organizations as agreed with the Commission

Tasks: One mission for one person for participation in the Codex Committee meeting on Pesticide Residues in Beijing, China.
Other missions will be carried out as agreed with the Commission

A.6 CRL-Web-Service (Horizontal Task)

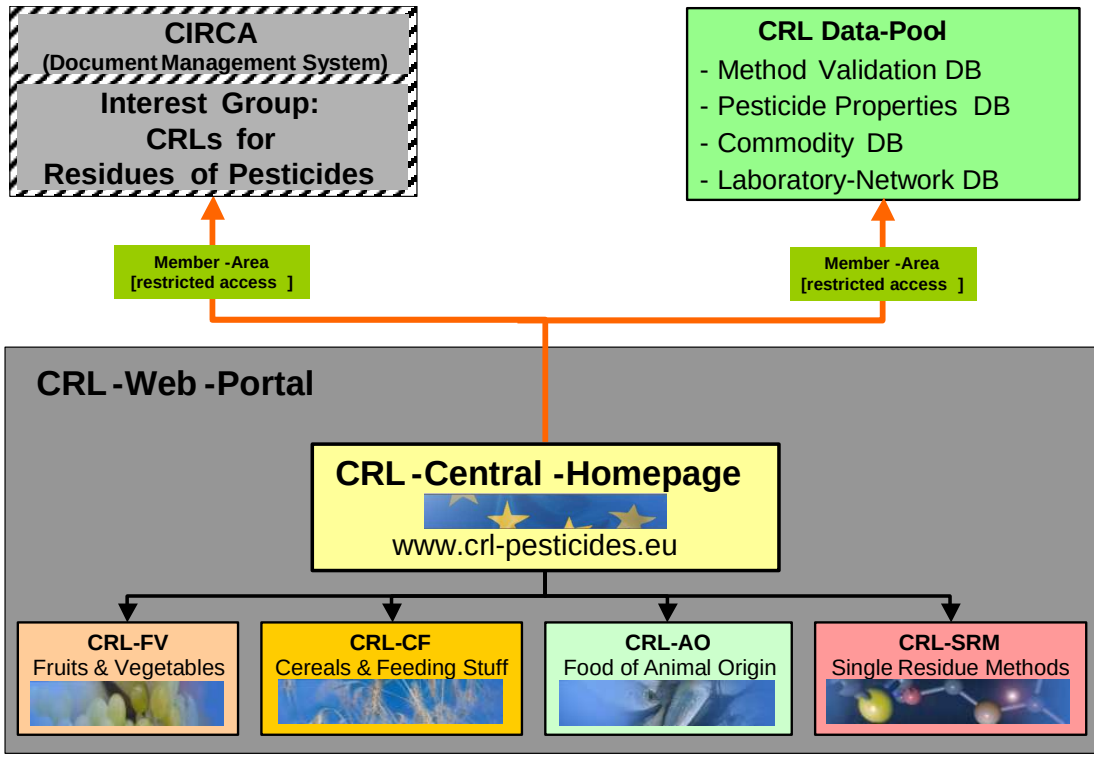
Background:
Among the duties of the CRLs is the creation of a laboratory Network and the coordination of the information flow within it. With this in mind the CRL-SRM has developed an internet-based platform (**CRL-Web-Service**) to facilitate the collection and timely dissemination of information, increase transparency and strengthen the Network between CRLs, NRLs and official laboratories.

The **CRL-Web-Service** mainly consists of the following elements:

1) a password protected **Document Management and Communication Module** based on the **CIRCA** system, which should be directed only to the network members;
2) a **CRL-Web-Portal** containing, among others, basic introductory information about the CRLs, news and announcements as well as links to the **individual CRL-websites**; and
3) a gradually expandable "**CRL Data-Pool**" containing various databases with information of practical use for pesticide residue analysts.

In order to assess the needs and expectations of the various laboratories as regards the information to be included in the CRL-Web-Service, a survey has been performed (**CRL-Survey**) the results of which have been taken into consideration in the construction of the CRL-Web-Service.

The Principle Structure of the CRL-Web-Service is shown in the figure below:



Tasks: see below

A.6.1 **CRL-Web-Portal, upgrading and maintenance**

The Internet Portal of the four pesticide CRLs (www.crl-pesticides.eu) has been in operation since 2007. It aims to facilitate dissipation of information from CRL to NRLs and official laboratories in a transparent way. Several improvements and extensions have been introduced in 2008.

Task: In 2009 the portal and the individual web-sites of the CRLs will be further expanded and gradually filled with valuable information. Still missing features will be gradually programmed according to the needs of the CRLs and the Network. The strategy to be followed should be discussed and aligned at the inter-CRL-meetings in close consultation with the COM.

A.6.2 **CRL Data-Pool**

A "**CRL Data-Pool**" entailing numerous databases with information of practical interest to the laboratories within the Network has been installed and expanded within the frame of the previous work programs (www.crl-pesticides-datapool.eu). This data-pool will be gradually expanded. The Table 1 gives an overview of the databases

Table 1: Overview of the CRL-Datapool: (status August 2008)

Database/Tool	Drafting of a plan	Programming of base structure	Structural improvements	Collection of data
A.6.2.1 **Method Validation DB**	Done	Done	Ongoing	Ongoing
A.6.2.2 **Methods DB**	2009	2009	2010-	2009-
A.6.2.3 **Pesticides DB**	Done	Done	Ongoing	Ongoing
A.6.6.3.1 **Stability of Standards DB**	2009	2010	2011-	2009-
A. 6.6.3.2 **Check your Scope Tool**	2009	2009	2010	-
A.6.2.4 **Commodities DB**	Done	In progress 2008	2009-	Ongoing
A.6.2.5 **Laboratory- Network DB**	Done	In progress 2008	2009-	Ongoing
A.7.1 **CRL-Survey Data Collection Tool**	2009	2009	2010-	2009/2010
A.6.2.5 **PT-Archive DB**	2009	2009	2010-	2009-

Tasks: see sub-topics below

A.6.2.1 **Method Validation DB, upgrading and maintenance**

Background: With method validation being compulsory for accreditation purposes, numerous validation experiments are being performed by various laboratories to evaluate analytical procedures as to whether they can meet the specified criteria. The **"CRL-Method Validation Database"** has been developed to allow a systematic collection of this great amount of data produced within the frame of intra- and inter-laboratory validation experiments. Online search tools allowing customized filtering and sorting of the data give laboratories the possibility to better assess the suitability of analytical methods for the analysis of various pesticide-commodity combinations. The potential of this website has already been recognized by Codex that has prompted the member countries to contribute to the database. Two recently published CEN standards refer to the method validation database of the CRL for updated information concerning validation data.

Task: In 2009 the database and its data retrieval tools will be further upgraded to accommodate specific user needs. Furthermore, data should be collected from NRLs and other laboratories and included into the database to expand the volume of data.

A.6.2.2 **Methods DB**

Background: With the creation of the method validation database (6.2.1) the laboratories were provided with the ability to store the results of their method validation experiments in a database. Important for the labs is furthermore the availability of data concerning the methodology of single and multiresidue procedures. Such data are intended to be stored in the "**Methods Database"** that should also provide reference to the source of information as well as links to online documents (e.g. the list of methods collected by the FAO/IAEA) and where applicable be interlinked with the method validation database.

Task: In 2009 the database will be designed and programmed in its base structure

A.6.2.3 **Pesticide DB, upgrading and maintenance**

Background: Pesticide residue analysts have to deal with a vast number of different pesticides and metabolites. With each pesticide behaving differently it is difficult for the analysts to maintain an overview of the situation. A differentiated and detailed knowledge of the properties of the different pesticides is necessary for understanding and predicting their behavior during analysis and thus essential when it comes to making the right decisions in method development, method validation and routine analysis. Several sources of information about the properties of pesticides already exist in literature as well as the internet, however their practical usefulness for pesticide residue analysts is limited. A main problem is that existing information is dispersed among countless sources. This not only makes the information extremely difficult to systematically retrieve, but it also does not support the formation of a global overview, which is essential for strategic planning.

The **"Pesticides Database"** aims at providing pesticide residue analysts with valuable pesticide-related information within a single platform in order to help them save time and improve the design of efficient analytical strategies.

In addition to the information collected from various sources the database will also contain useful experimental information generated by applying appropriate tests to systematically study the behavior of pesticides during the various critical stages of analysis such as sample comminution, extraction/partitioning, cleanup, storage of extracts and standards, chromatography and detection.

The data collected should allow to predict the analytical behavior of pesticides during analysis and to classify pesticides into categories (profiling), thus allowing the selection of representative pesticides based on scientifically sound evaluations. The selection of representative pesticides is important when it comes to simplifying validation procedures. The data generated should furthermore help to pinpoint the potential critical points in the analysis of pesticides, facilitate targeted method development and finally allow the classification of pesticides as multiresidue or single residue compounds.

Task: In 2009 the focus will be in improving the existing "Pesticide Properties Database" and in the collection of data both from various sources as well as from experiments performed by the CRL-SRM. The priority should lay on new pesticides as well as on pesticides with high analytical relevance (e.g. because of frequent usage in agriculture, high toxicity or inclusion in community monitoring programs).
The laboratory tests should be such to enable the identification of potential sources responsible for losses of the individual pesticides such as unfavorable partitioning and adsorption phenomena, as well as the exposure to certain conditions (e.g. extreme pH-values, temperature, light, air, enzymes etc). Information necessary for the chromatographic analysis and detection of pesticides such as mass spectra, chromatographic behavior information, and detection sensitivities achieved with various commonly used instruments will also be generated and collected. Pesticide recovery tests using common multiresidue procedures are also part of this scheme.

A.6.2.3.1 **Pesticide Stability DB, design**

A major source of errors in pesticide residue analysis is the degradation of standards in stock solutions, working solutions (e.g. mixtures), as well as in extracts. Quality Control protocols always require from laboratories to take the necessary measures in order to make sure that this source of errors remains insignificant. As a result many laboratories continuously check the stability of their standards. However, due to the high costs and lots of labor involved many laboratories are not in the position to do this control as required by the AQC-protocols. A common database, where information about the stability of pesticides can be stored is thus of high value and would help to exploit the existing synergy potential in this area.

Task: In 2009 the structure of database will be designed in order to be programmed in 2010

A.6.2.3.2 "**Check Your Scope" - Tool for the optimization of the pesticide scope targeted by laboratories**

Background: Regulation 396/2005 states that Member States shall establish multi-annual national control programmes for pesticide residues based on risk and they shall update them every year. Risk-based analytical strategies are not only requested by regulation but are also indicated by common sense as they contribute to a more efficient control. Within the aim of optimizing and improving the scope of the EU-coordinated control program the CRL-SRM has developed a pesticides ranking list based on a points system which takes into account various aspects indicating the relevance of pesticides such as toxicology, residue findings in food samples and pesticide use in agriculture.
By comparing their own pesticide scope with this ranking list laboratories will be able to detect gaps and gain the ability to thoughtfully expand and adjust their analyte scope. In order to encourage and facilitate this venture, an online tool will be programmed where the laboratories can indicate their current scope of pesticides in order to receive back a list with pesticides of high relevance that they do not cover. Appropriate filters regarding analytical equipment

available should allow the refinement of queries. At a future stage it is intended to generate customized ranking lists based on criteria/filters selected by the users (e.g. commodity type and sample origin).

Task: In 2009 a base structure of this tool will be programmed and made available on-line

A.6.2.4 **Commodity DB, upgrading and maintenance**

Background: Pesticide residue analysts have to deal with a vast number of different commodities. With each commodity having a different influence on analysis it is difficult to maintain an overview of the situation. A differentiated and detailed knowledge of the properties of the different commodities is paramount for the understanding of their behavior during analysis and helps the analyst to make the right decisions in method development, method validation and routine analysis. Several sources of information about the properties and the composition of commodities already exist in literature as well as the internet, however their practical use for pesticide residue analysts is limited. A main problem is that the information provided is dispersed among countless sources. This not only makes the information extremely difficult to systematically retrieve, but it also does not support the formation of a global overview, which is very valuable in strategic decision-making.
The **Commodity Database** that is currently being constructed should allow a systematic collection of commodity-related information that is useful for pesticide residue analysts. In addition to the information collected from various sources the database should also contain useful information generated by the CRL-SRM by applying a number of simple experiments designed to elucidate the behavior of the various commodities and their components during the various stages of pesticide residue analysis and their influence on analysis. In the future, these experiments may entail the measurement of the matrix load in the extracts before and after cleanup, the influence of matrix on pesticide degradation, the responsiveness of matrix components to various common cleanup approaches, and the study of interferences in measurement including matrix effects.

The data collected should allow to predict the potential influence of commodities on the analysis of pesticides and furthermore give the possibility to classify the commodities into categories (profiling), thus allowing the selection of representative commodities based on a scientifically sound evaluation. The selection of representative commodities is important when it comes to rationalize validation procedures.

Having all (the collected and generated) information in a single platform will help residue analysts to get a better overview of the various commodity types and help them in solving analytical problems. The base structure of the "**Commodity Database**" is being constructed within 2008.
In combination with the Pesticide DB, this database will form a highly valuable tool for pesticide residue analysts providing them with a convenient and efficient access to information needed for proper decision-making.

Task: In 2009 the database will be improved and fed with information gathered from various sources as well as with experimentally generated data.

A.6.2.5 **Laboratory-Network-DB, upgrading and maintenance**

Background: A **"Laboratory-Network-Database"**, with information about all laboratories within the CRL-NRL-Official Laboratories network is currently under construction. The information stored may entail lab-specific information such as address, lab-functions/fields of work and corresponding contact persons, instrumentation available, interest for collaborations etc. The laboratories will have the opportunity to submit their data online using a template profile-form. The database will allow customized online searches to quickly select/filter specific laboratories having common profiles (e.g. NRLs or official laboratories dealing with the same commodity group etc.).

Task: In 2009 the database will be considerably upgraded and fed with laboratory data

A.6.2.6 **PT-Archive Database, design and programming of base structure**

Background: Among the duties of the CRLs is to improve the performance of the official laboratories within the network (in particular the NRLs). Among the tools used to evaluate the performance of the laboratories is the conduction of proficiency tests. Currently 3-5 proficiency tests are performed annually by the CRLs with lot's of data being generated every year. The evaluation of the laboratory performance over the years is difficult not only because of this great amount of data incurred but also because of the stipulated coding policy. The creation of a database for the systematic collection of all PT-data will improve the overview and help to evaluate the overall performance of laboratories. With the help of appropriate filters and sorting options the database should allow customized PT-, laboratory- or pesticide-specific searches on-line.

Task: In 2009 the database will be designed in collaboration with the CRL for Fruits and Vegetables and its base structure will be programmed. Data from the previous proficiency tests run by the CRLs will be collected.

B. Development and Validation of Analytical Methods

B.1 Interlaboratory Validation of a method for the simultaneous analysis of various polar pesticides

Background: Multiresidue methods aim to cover pesticides of a broad polarity scope. However, there are some limitations especially towards the polar end of the scope, because polar matrix components, such as sugars and proteins, tend to negatively affect chromatography and detection. Current multiresidue procedures are thus designed to remove those interfering components during partitioning and cleanup. This however, also inevitably results in a loss of some very polar but still important pesticides. Not being amenable to multiresidue procedures, such pesticides have thus traditionally been a weak point in routine pesticide residue surveillance.
A method for the simultaneous analysis of the highly polar pesticides ethephon, glyphosate, glufosinate, maleic hydrazide and fosetyl aluminium involving a common extraction followed by different LC-MS/MS runs is currently being finalized.

Tasks:
In 2009 the finalized method will be distributed to other laboratories in order to perform an inter-laboratory test in 2009. Further method development will be performed to expand the scope of the method by some additional highly polar pesticides and metabolites (e.g. paraquat, diquat, amitrole).

B.2 Study of pesticides requiring modified multi-residue methods

Background: Several pesticides and legally relevant metabolites are known to pose problems in analysis and are thus considered as “difficult” or non-amenable to multiresidue methods. In many cases analysis is possible following certain modifications of classical multiresidue methods. Such modifications may entail pH-adjustment, temperature control, special measurement conditions etc.

Tasks:
Studies will be performed to identify, characterize and group these types of pesticides. Modifications of the multiresidue methods will be introduced. Priority will be given to pesticides and metabolites of high relevance in agriculture or that are included in coordinated control plans of the EU. The results will be communicated to the laboratories within the network

B.3 **Examination of existing analytical procedures for dithiocarbamates in order to evaluate their practical usefulness for routine pesticide residue testing in accordance with regulatory requirements**

Background
Dithiocarbamates (DTCs) are among the pesticides most widely used in agriculture. The extreme instability of the polymeric dithiocarbamates makes their direct analysis virtually impossible. MRLs are thus traditionally referring to the common carbon disulfide moiety. This analysis involves a cleavage step followed by the analysis of the released CS_2. This has been traditionally performed using a photometer, following a derivatization of the CS_2. The gas chromatographic determination of the CS_2 following its partitioning into a non-polar solvent is an increasingly used approach. The common moiety approach does, however, not allow a differentiation of the DTCs. This may be important, however, due to differences in the toxicology and legal requirements. A recent EU-Regulation *(Commission Directive 2007/57)* requires the application of methods for the differentiated analysis of propineb, ziram and thiram on a case by case basis when specific quantification is required. Alternative analytical procedures for dithiocarbamates have been developed allowing the differentiated determination of the most important groups of the DTCs, i.e. the propylene-bis-dithiocarbamates (propineb) and the ethylene-bis-dithiocarbamates (maneb, mancozeb, nabam) as well as N,N-dimethyl-dithiocarbamates (ziram, ferbam) via their corresponding monomers.

Tasks:
The most prominent existing approaches for the analysis of dithiocarbamates will be examined and their practical usefulness will be evaluated in the light of the existing regulations and considering technical and practical feasibility aspects. A team of expert on this topic will be consulted and the results of this initiative will be distributed among the network labs.

B.4 **Illegal or non-authorized pesticides (pesticide misuse)**

In collaboration with the CRL for Fruit and Vegetables the CRL-SRM will work on the collection and dissemination of information about illegally used pesticides as well as the development of methods for the analysis of illegal or non-authorized pesticides.

Tasks:
1) Method development and validation:
Experiments will be performed to determine whether the pesticides concerned are amenable to multiresidue methods, modified multiresidue methods or single residue methods. In the latter two cases suitable methods will be developed and validated. The generated data will be collected and stored in the method validation database.
2) Collection of information regarding misuse-cases
Pesticide-misuse-cases will be localized by comparison of available residue data with data about the authorized uses of pesticides in Europe as well as in specific countries as far as available. Information regarding misuse-cases will be collected and distributed to the labs within the network, where indicated.

C. Quality Assurance and Quality Control

C.1 Performance of an Interlaboratory Proficiency Test for "single residue analytes" (EUPT-C3/SRM4) together with the CRL for Cereals

A proficiency test covering multi residue and single residue methods will be performed in collaboration with the CRL for Cereals and Feeding Stuff.
Participants will be able to receive documents and instructions through the specific section of the CRL website.
Each participant will receive a detailed electronic interim report, which will allow the laboratories to interpret their results and also to identify possible sources of procedural errors.
A final report summarizing the scope, results, data treatment and additional information of the methods used will be printed and made available to every participant laboratory.

D. Technical and Scientific Support to NRLs/EU official labs and Third Country laboratories

D.1 Dissemination of Information and Networking

The dissemination of information to NRLs, EU-Official laboratories and third country laboratories is achieved via personal communication and presentations in conferences and workshops (see D.2 and D.3) as well as with the help of the CRL-Web-Portal (A. 6.2.1) and the CRL-Datapool (A. 6.2.2).
The networking activities include personal contacts including e-mail and telephone call exchange, the conduction of training workshops but also the creation of the CRL-Network-Database (A. 6.2.5).

D.2 Joint Training-Workshop for NRLs in Copenhagen (HORIZONTAL)

A training-workshop will be performed in collaboration with the three other CRLs (for Fruit and Vegetables (FV), Cereals and Feeding Stuff (CF), and Animal Origin (AO)) and all corresponding NRLs will be invited to participate.
The training-workshop will cover technical aspects including hands-on training as well as lectures and discussions on analytical as well as QC aspects. Special needs and problems of the laboratories selected to participate will be considered in the design of the training program.

D.3 **Seminars at one selected laboratory**

An NRL-visit will be conducted to one laboratory (selected in agreement with the COM) where the EUPTs results have been problematic over the last four years. Before the seminar a detailed study of the EUPT results obtained during the last four years will be carried out.
During the visit the possible reasons for the bad performance will be discussed and advices will be given to the laboratory on how to improve its performance. The objective of these seminars will be to evaluate “in situ” the technical capabilities of the selected laboratory as well as to promote future improvement. The CRL-SRM will send 2 representatives (one representative for theoretical and one for complementary technical assistance) to the seminar.

D.4 **Analysis of official samples, counter analysis**

Analyses of samples will be conducted following consultation with the Commission. The CRL will ask the commission for approval of additional eligible budget, if required.

D. 5 **Second Comprehensive CRL-Survey**

Background: At the end of 2006 and beginning of 2007 a first comprehensive survey of the NRLs and Official laboratories was conducted. The main aims were to assess the Status-Quo of the labs within the network (abilities and disabilities); to assess the needs and requirements of the labs; to gain the ability to plan and justify the CRL-activities based on sound data; and to give the possibility to the labs to compare themselves with other labs (see where they stand and get ideas on what could be done). Furthermore the survey had the aim to initiate a thinking process among the analysts within the network and to increase the awareness about certain aspects. With this follow-up Survey the CRLs will provide the necessary information to assess the development of the laboratories within the network.

Task: In 2009 the Survey questionnaire should be drafted and an online survey tool should be programmed so that the actual Survey can be launched either at the end of 2009 or the beginning of 2010. The Survey-Report will be drafted in 2010.