ANSES-Fougeres - EUROPEAN UNION REFERENCE LABORATORY for VMP Residues of Groups A6, B1, B2f, B3e

Funded by:

WORK PROGRAMME of the EU-RL for ANTIMICROBIALS AND DYES GROUP SUBSTANCES: B1, A6, B2f, B3e

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SUMMARY

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INTRODUCTION

The functions and duties of the Reference Laboratory are described in Article 94 of Regulation (EU) No 2017/625 of the European Parliament and of the Council of 15 March 2017 (Official Journal of the European Union L 95, 07.04.2017, pp. 1-142).

Regulation (EU) 625/2017 Art 94(2):
European Union reference laboratories designated in accordance with Article 93(1) shall be responsible for the following tasks insofar as they are included in the reference laboratories' annual or multiannual work programmes that have been established in conformity with the objectives and priorities of the relevant work programmes adopted by the Commission in accordance with Article 36 of Regulation (EU) No 652/2014:
(taking into account Art 147 of (EU) 625/2017)

1 TO ENSURE AVAILABILITY AND USE OF HIGH QUALITY METHODS AND TO ENSURE HIGH QUALITY PERFORMANCE BY NRLs.

Please, provided activities related to Regulation (EU) 2017/625:

- *Art. 94.2.a* ***Providing national reference laboratories with details and guidance on the methods of laboratory analysis, testing or diagnosis, including reference methods.***
  List of EU-RL analytical methods and their SOPs made available through the EU-RL website
- *Art. 94.2.b* ***Providing reference materials to national reference laboratories***
  Production of incurred testing materials, animal experiments, homogeneity testing, stability testing, storage, post-PT testing and shipment during PT and post-PT
- *Art. 94.2.c* ***Coordinating the application by the national reference laboratories and, if necessary, by other official laboratories of the methods referred to in point (a), in particular, by organising regular inter-laboratory comparative testing or proficiency tests and by ensuring appropriate follow-up of such comparative testing or proficiency tests in accordance, where available, with internationally accepted protocols, and informing the Commission and the Member States of the results and follow-up to the inter-laboratory comparative testing or proficiency tests.***
  Providing Proficiency Testing Studies and follow-up of these PTS
- *Art. 94.2.l* ***Where relevant for their area of competence, cooperate among themselves and with the Commission, as appropriate, to develop methods of analysis, testing or diagnosis of high standards.***
  Research and Development on future or updated analytical methods for VMPRs

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1.1. Provide NRLs with details and guidance on the methods of laboratory analysis, testing or diagnosis, including reference methods. (a)

Sub-activity 1.1.1. - To provide an updated survey of available EU-NRL network analytical methods

Over the year 2019: Sub-activity 1.1.1.a
Over the year 2020: Sub-activity 1.1.1.b

Objectives: To provide an updated survey of available EU-NRL network analytical methods
Description: This survey allows EU-RL and the EU-NRLs network to share a set of information on analytical methods (those for screening and those for confirmation) in use across the EU network and to provide their status in terms of level of validation (A *in-prep* to E *full-valid* levels) and of accreditation (*not accred or under fixed or flexible scopes*)
Expected Output: Report sub-divided in screening methods / confirmatory methods / analytical experts for each method in the NRLs. To be made available to NRLs and DG-SANTE posted onto the EU-RL website *(http://eurl-fougeres-veterinaryresidues.anses.fr)*
Duration: This activity is due to be scheduled over a period of five years. Last update was released in 2013. Next update will be prepared to be finalized and released over the period 2019-2020.
EU-RL staff considered for the task: Scientist + Secretary

Sub-activity 1.1.2. - Follow-up and update of the EU-RL Website

Over the year 2019: Sub-activity 1.1.2.a
Over the year 2020: Sub-activity 1.1.2.b

Objectives: Follow-up and update of the EU-RL Website
Description: Follow-up and improvement of the EU-RL Website including specific management of the new transfer into the global ANSES-EU-RLs mini-website platform built under the ANSES-format and fully connected to the ANSES-DG public internet system: www.anses.fr - http://eurl-fougeres-veterinaryresidues.anses.fr
Expected Output: Update of webpages and Postage of Documentation for COMM, for NRLs, for Third Country Official Laboratories (**Output 1**) and Survey of Documentation provided through the years 2019-2020 (**Output 2**)
Duration: Over the 24 months
EU-RL staff considered for the task: Scientists + Secretary

Sub-activity 1.1.3. – Publications on the public EU-RL website

Over the year 2019: Sub-activity 1.1.3.a
Over the year 2020: Sub-activity 1.1.3.b

Objectives: Follow-up and update of the EU-RL Website in regard to analytical method publication
Description: As a follow-up of a recent request from the Commission DG-SANTE, some publication of analytical methods will be posted on the public part of our EU-RL website: http://eurl-fougeres-veterinaryresidues.anses.fr
Expected Output: Provision of information on analytical methods; publication of the list of EU-RL available analytical methods via the EU-RL website
Duration: Over the 24 months
EU-RL staff considered for the task: Scientists + Secretary

1.2. Follow up on requests from NRLs for providing analytical standards. (b)

Sub-activity 1.2.1. - Procurement of reference analytical standards to the network of EU-NRLs

Over the year 2019: Sub-activity 1.2.1.a
Over the year 2020: Sub-activity 1.2.1.b

Objectives: Procurement of reference analytical standards to the network of EU-MS-NRLs
Description: All the NRL requests considering standard VMP substances will be investigated but satisfied only according to the commercial availability or non-availability of the substances.
Expected Output: EU-RL list of reference analytical VMP standards and their suppliers/manufacturers will be made available through the EU-RL website (http://eurl-fougeres-veterinaryresidues.anses.fr) (**Output 1**) and for shipment to the EU-MS NRLs upon their specific request according to our EU-RL website procedure but only for the non-commercially available standards (**Output 2**)
Duration: Over the 24 months
EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.2.2. - Procurement of reference tissue sample materials to the network of EU-NRLs

Over the year 2019: Sub-activity 1.2.2.a
Over the year 2020: Sub-activity 1.2.2.b

Objectives: Procurement of reference sample materials to the network of EU-MS-NRLs
Description: The PT testing materials under convenient and reliable EU-RL storage and subjected to periodic control at EU-RL level will be made available to the NRL-network
Expected Output: EU-RL PT testing materials will be made available through the EU-RL website (http://eurl-fougeres-veterinaryresidues.anses.fr) (**Output 1**) and for shipment to the EU-MS NRLs upon their specific request through our EU-RL website procedure (**Output 2**)
Duration: Over the 24 months
EU-RL staff considered for the task: Scientists + Technicians + Secretary

1.3 Organisation of proficiency tests and follow up on the results (c)

1.3.1 Organisation of PTs + 1.3.2 Follow up on and communication of the PT results

EILA de screening pour toutes les substances antimicrobiennes autorisées (B1) ou non-autorisées (A6-B2f) dans une matrice sélectionnée spécifiquement chaque année en essayant de passer en revue tous les produits d'intérêt sur 7 ans ou avec un turn-over de 3 ans avec 2 matrices par an :
Viande rouge / Volaille/ Lait / Miel / Œuf / Poisson / Crevettes
Prévoir ensuite un second EILA en fin d'année pour la confirmation sans re-préparation des matériaux ESEA

Sub-activity 1.3.1.a. / 1.3.2.a. - Provision of Proficiency or Collaborative Testings for MULTI-SCREENING and CONFIRMATION of Authorized and/or Prohibited substances from Group A6, B1, B2f and/or B3e (1 PT round each year in a different species/matrix) for the year 2019 Sub-activity 1.3.1.a. / 1.3.2.a.

Objectives: Providing to the NRL network under accreditation ISO 17043 one PT including testing for residues of several authorized and/or prohibited antimicrobial substances including their possible metabolites in specific species/products of concern chosen either for their domestic monitoring or for their import control.
Description: As a follow-up of new PT organization launched during the program 2016-2017, the substances of choice might be a combination of non-authorized substances chosen among the groups A6 (antimicrobials), B1 (MRL substances non-authorized in certain species/products), B2f (quinoxalines) and B3e (dyes). The matrix of choice for the PT materials will be selected from at least one of the different possible species/products (red meat, poultry meat, milk, eggs, honey, and aquaculture species) not excluding in certain circumstances on-farm control matrices (urine or drinking water) and with options proposed in relation to the appropriate issues of preceding years. The EU-NRLs method(s) to be controlled will be all considered collectively but the possible 2-step strategy of analysis (screening + confirmation) will primarily be considered for evaluation during this PT round.

Expected Output: Will be delivered by the EU-RL to the participants and to DG-SANTE desk officer within the 6 months following the end of the PT round of analyses by EU-NRLs, a final report on the results obtained by the participating laboratories (**Output 1**). The report will also be posted in due time on our EU-RL website to the attention of the DG-SANTE exclusively (**Output 2**). A specific follow-up by the EU-RL of corrective actions after non-compliant results will also be undertaken in line with Commission requirements and specific information will be attached to the final report posted to the attention of the DG-SANTE exclusively (**Output 3**) and sent to the Competent Authority (**Output 4**).
Duration: 8 to 9 months for the organisation and delivery of the PT round and release of final report + 2 to 4 more months for the follow-up of possible corrective actions at some NRLs after the final report delivery
EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.3.1.b. / 1.3.2.b. - Provision of Proficiency or Collaborative Testings for MULTI-SCREENING and CONFIRMATION of Authorized and/or Prohibited substances from Group A6, B1, B2f and/or B3e (1 PT round each year in a different species/matrix) for the year 2020 Sub-activity 1.3.1.b. / 1.3.2.b.

Objectives: Providing to the NRL network under accreditation ISO 17043 one PT including testing for residues of several authorized and/or prohibited antimicrobial substances including their possible metabolites in specific species/products of concern chosen either for their domestic monitoring or for their import control.
Description: As a follow-up of new PT organization launched during the program 2016-2017, the substances of choice might be a combination of non-authorized substances chosen among the groups A6 (antimicrobials), B1 (MRL substances non-authorized in certain species/products), B2f (quinoxalines) and B3e (dyes). The matrix of choice for the PT materials might be selected from at least one of the different possible species/products (red meat, poultry meat, milk, eggs, honey, and aquaculture species) not excluding in certain circumstances on-farm control matrices (urine or drinking water) and with options proposed in relation to the appropriate issues of preceding years. The EU-NRLs method(s) to be controlled will be all considered collectively but the possible 2-step strategy of analysis (screening + confirmation) will primarily be considered for evaluation during this PT round.
Expected Output: Will be delivered by EU-RL to the participants and to DG-SANTE desk officer within the 6 months following the end of the PT round of analyses by EU-NRLs, a final report on the results obtained by the participating laboratories (**Output 1**). The report will also be posted in due time on our EU-RL website to the attention of the DG-SANTE exclusively (**Output 2**). A specific follow-up by the EU-RL of corrective actions after non-compliant results will also be undertaken in line with Commission requirements and specific information will be attached to the final report posted to the attention of the DG-SANTE exclusively (**Output 3**) and sent to the Competent Authority (**Output 4**).
Duration: 8 to 9 months for the organisation and delivery of the PT round and release of final report + 2 to 4 more months for the follow-up of possible corrective actions at some NRLs after the final report delivery
EU-RL staff considered for the task: Scientists + Technicians + Secretary

1.3.3 Production of incurred materials for PT testing

Sub-activity 1.3.3. - Production of incurred sample materials for the Proficiency or collaborative Testing issues

Sub-activity 1.3.3.a: over the year 2019 for PT 1.3.1.a/1.3.2.a or for the collaborative study combined with sub-activity 1.5.3

Sub-activity 1.3.3.b: over the year 2020 for PT 1.3.1.b/1.3.2.b or for the collaborative study combined with sub-activity 1.5.3

Objectives: Production of incurred sample materials for the Proficiency Testing task and relevant for authorized and /or non-authorized substances from Group A6, and/or B1, and/or B2f and/or B3e

Description: According to the sub-activity 1.3 here-above for testing relevant authorized and/or non-authorized substances from Groups B1 (*MRL-antimicrobials*), A6 *(CAP, NIFU)* and/or B2f *(QUINOXALINES)* and/or B3e (*FISH-FARMING DYES*), the requested reference sample materials (as far as possible being prepared naturally incurred materials) will be produced at the experimental farms of Anses laboratories and prepared in accordance with the standards of PT testing material preparation (homogeneity and stability studies) and under our recognized quality assurance scheme (accreditation N° 1 – 2294 - www.cofrac.fr)
Expected Output: Production of at least 3 new Testing Materials per PT round for year 2019 (**Output 1**) and for year 2020 (**Output 2**)
Duration: Over 3 months per year
EU-RL staff considered for the task: Scientists + Technicians + Secretary

1.3.4 Preparation for transfer of incurred samples

Sub-activity 1.3.4 - Transfer of the produced reference materials to convenient storage, stability control and use for the EU-MS-NRLs network.

Over the year 2019: Sub-activity 1.3.4.a
Over the year 2020: Sub-activity 1.3.4.b

Objectives: Maintenance and testing of incurred sample materials prepared for previous Proficiency Testing task and relevant for authorised and /or non-authorised substances from Group A6, and/or B1, and/or B2f and/or B3e
Description: According to the sub-activity 1.3 here-above for testing relevant authorized and/or non-authorized substances from Groups B1 (*MRL-antimicrobials*), A6 *(CAP, NIFU non-authorised antimicrobials)* and/or B2f *(QUINOXALINES)* and/or B3e (*FISH-FARMING DYES*), the requested reference sample materials (as far as possible being prepared naturally incurred materials) will be stored, maintain and retested prior to transfer to NRL after their specific request and under our recognized quality assurance scheme.
Expected Output: Evaluation and transfer of at least 4 Testing Materials in four different destinations each year
Duration: Over the 24 months of the program
EU-RL staff considered for the task: Scientists + Technicians + Secretary

1.4 Cooperation collaboration and meetings with other EURLs and scientific exchange (l)

Sub-activity 1.4.1. - Meeting of the cluster of EU-RLs, EU-RLs residues management *(at least 4 of 2 days per year meaning 4 meetings in 2019 as sub-activity 1.4.1.a and 4 meetings in 2020 as sub-activity 1.4.1.b)*

Objectives: Meeting with the Commission DG-SANTE and/or with the cluster of EU-RLs for VMPR
Description: Upon the request from or agreement with the Commission DG-SANTE
Expected Output: Up to 4 missions per year for one EU-RL delegate including the annual general meeting of the EU-RLs
Duration: Over 2 days per mission
EU-RL staff considered for the task: Scientists

Sub-activity 1.4.2. – Updating the Decision 2002/657 and the 2 additional guidelines attached to it to be carried out over 2019 (sub-activity 1.4.2.a) and 2020 (sub-activity 1.4.2.b)

Objectives: Drafting together with the Cluster of 4 EU-RLs and with the network of NRLs the Technical Guidelines for the validation of performance of VMPR analytical methods that will be updating/replacing those under the current Decision (EC) No 2002/657
Description: As requested from the Commission and from the EU-MS CA expert residue working group on residues of VMPs as of its 23 June 2015 meeting in Brussels, a new Regulation is foreseen to update/replace the Decision (EC) No 2002/657 including all technical guidance for validation of screening and confirmatory VMP residue analytical methods, i.e. Document SANCO/2004/2726 rev4 and CRL Guidelines of 10/1/2010 for validation of the VMPR screening methods. The first draft was prepared in 2018. In 2019 this will be discussed with the NRLs. A final version will be prepared in 2019 including the comments from MS and COM.
Subsequently – if needed – the preparation of practical guidance documents will be started on certain subjects such as: 1- for validation of screening methods; 2- for validation of confirmatory methods; 3- for extension of validated methods.
Expected Output: Revised version of Decision (EC) 2002/657 (Output 1) and Updated Technical Guidelines for Validation of VMPR Analytical Methods complementing the foreseen Regulation (Output 2). All documentation will be posted onto our EU-RL website to the attention of Commission (http://eurl-fougeres-veterinaryresidues.anses.fr) (Output 3).
Duration: Over the years 2019 and 2020
EU-RL staff considered for the task: Scientists

Sub-activity 1.4.3. – Building a common portal with the DG-SANTE for facilitated access to the websites for the "VMPR" EURLs to be carried out over 2019 (sub-activity 1.4.3.a) and 2020 (sub-activity 1.4.3.b)

Objectives: Follow-up of the organisation for a common Internet approach to disseminate VMPR information throughout the cluster of "EU-RLs" to the attention of the network of NRLs and further outside EU
Description: Discussions started during the year 2018 within the cluster of VMPR EU-RLs to check technical feasibility for implementing a better coverage of the links toward the EU-RL websites will be further carried out to finalize the project together with links to the COMMISSION DG-SANTE website
Expected Output: Building and maintenance/improvement of a website portal able to give enough visibility for the different EU-RL websites already in place (Output 1). Linkage between EU-RL websites of the VMPR cluster and the Portal possibly supported by the DG-SANTE website platform (Output 2).
Duration: Over the years 2019 and 2020
EU-RL staff considered for the task: Scientists

Sub-activity 1.4.4. – Harmonisation of PT performance criteria within the "VMPR" EURLs to be carried out over 2019 (sub-activity 1.4.4.a) and 2020 (sub-activity 1.4.4.b)

Objectives: Preparing a common protocol through the cluster of "EU-RLs" for assessing the PT performance of NRLs for VMP residue testing.
Description: Discussions started during the year 2018 within the cluster of VMPR EU-RLs to try implementing a harmonised approach on PT-Evaluation via an agreed PT-protocol taking into account the individual factors of the EURLs will be further carried out to finalize the project to be presented to the network of EU-MS NRLs.
Expected Output: Common PT performance criteria drafted in a protocol delivered to the network of NRLs (Output 1) and posted onto the EU-RL website (Output 2).
Duration: Over the years 2019 and 2020
EU-RL staff considered for the task: Scientists

Sub-activity 1.4.5. – Identification and Quantification of VMP residues down below the MRL at low ppb-level to be carried out over 2019 (sub-activity 1.4.5.a) and 2020 (sub-activity 1.4.5.b)

Objectives: Preparing a common protocol through the cluster of VMPR "EU-RLs" for extending the range of concentration to validate MRL analytical methods down below the MRL at low ppb-level.
Description: Quantitative results for compliant samples below the MRL will need to be submitted to EFSA in the future through the SSD2 in order to allow future risk exposure assessments. The update of the Decision 2002/657 will be part of the legal basis to implement these additional requirements from the COM. Furthermore validation studies of analytical methods for MRL substances should aim to be able to provide also results down to approximately 0.1 x MRL as this is the requirement that forms the current state of discussion with EFSA (provision of sub-MRL results). Anyhow requirements are not fixed and may change along with future revision of Decision 2002/657.
Expected Output: Update of the Decision 2002/657 (Output 1) and Postage of Technical documentation on the EURL website (Output 2).
Duration: Over the years 2019-2020
EU-RL staff considered for the task: Scientists

1.5 Development and validation of analytical methods (l)

PHYSICO-CHEMICAL METHODS

Sub-activity 1.5.1. - Development and Validation of Analytical Methods - Extending LC-HRMS screening analysis to all Group B1 antimicrobial residues and some other VMP groups in different species/products and validating according to new regulations (DEMAHR part 2)

Over the year 2019: Sub-activity 1.5.1.a
Over the year 2020: Sub-activity 1.5.1.b

Objectives: To demonstrate the adaptation and the validation of a full-scan High Resolution MS analytical method for delivery to field laboratories in a large scope of VMPRs and with high-throughput screening option.
Description: The context of the evolution of screening strategies put the new LC-HRMS analytical systems at the premier place of advanced technologies dedicated to VMP residue control in balance with the now well-known targeted LC-MS/MS instruments. Considering the broad network of NRLs and of field laboratories within the EU, the EU-RL considers of high interest to develop and propose a multi-VMP residue screening method including as many Group B1 antibiotic residues as possible and also including some other relevant classes of VMP residues (Benzimidazoles, Avermectins, Anticoccidials, NSAIDs, …) within a single Full Scan High Resolution Mass Spectrometric instrument. This project was started mid-2017 after the EU-RL acquisition of a Q-Exactive^{+} LC-HRMS equipment. During the 2018 programme, advances in the development of this LC-HRMS strategy for controlling VMPR in meat have been presented to the NRLs at the annual workshop of June 2018; and this first presentation was posted in July 2018 onto the EU-RL website to the attention of the network of NRLs. A validation in Meat of Bovine, Porcine and Poultry was carried out by the EU-RL in the 2nd part of 2018 with the transfer to the NRLs network forecast at the next annual workshop of 2019. This developing project will be now followed-up during the programme over the years 2019 and 2020 with first extending in meat to other VMPs having an MRL set in Reg 37/2010 (basic NSAIDs, new antimicrobials considering the cascade, …) and also to validate the method for relevant VMP substances in Milk. In future programmes, ie. 2021-2022 will also have to be considered possibly enlarging to further substances whenever there will be interest to include some of them in the screening for surveillance programme (in Meat as well as in Milk).
Expected Output: In 2019, after a formal validation of the developed method extended to milk and the meat method enlarged to other relevant substances (basic NSAIDs, new antimicrobials, …), an hands-on training dedicated to LC-HRMS strategy (Output 1) will be presented to the network of EU-NRLs during the next annual

workshop of 2020 together with the release of a Standard Operating Procedure (Output 2); also a report of validation according Decision (EC) No 2002/657 to be drafted (Output 3);
Presentations together with SOPs and summary of validation reports to be posted in due times over 2019 and 2020 on our EU-RL website to the attention of the network of NRLs (Output 4); communication to the international scientific community should be delivered in a symposium and/or through an article in an international peer-reviewed scientific journal in 2020 (Output 5).
Duration: Over 2019-2021
EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.5.2. - Development and Validation of Analytical Methods – Confirmation of beta-lactam residues in milk (BETA2LAC)

Over the year 2019: Sub-activity 1.5.2.a

Objectives: To finalize and to disseminate the method during a hands-on training of the 2019 workshop
Description: Beta-lactam antibiotics are the most important VMP products used in food-producing livestock animals and in milking cows-sheep and goats. Additionally some of them (3rd & 4th generation cephalosporins) are considered critically-important antibiotics in regard to the still-relevant antimicrobial resistance issue. Therefore, the EU-RL considers the quality of the confirmatory control of these residues in meat and in milk is still to be improved within the EU-MS NRLs network. As a follow-up of the 2017 development and validation of a LC-MS/MS confirmatory method able to include beta-lactam MRL substances in meat, it was intended to develop in 2018 a LC-MS/MS confirmatory method able to include beta-lactam MRL substances in milk, and to validate the performance of the method in milk in line with the standardised criteria according to the Decision (EC) no 2002/657.
Expected Output: To deliver a SOP in milk to be presented to the network of NRLs (Output 1); a report of validation according to Decision (EC) no 2002/657 will be drafted (Output 2); a presentation of the method will be given during the next annual workshop (Output 3); SOPs and validation reports for meat and later for milk to be posted in due times on our EU-RL website to the attention of the network of NRLs (Output 4); a communication to the International Scientific Community to be delivered in a symposium and/or through an international peer-reviewed scientific journal (Output 5).
Duration: 2017-2019
EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.5.3. - Development and Validation of Analytical Methods – An evaluation of the state-of-the-art in EU-MS NRLs analytical instrumentation and of their advanced analytical strategies for a Multi-Antimicrobial and other VMP Method using suitable LC-MSMS & LC-HRMS instruments

Over the year 2019: Sub-activity 1.5.3.a
Over the year 2020: Sub-activity 1.5.3.b

Objectives: 1 - To demonstrate the current state-of-art of the NRLs network for the use of LC-HRMS and LCMSMS instrumentations as screening tools for multiple VMPs. 2 – To deliver the NRLs network' data raised by a collaborative interlaboratory round for LC-HRMS and/or LCMSMS screening of VMPs in meat samples.
Description: Considering the advances in mass spectrometric high resolution technologies (i.e. time-of-flight and orbital trap instruments) and the current level of acquisition by EU-MS NRLs of such instruments over the 5 past years, it is now our collective concern to evaluate and to demonstrate the possible future of the analytical strategies to screen and to confirm as many as possible regulated VMP residues in food by means of this new innovative instrumentation. A preliminary study was implemented over the period 2017-2018 as a collaborative study with the aim to strictly assess the LC-HRMS instruments' capabilities to be used as reliable screening tools. Extracts spiked with various VMPs were prepared and blindly distributed to the 14 participants joining the collaborative study. The analyses focused on Full Scan MS schemes using if possible the currently 4 different

types of HRMS instruments (ToF, Orbitrap, Q-ToF, and Q-Orbitrap). No evaluation of the complete analysis including sample preparation had been undertaken in this previous study. Only detection capability of various instruments as regard to VMP residues was evaluated. Thanks to the results collected during this preliminary study, a second project will be implemented over the period 2019-2020 to further investigate the outcomes and benefits of these multi-screening methods whatever Low Resolution or High Resolution mass spectrometric detection. For this purpose a new collaborative study will be carried out enlarged to all NRLs network LC-LRMS and LC-HRMS systems provided they are used for a large screening of VMP substances. The participants will be authorized to use their own strategy of separative LC conditions. It is intended to produce enough data to assess parameters such as detection capabilities, false-positive rates and false-negative rates. The study will also provide details on the analytical performances of analyses and further contribute to EU recommendations on criteria dedicated to the evaluation of analytical performance of methods for control (screening / confirmation) by LRMS and HRMS systems.

Expected Output: The following items will be delivered to the network of NRLs the report of the state-of-the-art and comparative scope in LC-HRMS & LC-LRMS instrumentations in EU (Output 1); the report of the collaborative inter-laboratory study (Output 2); these reports will also be presented thoroughly during one of our EU-RL workshops (Output 3) and also posted onto our EU-RL website to the attention of the network of NRLs (Output 4). A scientific presentation will be delivered in at least one international scientific symposium (Output 5). A publication might be further submitted to a peer-reviewed international scientific journal (Output 6).

Duration: Over 2019-2021

EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.5.4. - Development and Validation of Analytical Methods - Enhancing the control for multi-dye residues in aquaculture products by targeted method with LC-MSMS and untargeted approach using LC-HRMS (METACOLOR)

Over the year 2019: Sub-activity 1.5.4.a
Over the year 2020: Sub-activity 1.5.4.b

Objectives: 1 - To release an updated and extended analytical method by LC-MS/MS and/or LC-HRMS for multi-dye residues in aquaculture. 2 – To deliver to the EU-NRLs network and to the scientific community new insights in the metabolomics approach applied to search for dye residue metabolic biomarkers in aquaculture products.

Description: After its ban in 2004 in the EU, the occurrence of malachite green and its leucobase in aquaculture products has been reduced and adequately monitored for several years now. This issue is also well documented in the literature. Recently, the interest in dye residue control was extended to several other dyes closely related to malachite green, *i.e.* crystal violet and brilliant green. Still possibly used as biocides in aquaculture products imported from other regions of the world, it is also of interest to develop a control strategy able to counteract any attempt of misuse for other chemical substances from the same triarylmethane family (group substitution) or from other related dye families (phenothiazines, xanthenes, phenylazoic dyes, etc...). A first project called "Multicolor" was carried out during our "2016-2017" program with the objectives to contribute in developing a multi-dye LC-MSMS method able to demonstrate the scope of possible future extension from our current 5-compound LC-MSMS method to cover up to 10-15+ dye compounds. The outputs of this first phase have been fully reported in the final activity report of our "2016-2017" program. Additionally, this project included in its second part, a metabolomics approach by LC-HRMS opened to the Malachite green and the Victoria Pure Blue bo respectively. It was evaluated for the first time for this class of compounds how to track possible endogenous and/or exogenous biomarker(s) of metabolic effects for, at least these two dyes and by means of an *in vitro* experiment in aquaculture products. As a follow-up of this first project, it is intended to start since 2018 and up to 2020 a second phase project named METACOLOR in order to investigate the presence of potential metabolites of the Victoria blue family of compounds by comparing and challenging them in *in-vitro* experiments (trout fish microsomes, …) and in *in-vivo* experiments (trout fish species, …) after a Victoria Pure Blue BO treatment of farmed fishes. The final part of the project will be to reviewing the analytical multi-dye LC-MS/MS method in terms of robustness and scope of relevant dye substances and treatment-tracer metabolites. It is also intended to possibly extend the method to different other aquaculture species of interest in terms of worldwide import control of farmed seafood (like salmon, tilapia, catfish, flat fish, sea bream, sea bass, eel, shrimp, and prawn, …).

Expected Output:
As a follow-up to the advances in the project along the years 2019 and 2020, a display of the metabolic study to track possible biomarkers of dye treatment in fish will be delivered to the network of EU-MS. Also an updated standard operating procedure for the confirmatory LC-MS/MS method of multi-dyes in aquaculture products including extension to new metabolites and/or new fish species and a report of validation of the performance of the method will be delivered and will be presented at our annual Workshops in 2019 (Output 1-advances) and in 2020 (Output 2-final). Then the SOP will be also posted on our EU-RL website to the attention of the network of NRLs (Output 3). A communication will be displayed on this issue to the attention of the scientific community during an international symposium dedicated to the veterinary drug residue analysis, namely Euroresidue IX (May 2020) or any other suitable international symposium in the 2019-2020 period (Output 4). Scientific publications will also be submitted to peer-reviewed international journals in relation to the different results of the project in the period 2020-2021 (Output 5).
Duration: Over 2018-2020
EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.5.5. - Development and Validation of Analytical Methods - Validation of new confirmatory LC-MS/MS monitoring of nitrofuran residues in tissues and including the nifursol metabolite (NITRO5)

Over the year 2019: Sub-activity 1.5.5.a

Objectives: 1 – Adaptation to new instrumentation of a LC-MS/MS method capable of monitoring 5 nitrofuran metabolites and including the nifursol DNSAH metabolite in meat tissues; 2 - To validate the performance of the method in meat at lower level than the current RPA of 1 µg/kg and according to Decision (EC) no 2002/657.
Description: The current analytical method provided to control nitrofuran banned substances is derived from the method developed in 2002 in a UK-NRL and a NL-NRL and dedicated to 4 metabolites, AOZ, AMOZ, AHD and SEM. Today, there is also an interest to enlarge this control to a 5th nitrofuranic substance called nifursol. Banned since 2005, and previously used as feed additive for chicken and turkey flocks the nifursol is rapidly metabolised in DNSAH. This metabolite could possibly be introduced in a global nitrofuran metabolite method robust and sensitive enough to monitor all 5 nitrofurans at once at the RPA of 1.0 µg/kg (CCalpha at 0.5 µg/kg). The chemical synthesis of a labelled-DNSAH will be considered to be used as internal standard for more accurate mass spectrometric quantitation. Therefore, the EU-RL will consider the development and transfer of such a confirmatory method based on one of its projects published 10 years ago and now to be updated and adapted to the current instrumentation.
Expected Output: The phase of development of the adapted analytical method on a new LC-MS/MS instrument was started in 2018 followed by its validation process; In early 2019, a SOP will be prepared for dissemination to the network of NRLs during the next workshop (Output 1); a report of validation according to Decision (EC) no 657/2002 will be drafted (Output 2); SOP and validation report to be posted in due time onto our EU-RL website to the attention of the network of NRLs (Output 3); a hands-on training for nitrofuran metabolites in meat will be proposed during the next appropriate annual workshop (Output 4); a communication to the international scientific community to be delivered in Symposium and/or through an international peer-reviewed scientific journal (Output 5).
Duration: 2018-2019
EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.5.6. - Development and Validation of Analytical Methods - Confirmatory LC-MS/MS monitoring of colistin residues in feed and in meat

Over the year 2019: Sub-activity 1.5.6.a
Over the year 2020: Sub-activity 1.5.6.b

Objectives: 1 – Adaptation of a LC-MS/MS method able to monitor the authorised-MRL colistin substance in porcine and in poultry meat; 2 - To validate the performance of the method in meat in line with the Decision (EC) no 2002/657; 3 - To release the analytical method to the network of NRLs; 4 – Adaptation of a LC-MS/MS method able to monitor authorised-MRL colistin substance in porcine and in poultry feed; 5 - To validate the performance of the method in feeds in line with the new standardised criteria according to the Decision (EC) no 2002/657; 6 - To release the analytical method to the network of NRLs

Description: Colistin is an important VMP product used in food-producing livestock especially in pigs, cattle, sheep, goats, rabbit and in poultry. Additionally it is one of the most critically important antibiotics (CIA) in regard to the still-relevant antimicrobial resistance issue and considering the 2016 Revision 5 of the WHO list of CIAs for human medicine and the current EMA-AMEG list of CIAs in animal husbandry based on degree of risk to humans due to antimicrobial resistance development following use in animals. Therefore, the EU-RL considers of particular interest the quality of the confirmatory control of these residues in meat from food-producing animals and other animal-derived food products and in feed as well. This control is still to be improved within the EU-MS NRLs network. A collaboration with the Cypriot NRL has been started in 2018 and will follow-up throughout a 3-year project up to 2020 and considering both controls in meat and in feed.

Expected Output: First analytical developments will be started in SGL-Nicosia in 2018 and also combined in Anses-Fougeres in 2019 (Output 1). It is expected to end up with delivering a SOP in meat and another in feed presented to the network of NRLs by 2020 (Output 2); a report of validation for each of the analytical methods according to Decision (EC) no 2002/657 will be drafted (Output 3); a hands-on training for colistin in meat and feed to be delivered during the next appropriate annual workshop (Output 4); SOP and validation report to be posted in due times on our EU-RL website to the attention of the network of NRLs (Output 5); a communication to the international scientific community to be delivered in symposium and/or through an international peer-reviewed scientific journal (Output 6).

Duration: 2018-2020

EU-RL staff considered for the task: Scientists + Technicians + Secretary

⇨ Sub-activity 1.5.7. for *Development and Validation of Confirmatory LC-MS/MS monitoring of banned VMP substance residues* will be reported to next WP 2021. It will be here replaced in the Work programme 2020 by the Sub-activity 1.5.7.bis as follows :

~~Sub-activity 1.5.7. - Development and Validation of Analytical Methods - Confirmatory LC-MS/MS monitoring of banned VMP substance residues~~

~~Over the year 2019: Sub-activity 1.5.7.a~~
~~Over the year 2020: Sub-activity 1.5.7.b~~

~~**Objectives**: 1 - To develop a LC-MS/MS method capable of including low Reference Point for Action (RPA) level of control for banned antimicrobials (chloramphenicol, nitrofuran metabolites, dapsone) and banned nitroimidazoles in meat products; the production of first choice would be the poultry production. 2 - To validate the performance of the method in line with the new regulation for monitoring of unauthorised substances and the new standardized criteria according to the 2019-2020 forecast revised Decision (EC) No. 657/2002~~

~~**Description**: There is more and more concern in reducing the number of samples to be controlled in regard to the numerous analytical methods implemented into the annual national residue control plans of the 28 EU-MS. In order to try reducing this number of implemented analytical methods, it is of interest to combine them when possible but with keeping high standard level of reliability of the official control. Therefore the EU-RL considers of particular need to evaluate a new challenge to merge as many banned antimicrobial substances as possible within the very same unique routine control method.~~

~~**Expected Output**: A report of evaluation of the capability to develop combined CAP, NIFU, NIIM residue method (Output 1); To deliver a Standard Operating Procedure presented to the network of NRLs (Output 2); a~~

~~report of validation according to new revised Decision (EC) no 657/2002 will be drafted (Output 3); a hands-on training will be delivered during the next annual workshop (Output 4); SOP and validation report to be posted in due times on our EU-RL website to the attention of the network of NRLs (Output 5); a communication to the International Scientific Community to be delivered in Symposium and/or through an International Peer-reviewed Scientific Journal (Output 6).~~

~~**Duration**: 2019-2020~~

~~**EU-RL staff considered for the task**: Scientists + Technicians + Secretary~~

⇨ Replacement:

Sub-activity 1.5.7. bis - Development and Validation of Analytical Methods - Extending LC-HRMS screening analysis to all Group B1 antimicrobial residues and some other VMP groups in egg products and validating according to new regulations

Over the year 2020: Sub-activity 1.5.7.b

Objectives: To demonstrate the adaptation and the validation of a full-scan High Resolution MS analytical method for delivery to field laboratories in a large scope of VMPRs and with high-throughput screening option by means of using a LC-QTOF-MS system and focusing the method to control in egg products.

Description: The context of the evolution of screening strategies put the new LC-HRMS analytical systems at the premier place of advanced technologies dedicated to VMP residue control in balance with the now well-known targeted LC-MS/MS instruments. Considering the broad network of NRLs and of field laboratories within the EU, the EU-RL considers of high interest to develop and propose a multi-VMP residue screening method for egg products and including as many relevant Group B1 antibiotic residues as possible and also including some other relevant classes of VMP residues (Benzimidazoles, Avermectins, Anticoccidials, …) within a single Full Scan High Resolution Mass Spectrometric instrument : an LC-QTOF-MS instrument.

Expected Output: In 2020, will be started the development of the egg product LC-HRMS screening method. A first presentation of this project will be made to the EU-MS NRLs network during the workshop of June 2020 (Output 1). As a follow-up of the validation of the method to occur in the course of 2020 and early 2021, an hands-on training dedicated to this LC-HRMS method (Output 2) will be presented to the network of EU-NRLs during the next annual workshop of 2021 together with the release of a Standard Operating Procedure (Output 3); also the report of validation according to revised Decision (EC) No 2002/657 and the SOP will be posted into the EU-RL Website (Output 4);

Communications to the international scientific community should be delivered in a symposium and/or through an article in an international peer-reviewed scientific journal in 2021 (Output 5).

Duration: Over 2020-2021

EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.5.8. - Development and Validation of Analytical Methods - Confirmatory LC-MS/MS monitoring of fumagillin residues in Honey

Over the year 2020: Sub-activity 1.5.8.b

Objectives: To develop a LC-MS/MS method for the determination of Fumagillin (or its metabolites) residues in honey. To validate the performance of the method according to Decision (EC) No. 657/2002

Description: To apply efficient treatment against microsporidian parasites *Nosema apis* infections in honey bees, fumagillin antimicrobial substance was considered a relevant medication with also disinfecting capacities. It is used for many years in bees feeding to reduce the risk of mortality. The substance is registered in use in Northern America. However it has been suspended for use in apiaries within the EU since 2002. Currently subjected to evaluation for a new MRL dossier application received by the EMA in 2016, the control of the substance will request to possibly monitor several residues within the same LC-MS/MS method. After a complete bibliography review (use, chemical properties, stability, analytical method, marker residues, stability) a development of an analytical method will be started in 2020 to determine fumagillin or its potential marker residues in honey.

Expected Output: To deliver a Standard Operating Procedure accessible to the network of NRLs (Output 1); a report of validation according to Decision (EC) no 2002/657 will be drafted (Output 2); a hands-on training will be delivered during the next annual workshop (Output 3); SOP and validation report to be posted in due times on our EU-RL website to the attention of the network of NRLs (Output 4); a communication to the International Scientific Community to be delivered in Symposium and/or through an International Peer-reviewed Scientific Journal (Output 5).
Duration: 2020-2021
EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.5.9. - Development and Validation of Analytical Methods - Confirmatory LC-MS/MS monitoring of florfenicol and florfenicol amine residues in Meat and Aquaculture products

Over the year 2020: Sub-activity 1.5.9.b

Objectives: To develop a LC-MS/MS method for the determination of Florfenicol (or its metabolites) residues in fish farming and in meat. To validate the performance of the method according to Decision (EC) No. 657/2002
Description: Florfenicol (FF) is an authorized compound from the amphenicol antibiotic VMP family. The FF has got MRL set up in all food-producing species listed in Table 1 of Commission Regulation (EU) No. 37/2010 (with the marker residue defined as '*the sum of florfenicol and its metabolites measured as florfenicol amine*'. A specific method for accurate measurement of FF and its metabolites as FFA will be developed, including a hydrolysis step prior to sample extraction to convert the parent drug and its metabolites to the single marker residue FFA.
Expected Output: To deliver a Standard Operating Procedure accessible to the network of NRLs (Output 1); a report of validation according to Decision (EC) no 2002/657 will be drafted (Output 2);
Duration: 2020-2021
EU-RL staff considered for the task: Scientists + Technicians + Secretary

BIOLOGICAL-BIOCHEMICAL METHODS

Sub-activity 1.5.10. - Development and Validation of Analytical Methods - Evaluation of innovative technologies for rapid screening of veterinary antimicrobial residues in Foodstuffs - Electrochemical biosensors (Potentiometric Vantix – Amperometric Magnetic beads) for screening prohibited substances (VAMP & SUSANA)

Over the year 2019: Sub-activity 1.5.10.a
Over the year 2020: Sub-activity 1.5.10.b

Objectives: 1 – Our first action within the program of 2018 was to evaluate the specificities of both electrochemical systems here-after described in order to develop new multiplex screening methods applicable to multiple prohibited antibiotics and dyes (chloramphenicol, nitrofuran metabolites, dyes) in different matrices (*e.g.* aquaculture products, and honey). A first method was developed and optimised for the screening of CAP in milk down below the MRPL/RPA. 2 - The next objective now pending over 2018-2019 is to continue to develop with some other single family screening methods for other banned substances in milk (nitrofuran metabolites, and dyes). 3 - Then to extend to a new multiplex method combining all these prohibited substances first in the milk product. 4 - Afterwards, we will try to adapt the new multiplex method for banned substances in other matrices (eg. honey, aquaculture products). Overall, this project allows to compare the performances of these 2 electrochemical biosensors, based on similar bioreceptors (eg. antibodies, binding proteins, and aptamers).
Description: Two different electrochemical biosensors were identified during the programs for 2015 & 2016-2017 which are able to perform multiplex screening of antibiotic residues:

- A commercial system named Vantix™ (from Vantix Diagnostics™) is a potentiometric biosensor, claimed to provide a reproducible platform on which sensitive and robust assays can be developed. The main advantages of this platform are firstly a reduced investment; secondly each user could perform his own development, using antibodies and antibiotic-enzyme conjugates and thirdly the sample preparation is usually easily manageable (even no preparation for milk). The combs are constituted of 12 channels, which allow the simultaneous analysis of 12 analytes or 12 samples or a mix. The system was evaluated in 2017 to perform the first developments of analytical methods for the specific screening of chloramphenicol residues in milk. The objective in 2018-2019 will be to go on with the development of new methods for a multi-residue screening of authorised substances (eg. tetracyclines, quinolones, sulfonamides, aminoglycosides, macrolides) in milk, honey, tissues (including aquaculture products) and eggs for example and for the screening of multiple banned antibiotics (*e.g.* chloramphenicol, nitrofuran metabolites, dyes) in different matrices (eg. aquaculture products, honey).
- An amperometric biosensor has been developed by a Spanish research team. Their research interests focus on analytical electrochemistry, nanostructured electrochemical interfaces and electrochemical and piezoelectric sensors and biosensors. The multiplexed detection relies on the use of a mixture of target-specific modified magnetic beads and application of direct competitive assays using horseradish peroxidase (HRP)-labelled tracers. The cost of the amperometric biosensor is low. Moreover, the development of methods is manageable, using antibodies and antibiotic-enzyme conjugates. Finally, sample preparation time can be much reduced. In 2017, a technical evaluation of the system was performed in our laboratory. The development of specific method for chloramphenicol detection in milk was started in 2017 and extended over 2018. The objective in the 2019-2020 programme period will be to go on and enlarge with the development of new methods for a multi-residue screening of multiple banned antimicrobials (*e.g.* chloramphenicol, nitrofuran metabolites, dyes) in different matrices (*e.g.* aquaculture products, honey).

Expected Output: An intermediate report of the advances in the project will be delivered for the next workshop by end of 2019 (Output 1). It will contain the advances on a single compound method for a banned substance (chloramphenicol) that was developed and validated by end of 2018. A presentation of the advances on the Vantix project will be delivered during the EU-RL workshop of 2019 (Output 2) and disseminated to an enlarged community during an international congress in 2019 (Output 3). A multiplex method screening for several prohibited substances will be developed in 2019. Two evaluation reports will be delivered by the end of 2019 to the network of NRLs considering the 2 electrochemical biosensors tested (Output 4). The evaluation reports will be then posted on our EU-RL website to the attention of the network of NRLs (Output 5). A formal presentation of the final advances on the project will be delivered during the workshop organised in 2020 to the attention of the NRLs experts (Output 6). Then publications in peer-reviewed scientific journals might be also considered (Output 7).

Duration: 2018-2020

EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.5.11. - Development and Validation of Analytical Methods – Evaluation of a screening method for the colistins, a critically important antibiotic, by means of ELISA in porcine and poultry meats

Over the year 2019: Sub-activity 1.5.11.a

Objectives: 1 - Evaluation of the performance of 3 commercially available ELISA kits (from Europroxima, The Netherlands; Creative Diagnostics, US; Bioo Scientific, US) aimed at screening of colistin in porcine and poultry meats. 2 - Comparison of the results of the 3 ELISA kits validations.

Description: The screening of colistin with immunoassays is an interesting alternative to LC-MS/MS methods because of its lower investment in analytical equipment. Three different manufacturers of ELISA kits for the screening of colistin have been identified. Therefore the 3 ELISA kits will be evaluated in line with the Decision (EC) No 2002/657 and with the European guideline for the validation of screening VMP residue methods (2010).

Expected Output: One evaluation report per kit will be delivered by the end of 2019 to the network of NRLs (Output 1). The evaluation reports will then be posted on our EU-RL website to the attention of the network of NRLs (Output 2). A formal presentation of the advances on the project will be offered to the attention of the NRL experts during the workshop organised in 2019 (Output 3). A communication in an international symposium

and/or a scientific publication in a peer-reviewed journal might be also further considered for dissemination (Output 4).

Duration: 2019

EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.5.12. - Development and Validation of Analytical Methods - Evaluation of innovative technologies for rapid screening of veterinary antimicrobial residues in Foodstuffs - Electrochemical biosensors (Potentiometric Vantix – Amperometric Magnetic beads) for screening authorised MRL antimicrobial substances

Over the year 2020: Sub-activity 1.5.12.b

Objectives: 1 - Our first action in 2020 will be to go on with the evaluation of both systems here-after described in order to develop new multiplex methods applicable to the screening of authorised antibiotics (eg. tetracyclines, quinolones, sulfonamides, aminoglycosides, macrolides) in milk. A method will be developed and optimised for the screening of one to 3 antibiotic families below MRL in milk. 2 - The second objective in 2021 will be to develop one new multiplex method for these 2 to 3 families in milk. Afterwards we will try to adapt the new multiplex method for authorised substances in other matrices (eg. honey, aquaculture products). This project will allow the comparison of the performances of these 2 electrochemical biosensors, based on the same bioreceptors (eg. antibodies, binding proteins, and aptamers).

Description: Two different electrochemical biosensors have been identified during the programs for 2015 & 2016-2017 & 2018 which are able to perform multiplex screening of antibiotics:

- A commercial system named Vantix™ (from Vantix Diagnostics™) is a potentiometric biosensor, claimed to provide a reproducible platform on which sensitive and robust assays can be developed. The main advantages of this platform are firstly a reduced investment; secondly each user could perform his own development, using antibodies and antibiotic-enzyme conjugates and thirdly the sample preparation is usually easily manageable (even no preparation for milk). The combs are constituted of 12 channels, which allow the simultaneous analysis of 12 analytes or 12 samples or a mix. The system was evaluated in 2017 to perform the first developments of analytical methods for the specific screening of chloramphenicol residues in milk. The objective in 2020-2021 will be to go on with the development of new methods for a multi-residue screening of authorised substances (eg. tetracyclines, quinolones, sulfonamides, aminoglycosides, macrolides) in milk first and if possible in, honey, tissues (including aquaculture products) and eggs for example.
- An amperometric biosensor has been developed by a Spanish research team. Their research interests focus on analytical electrochemistry, nanostructured electrochemical interfaces and electrochemical and piezoelectric sensors and biosensors. The multiplexed detection relies on the use of a mixture of target-specific modified magnetic beads and application of direct competitive assays using horseradish peroxidase (HRP)-labelled tracers. The cost of the amperometric biosensor is low. Moreover, the development of methods is manageable, using antibodies and antibiotic-enzyme conjugates. Finally, sample preparation time can be much reduced. In 2017, a technical evaluation of the system was performed in our laboratory. The development of specific method for chloramphenicol detection in milk started in 2017. The objective in the 2020-2021 period will be to go on and enlarge with the development of new methods for a multi-residue screening of authorized substances (*e.g.* tetracyclines, quinolones, sulfonamides, aminoglycosides, macrolides) in milk, honey, tissues (including aquaculture products) and eggs for instance.

Expected Output: An intermediate report of the advances in the project will be delivered by end of 2020 (Output 1). It will contain the advances on the single compounds methods for authorised substances that will be developed and validated in 2020. A presentation of the advances on the project will be delivered during the EU-RL workshop of 2020 (Output 2) and/or during an international congress in 2020 (Output 3).

In 2021, a multiplex method for several authorised substances will be developed and validated. Two evaluation reports will be delivered by the end of 2021 to the network of NRLs considering the 2 biosensors tested (Output 4). The evaluation reports will be then posted on our EU-RL website to the attention of the network of NRLs (Output 5). A formal presentation of the final advances on the project will be delivered during the workshop organised in 2021 to the attention of the NRLs experts (Output 6). Then publications in peer-reviewed scientific journals might be also considered (Output 7).

Duration: 2020-2021

EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.5.13. - Development and Validation of Analytical Methods - Evaluation of innovative technologies for rapid screening of veterinary antimicrobial residues in Foodstuffs - electrochemical biosensors other than potentiometric and amperometric: the voltammetric device; and amplification strategies to improve the sensitivity of electrochemical biosensors (eg. nanostructures, enzyme amplification)

Over the year 2020: Sub-activity 1.5.13.a

Objectives: 1 - The voltammetric detection will be evaluated as a follow-up of project launched during our earlier programme 2016/2017. 2 - The second combined objective is to test nanoparticles (ie. carbon-based, metal-based and/or uncommon nanomaterials: nanohorns, fullerenes) to try improving the sensitivity of the electrochemical biosensors which were tested in 2016/2017. The model compound will be chloramphenicol.

Description: From 2016/2017, we have tested amperometric and potentiometric detection systems to develop single compounds and multiplex methods for the screening of antibiotic residues. Other electrochemical detection systems are available and fitted to the screening of contaminants in foodstuffs (eg. Electrochemical impedance spectroscopy, voltammetry). Furthermore different kinds of nanoparticles (ie. Carbon based, metal based and/or uncommon nanomaterials: nanohorns, fullerenes) are used to enhance the electron transfer in electrochemical biosensors, which allow to improve the sensitivity of the methods. The objective in the 2020-2021 period will be to develop methods for the screening of CAP in milk as a model compound with new electrochemical detection systems (eg. Electrochemical impedance spectroscopy, voltammetry), with and without the use of nanoparticles. These results will be compared together and also with the previous results obtained with amperometric and potentiometric systems.

Expected Output: An intermediate report of the advances in the project will be delivered by end of 2020 (Output 1). It will contain the advances on the development of a CAP method using different electrochemical systems and / or nanoparticles that will be developed and validated in 2020. A presentation of the advances on the project will be delivered during the EU-RL workshop of 2020 (Output 2) and/or during an international congress in 2020 (Output 3).

In 2021, a multiplex method for several authorised substances will be developed and validated. One evaluation report will be delivered by the end of 2021 to the network of NRLs (Output 4). The evaluation report will be then posted on our EU-RL website to the attention of the network of NRLs (Output 5). A formal presentation of the final advances on the project will be delivered during the workshop organised in 2021 to the attention of the NRLs experts (Output 6). Then publications in peer-reviewed scientific journals might be considered (Output 7).

Duration: 2020-2021

EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.5.14. - Development and Validation of Analytical Methods – Evaluation of new portable bio rapid methods for testing residues of antibiotics or dyes in food products from animal origin (meat, milk, eggs, …), by means of immunological techniques.

Over the year 2020 : Sub-activity 1.5.14.a

Objectives: The objective of this project is to test new portable immunological-based rapid methods for testing residues of antibiotics or dyes in food products from animal origin (meat, milk, eggs, …), when new possibilities appear on the market, to be reactive to give advices to the network of NRLs.

Description: In the field of biosensor technology, many researches are in progress to apply biosensors to the rapid screening of antibiotic residues in foodstuffs, especially to improve their sensitivity and specificity and to lower the cost of the screening step. Furthermore new compounds of interest could be targeted when needed, for example if no physicochemical is available. In these cases, the new technology and/or new kit will be evaluated. A new method will be developed if needed or a new kit

will be evaluated according to the decision EC/2002/657 and to the European guideline for the validation of screening methods (2010).

Expected Output: An intermediate report of the advances in the project will be delivered by end of 2020 (Output 1). It will contain the advances on the development and/or validation. The evaluation report will be then posted on our EU-RL website to the attention of the network of NRLs by end of 2020 (Output 2). A formal presentation of the final advances on the project will be delivered during the workshop organised in 2021 to the attention of the NRLs experts (Output 3). Then publications in peer-reviewed scientific journals might be also considered (Output 4).

Duration: 2020

EU-RL staff considered for the task: Scientists + Technicians + Secretary

1.6 Analysis of official samples (b)

Sub-activity 1.6.1. - ANALYSIS OF OFFICIAL SAMPLES in case of dispute or as third-part evaluation

Over the year 2019: Sub-activity 1.6.1.a
Over the year 2020: Sub-activity 1.6.1.b

Objectives: As EU-RL, the ANSES-Fougères will continue with analysing at a reference status or after disputes some of the official samples coming from the NRLs and on their specific demand.

Description: The specific requests arising from certain NRLs to analyse in their place a part or all of the confirmatory sets of samples coming from their National Residue 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 EU-RL task requested by the Regulation (EU) 625/2017 and the Annex V of the Directive (EC) 96/23.

Expected Output: From 2 and up to 10 different requests may be considered

Duration: Requests' admissibility/acceptability evaluated and analysis carried out within 1 month

EU-RL staff considered for the task: Scientist + Technicians + Secretary

2 TO PROVIDE SCIENTIFIC AND TECHNICAL ASSISTANCE TO NRLs

Please, provided activities related to Regulation (EU) 2017/625:

- *Art. 94.2.d* ***Coordinating practical arrangements necessary to apply new methods of laboratory analysis, testing or diagnosis, and informing national reference laboratories of advances in this field.***
  GLOBAL TRAININGS DURING ANNUAL WORKSHOPS – ANALYSIS OF OFFICIAL SAMPLES
- *Art. 94.2.e* ***Conducting training courses for staff from national reference laboratories and, if needed, from other official laboratories, as well as of experts from third countries.***
  SPECIFIC ANALYTICAL TRAININGS ON-SITE or at EU-RL FACILITIES
- *Art. 94.2.g* ***Providing information on relevant national, Union and international research activities to national reference laboratories.***
  ANNUAL WORKSHOP / INTERNATIONAL SYMPOSIA / EU-RL WEBSITE

2.1 Providing technical and scientific support to NRLs (d)

Sub-activity 2.1.1. – Continuous technical and scientific communication with the network of EU-MS NRLs

Over the year 2019: Sub-activity 2.1.1.a
Over the year 2020: Sub-activity 2.1.1.b

Objectives: Delivering upon requests from the EU-MS-NRLs any technical and scientific advices and information related to the field of VMPR groups A6-B1-B2f-B3e
Description: Over the year, a continuous line of communication is carried out by any means like phone call, emails, EU-RL website, ….
Expected Output: Listing of the issues exchanged with the EU-MS NRLs by the continuous line of communication
Duration: Over 24 months
EU-RL staff considered for the task: Scientists + Secretary

2.2 Organisation of workshops (e)

Sub-activity 2.2.1. - Organisation of the annual workshop to the attention of EU-MS NRLs from 2019 and from 2020

Over the year 2019: Sub-activity 2.2.1.a
Over the year 2020: Sub-activity 2.2.1.b

Objectives: Organisation of the annual workshop to the attention of EU-MS NRLs
Description: A 2-day or 3-day workshop to the attention of the experts from the network of EU-MS NRLs and EU-CC-NRLs in charge of antimicrobial residue control in food will be organised in conformity with requirements of current enforced Regulation (EU) for Union financial aid to the EU reference laboratories. This annual workshop may also include when necessary a technical training session. The venue and a preliminary agenda will be announced at the beginning of the year and prepared according to main regulatory, scientific and technical issues to be exchanged with the EU-MS NRL network.
Expected Output: Announced at the beginning of the year 2018 (Output 1); Postage onto the EU-RL website (Output 2); Release of the programme and list of participants to the workshop (Output 3); Dissemination of all documents delivered during the workshop by posting onto the EU-RL website (Output 4)
Duration: Over 10 months for preparation-dissemination and over a 3-4 day venue
EU-RL staff considered for the task: Scientists + Technicians + Secretary

2.3 Organisation of training courses (e)

Sub-activity 2.3.1. – Analytical support and technical TRAININGS at the specific request of EU-NRLs or Official Laboratories of Candidate Countries

Over the year 2019: Sub-activity 2.3.1.a
Over the year 2020: Sub-activity 2.3.1.b

Objectives: These training sessions aim at providing additional scientific and technical service to some EU-NRLs or to some Official Laboratories of EU Candidate Countries after their request generally due to inadequate results in specific EU-PT or due to some other relevant VMPR control issues.
Description: Organisation at EU-RL-ANSES-Fougères premises or sometimes on-site of specific training courses toward scientists/analysts from Member States and/or EU-Acceding Countries and/or EU-Candidate Countries, only upon their request and after tailored training agenda to be agreed upon between the Parties.
Expected Output: A set of 4 separate trainings related to the screening and/or confirmation of antimicrobial or dye residues in meat and/or other relevant products (milk, fish, honey, egg, …) (Outputs 1-2-3-4) are foreseen for the period 2019-2020
Duration: Organised over 40 days maximum across the 24 months of the WP and in separate sets of 1-week (5-day) for up to 8 analysts or 2-week (10-day) max for up to 4 analysts

2.4 Visits of NRLs (d and e)

Sub-activity 2.4.1. - Projection of 4 visits (2 visits in 2019 and 2 visits in 2020) of EU-RL delegates to EU-NRLs from the Member States or from the Candidate Countries

Over the year 2019: Sub-activity 2.4.1.a
Over the year 2020: Sub-activity 2.4.1.b

Objectives: Projection of 4 visits of EU-RL delegates to EU-NRLs from the Member States or from EU-Candidate Countries
Description: The EU-RL-delegate visit to specific EU-NRLs is an occasion of privileged bilateral discussion on issues dedicated to the specificities of each NRL. It is part of the strengthening of the EU-MS NRL networking
Expected Output: Final Reports of the 4 visits (Output 1) (Output 2) (Output 3) (Output 4)
Duration: Organised for 2 EU-RL delegates and over a 2-5 day mission depending on the number of laboratories concerned by the NRL activities in the relevant country visited.
EU-RL staff considered for the task: Scientists

2.5 Providing to NRLs relevant information on National, Union and International research activities for VMPRs (g)

Sub-activity 2.5.1. – Continuous technical and scientific communication with the network of EU-MS NRLs by phone, email and any other type of communication

See for Budget under Sub-activity 2.1.1.

Over the year 2019: Sub-activity 2.5.1.a
Over the year 2020: Sub-activity 2.5.1.b

Objectives: Delivering upon requests from the EU-MS-NRLs any technical and scientific advices and information related to the field of VMPR groups A6-B1-B2f-B3e
Description: Over the year, a continuous line of communication is carried out by any means like phone call, emails, EU-RL website, ….
Expected Output: Listing of the issues exchanged with the EU-MS NRLs by the continuous line of communication
Duration: Over 24 months
EU-RL staff considered for the task: Scientists + Secretary

Sub-activity 2.5.2. - International missions of EU-RL delegates in several symposia, seminaries and workshops for enhancing dissemination of scientific information in the field of antibiotic and dye residues in food ***See for Budget under Sub-activity 3.3***

Over the year 2019: Sub-activity 2.5.2.a
Over the year 2020: Sub-activity 2.5.2.b

Objectives: International missions of EU-RL delegates in several symposia, seminars and workshops for enhancing dissemination of scientific information in the field of antibiotic and dye residues in food
Description: The active participation (organisation, scientific session chairing, oral communication, poster communication) to European/International workshops, seminaries and symposia are of utmost importance to disseminate the EU-RL information and activity. It is the right place to interact externally in our field of food safety control with the network of EU-NRLs and broader food control communities.
Expected Output: Several missions are scheduled for the attention of the scientists of the EU-RL and dissemination of information to be released at EU-RL workshops and posted onto the EU-RL website: (http://eurl-fougeres-veterinaryresidues.anses.fr)
Duration: Over the 24 months several missions scheduled on a 3 to 5 day travel basis each
EU-RL staff considered for the task: Scientists

2.6 Updating and publication of the list of NRLs

Sub-activity 2.6.1. - Update of the LIST of EU-MS NRLs in charge of VMPR Control in Food

Over the year 2019: Sub-activity 2.6.1.a
Over the year 2020: Sub-activity 2.6.1.b

Objectives: Follow-up and update of the LIST of EU-MS NRLs in CHARGE of VMPR CONTROL IN FOOD in regard to Groups Substances allocated to the tasks of the EU-RL: A6, B1, B2f, and B3e.
Description: as a new requirement of Regulation (EU) No. 2017/625, a list of the EU-MS NRLs in charge of VMPR Control in Food from Animal Origin will be regularly updated.
Expected Output: An updated list with NRLs contact details to be made publicly available and to the network of NRLs through the EU-RL website (http://eurl-fougeres-veterinaryresidues.anses.fr) (Output 1) (Output 2)
Duration: Over a 3 month exchange with NRLs and /or EU-MS Competent Authorities
EU-RL Staff considered for the task: Scientist + Secretary

3 TO PROVIDE SCIENTIFIC AND TECHNICAL ASSISTANCE TO THE EUROPEAN COMMISSION AND OTHER ORGANISATIONS

Please, provide activities related to Regulation (EU) 2017/625:

- *Art. 94.2.f* ***Providing scientific and technical assistance to the Commission within the scope of their mission.***

- *Art. 94.2.h* ***Collaborating within the scope of their mission with laboratories in third countries and with the European Food Safety Authority (EFSA), the European Medicines Agency (EMA) and the European Centre for Disease Prevention and Control (ECDC).***

3.1 Technical and scientific assistance to the Commission (f)

Sub-activity 3.1.1.a - **Analysis of National residue monitoring plans of the MS for 2019 (f)**

Objectives: For the year 2019, an evaluation of the National Residue Monitoring Plans of the 27/28 Member States in terms of analytical methods in use for VMPR substances of Groups A6 (*CAP, NIFU, DAP*), B1 (*MRL-antimicrobials*), B2f (*CBX, OQX*), B3e (*Dyes*)
Expected Output: Release of a final report to the Commission DG-SANTE and FVO (Output 1) and posted onto our EU-RL website to the exclusive attention of the Commission (http://eurl-fougeres-veterinaryresidues.anses.fr) (Output 2) and afterwards comments from and technical exchange with the MS-CAs and MS-NRLs a presentation of main findings to the SC PAFF (Output 3)
Duration: Over 3 months
EU-RL staff considered for the task: Scientists

Sub-activity 3.1.1.b - **Analysis of National residue monitoring plans of the MS for 2020 (f)**

Objectives: For the year 2020, an evaluation of the National Residue Monitoring Plans of the 27/28 Member States in terms of analytical methods in use for VMPR substances of Groups A6 (*CAP, NIFU, DAP*), B1 (*MRL-antimicrobials*), B2f (*CBX, OQX*), B3e (*Dyes*)
Expected Output: Release of a final report to the Commission DG-SANTE and FVO (Output 1) and posted onto our EU-RL website to the exclusive attention of the Commission (http://eurl-fougeres-veterinaryresidues.anses.fr) (Output 2) and afterwards comments from and technical exchange with the MS-CAs and MS-NRLs a presentation of main findings to the SC PAFF (Output 3)
Duration: Over 3 months
EU-RL staff considered for the task: Scientists

Sub-activity 3.1.2.a – **Support to Commission on specific items upon request in 2019 (f)**

Objectives: Upon request from the Commission DG-SANTE, the EU-RL may have to deliver specific advice, survey, report … in line with the scope of VMPRs allocated.
Expected Output: 2 or 3 medium-large requests over the year 2019 of the WP 2019-2020
Duration: Over the 12 months of 2019
EU-RL staff considered for the task: Scientists

Sub-activity 3.1.2.b – **Support to Commission on specific items upon request in 2020 (f)**

Objectives: Upon request from the Commission DG-SANTE, the EU-RL may have to deliver specific advice, survey, report … in line with the scope of VMPRs allocated.
Expected Output: 2 or 3 medium-large requests over the year 2020 of the WP 2019-2020
Duration: Over the 12 months of 2020
EU-RL staff considered for the task: Scientists

3.2 Collaboration with European and international organisations and Third Countries (h)

Sub-activity 3.2.1. - *Co-operation with European / International organisations: DG-SANTE/FVO, EMA, EFSA, EURACHEM, AOACI, FAO-AIEA, ISO, CEN, FIL-IDF, IUPAC, …*

Over the year 2019: Sub-activity 3.2.1.a
Over the year 2020: Sub-activity 3.2.1.b

Objectives: Cooperation where relevant issues and requested with DG-SANTE / FVO, DG-Trade, DG-NEAR, EMA, EFSA, EURACHEM, AOACInt, FAO-IAEA, WHO-Codex, ISO, CEN, IDF, IUPAC, …
Description: There is every year several solicitations from the European or International levels requesting our EU-RL expertise
Expected Output: Exchange and release of reports for expertise data or advices delivered to these European or International Food Safety Official Entities
Duration: Over the 24 months
EU-RL Staff considered for the task: Scientist + Secretary

Sub-activity 3.2.2. - Participation to advanced schools for Third Countries Laboratories like SARAF or BTSF training courses upon request

Over the year 2019: Sub-activity 3.2.2.a
Over the year 2020: Sub-activity 3.2.2.b

Objectives: Dissemination of advanced VMPR information to EU-MS and Third Country Official Lab experts.
Description: Participation to advanced schools like SARAF or BTSF training courses upon request.
Expected Output: From 1 and up to 3 training courses per year lasting 2 to 5 h per course
Duration: over 24 months
EU-RL staff considered for the task: Scientists

Sub-activity 3.2.3. – Continuous technical and scientific communication with the network of EU-MS NRLs ***See for Budget under Sub-activity 2.1.1.***

Over the year 2019: Sub-activity 3.2.3.a
Over the year 2020: Sub-activity 3.2.3.b

Objectives: Delivering upon requests from the EU-MS-NRLs any technical and scientific advices and information related to the field of VMPR groups A6-B1-B2f-B3e
Description: Over the year, a continuous line of communication is carried out by any means like phone call, emails, EU-RL website, ….
Expected Output: Listing of the issues exchanged with the EU-MS NRLs by the continuous line of communication.
Duration: Over 24 months
EU-RL staff considered for the task: Scientists + Secretary

3.3 Participation in symposiums, workshops and seminars for the dissemination of scientific information. (h)

Sub-activity 3.3.1.a - International missions of EU-RL delegates in several symposia, seminaries and workshops for enhancing dissemination of scientific information in the field of antibiotic and dye residues in food for the year program 2019 ***See also 2.5.2.***

Sub-activity 3.3.1.b - International missions of EU-RL delegates in several symposia, seminaries and workshops for enhancing dissemination of scientific information in the field of antibiotic and dye residues in food for the year program 2020 ***See also 2.5.2.***

Objectives: International missions of EU-RL delegates in several symposia, seminars and workshops for enhancing dissemination of scientific information in the field of antibiotic and dye residues in food
Description: The active participation (organisation, scientific session chairing, oral communication, poster communication) to European/International workshops, seminaries and symposia are of utmost importance to disseminate the EU-RL information and activity. It is the right place to interact externally in our field of food safety control with the network of EU-NRLs and with the Official Laboratories of Third Countries worldwide.
Expected Output: Several missions are scheduled for the attention of the scientists of the EU-RL and dissemination of information to be released at EU-RL workshops and posted onto the EU-RL website: (http://eurl-fougeres-veterinaryresidues.anses.fr)
Duration: Over the 24 months of the WP several missions scheduled on a 3 to 5 day travel basis each
EU-RL staff considered for the task: Scientists

3.4 To ensure a sound and efficient management of the EURL/EURC funding cycle.

Sub-activity 3.4.1.a - Compilation of provisional programme, mid-term biannual report and cost estimates of the year 2019

Sub-activity 3.4.1.b - Compilation of provisional programme, final term biannual reports and cost estimates of the combined years 2019-2020

Objectives: Documents to be released to the Commission-DG-Santé in due time according to the contracted agreement.
Description: One programme for 2019-2020 including the scientific & technical tasks, a proposed 2-year budget for the proposed tasks. One final report for 2018 program including scientific & technical issues and budget execution.
Expected Output: By end of November 2018, the provisional Programme 2019-2020 including scientific & technical tasks, and a 2-year budget (Output 1) + Postage onto the EURL website to the exclusive attention of COMM (Output 2)
By March 2019, the Final Technical report of the programme for the period 2018 (Output 3) + Postage onto the EURL website to the exclusive attention of COMM (Output 4)

By March 2020, the mid-term biannual Technical report and year2019-budget of programme 2019-2020 (Output 5) + Postage onto the EURL website to the exclusive attention of COMM (Output 6) (http://eurl-fougeres-veterinaryresidues.anses.fr)
By March 2021, the Final Technical report of programme 2019-2020 (Output 7) + Postage onto the EURL website to the exclusive attention of COMM (Output 8) (http://eurl-fougeres-veterinaryresidues.anses.fr)
Duration: Over 28 Months
EU-RL staff considered for the task: Scientists + Secretary

4 REAGENTS AND REFERENCE COLLECTIONS

Please, provided activities related to Regulation (EU) 2017/625:

- *Art. 94.2.*j ***Coordinating or performing tests for the verification of the quality of reagents and lots of reagents used for the diagnosis of foodborne, zoonotic or animal diseases and pests of plants.***
- *Art. 94.2.k* ***Where relevant for their area of competence, establishing and maintaining:***
  - ***i. reference collections of pests of plants and/or reference strains of pathogenic agents;*** ***Not concerned***
  - ***ii. reference collections of materials intended to come into contact with food used to calibrate analytical equipment and provide samples thereof to national reference laboratories;*** ***Follow-up of Reference Materials from PTs***
  - ***iii. up-to-date lists of available reference substances and reagents and of manufacturers and suppliers of such substances and reagents.*** ***Follow-up of Reference Analytical Standards***

4.1 Up to date lists of available reference substances and reagents and of manufacturers and suppliers of such substances and reagents (k)

Sub-activity 4.1.1.a - Follow-up of the database of the analytical standards for 2019
Sub-activity 4.1.1.b - Follow-up of the database of the analytical standards for 2020

Objectives/Description: Follow-up of the list of the analytical standards commercially made available from authorised suppliers and of the database for the non-commercially available analytical standards proposed at the EU-RL facilities
Expected Output: A yearly updated report on the database of reference antimicrobial standards to be posted to the network of NRLs through the EU-RL website (http://eurl-fougeres-veterinaryresidues.anses.fr) (Output 1)
Duration: Over the year 2019
EU-RL staff considered for the task: Scientist + Secretary

Sub-activity 4.1.2.a - Follow-up of the database for the reference materials for 2019
Sub-activity 4.1.2.b - Follow-up of the database for the reference materials for 2020

Objectives/Description: Follow-up of the database for the reference materials prepared during EU-RL-organised proficiency testing studies and of the list of reference materials made available from authorised suppliers
Expected Output: A yearly updated report on the database of reference antimicrobial materials created starting from our PT materials and to be made available to the network of NRLs through the EU-RL website (**Output 1**). A yearly updated report on the list of marketed antimicrobial reference materials and to be made available to the network of NRLs through the EU-RL website (**Output 2**)
Duration: Over the year 2020
EU-RL staff considered for the task: Scientist + Secretary

5 REQUIREMENTS RELATED TO OTHER LEGISLATION

Please specify applicable legislation:

No activity related to this issue

Sub-activity 5.x *(name of Sub-activity)*

Objectives: Nil
Description: Nil
Expected Output: Nil
Duration: Nil
EU-RL staff considered for the task: Nil

REMARKS

No remark

(if necessary)

WORK PROGRAMME of EURL for

BVL BERLIN

PERIOD: 2019/2020

Version 1.0
(date 17/12/2018

CONTACT DETAILS

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SUMMARY

INTRODUCTION

The EUROPEAN UNION REFERENCE LABORATORY FOR RESIDUES OF VETERINARY MEDICINES AND CONTAMINANTS IN FOOD OF ANIMAL ORIGIN (EURL Berlin) with responsibilities for residues of beta-agonists, anthelmintics, non-steroidal anti-inflammatory drugs and anticoccidials including nitroimidazoles (groups of substances: A5-B2a-B2b-B2e) is part of Department 5 “Method Standardisation, Reference Laboratories, Antibiotic Resistance” of the BVL (Bundesamt für Verbraucherschutz und Lebensmittelsicherheit - Federal Office of Consumer Protection and Food Safety).

The analytical activities of the EURL Berlin are pursued by specialised sub-units, which are in charge of the different substance groups within the responsibility of the EURL Berlin. They are supplemented by a sub-unit in charge of the preparation of incurred test materials to be used as in-house reference samples and for proficiency testing.

The activities listed in the following correspond to the duties and operating conditions of EURLs as laid down in Regulation (EC) No. 2017/625, Article 94 (formerly: Article 32 of Regulation (EC) No. 882/2004).

Regulation (EU) 625/2017 Art 94(2):
European Union reference laboratories designated in accordance with Article 93(1) shall be responsible for the following tasks insofar as they are included in the reference laboratories' annual or multiannual work programmes that have been established in conformity with the objectives and priorities of the relevant work programmes adopted by the Commission in accordance with Article 36 of Regulation (EU) No 652/2014:
(taking into account Art 147 of (EU) 625/2017)

1 TO ENSURE AVAILABILITY AND USE OF HIGH QUALITY METHODS AND TO ENSURE HIGH QUALITY PERFORMANCE BY NRLs.

Please, provided activities related to Regulation (EU) 2017/625:
(Number of Sub-activity boxes can be adjusted by EURL)

- *Art. 94.2.a* ***Providing national reference laboratories with details and guidance on the methods of laboratory analysis, testing or diagnosis, including reference methods.***
- *Art. 94.2.b* ***Providing reference materials to national reference laboratories***
- *Art. 94.2.c* ***Coordinating the application by the national reference laboratories and, if necessary, by other official laboratories of the methods referred to in point (a), in particular, by organising regular inter-laboratory comparative testing or proficiency tests and by ensuring appropriate follow-up of such comparative testing or proficiency tests in accordance, where available, with internationally accepted protocols, and informing the Commission and the Member States of the results and follow-up to the inter-laboratory comparative testing or proficiency tests.***
- *Art. 94.2.l* ***Where relevant for their area of competence, cooperate among themselves and with the Commission, as appropriate, to develop methods of analysis, testing or diagnosis of high standards.***

Sub-activity 1.1 *(*Provision of up-to-date information to NRLs*)*

Objectives:
Provision of up-to-date information to NRLs

Description:
Technical, legal and scientific information is provided to NRLs and official routine laboratories as well as to official laboratories from third countries. The information is made available on the internet (FIS-

VL – permanently up-dated web portal of the EURL), where all relevant information can be found on validated methods, standard substances, reference materials, workshops, stability studies, and many more. Important current information is distributed to a mailing list (information service per e-mail). Moreover, specific information is provided on request via e-mail and by telephone support.

Expected Output:
Provision of information on analytical methods; publication of methods via the EURL website (following the procedure of the pesticide EURLs); scientific support via e-mail or telephone

Duration:
2019/20 and ongoing

Sub-activity 1.2 *(*Support to NRLs by provision of reference materials (reference standards and matrix reference materials)*)*

Objectives:
Support to NRLs by provision of reference materials (reference standards and matrix reference materials)

Description:
Suitable (pure) reference standards as well as incurred and blank reference materials are the basis of a successful method development, method validation and method performance control. Especially incurred matrix reference materials are essential for a harmonised residue control and comparable results. The EURL already has a large stock of incurred matrix reference materials, which are continuously controlled for stability, as well as standard substances. Nevertheless, several reference materials are still missing, and the need for additional materials, either due to their relevance for residue control or due to NRL requests, is permanently monitored. Moreover, the need for the substitution of already available reference materials due to instabilities is taken into account.

The production of new reference materials is planned according to these considerations as well as with respect to the future use of the materials in proficiency tests and the provision of incurred material to official control laboratories (OCL) for scientific purposes. Furthermore, it is an ongoing task to investigate possible new veterinary drugs, their metabolisation or degradation products.

Additionally, the availability of reference standards as well as of adequate internal – preferably isotopically labelled – standards is evaluated. Reference standards in stock are controlled according to the concept finalised and presented in the 2018 working period as far as feasible. In addition, we purchase substances, metabolites or internal standards which we presume to be required.

Reference standards (“standard substances”) and incurred reference materials are provided to NRLs and official control laboratories in third countries upon request (ordering form developed in 2016/17 and provided to the OCL via the FIS-VL).

Based on the above-mentioned considerations, the following animal studies for the production of incurred matrix materials are planned in 2019/20 :

Beta-agonists in hair of cows (multi-annual study; to be finalised in 2021)
Fluralaner in egg
Salinomycin in egg and tissue
Diclazuril in egg and tissue
Morantel in milk and tissue

Nitroimidazoles in plasma, serum and whole blood

Because of difficulties in obtaining the official permission for conducting animal experiments due to changed regulations, the following studies from 2018 were delayed :
Coccidiostats in laying hens
Beta agonists in urine and tissue of calves
Treatment with amitraz in combination with the above-mentioned animal studies

These studies will be finalised in 2019.

The production of the materials includes the treatment of the animals, the collection (if necessary including the slaughtering of the animals) of the materials and a pre-characterisation of the residues.

In addition, the production of reference materials from "raw" incurred sample materials is planned. The production process covers the following steps: dilution of the material if necessary, homogenisation of the material, aliquotation and packaging of test portions, tests on homogeneity and stability (short-term and mid-term), tests on hydrolysis effects (conjugated residues), tests on extraction efficiency (if applicable).

The following materials will be produced and characterised (cf. 1.3):
NSAID in horse muscle /another species (4 materials; 1 material was homogeneity-tested in 2018*)
Nitroimidazoles in fish
Avermectins in fish
Coccidiostats in egg
Beta-agonists in urine, hair or lung

* Stability testing (short-term and mid-term) for NSAIDs in horse muscle is planned for this period. Stability analyses in the past revealed that some NSAIDs degraded within the first 2 years of storage. Thereafter, they were stable.

Expected Output:
Pre-tested incurred matrix materials for proficiency tests and for scientific purposes; reference materials for NSAIDs in muscle, coccidiostats in egg, avermectins in fish, nitroimidazoles in fish, beta-agonists in hair or lung; support to NRLs/RFLs; cooperation with synthesis laboratories; synthesis of new standards; literature reviews on new substances, purity of selected important standard substances

Duration:
2019/20 and ongoing

Sub-activity 1.3 *(*Organisation and evaluation of proficiency tests and follow-up on result*)*

Objectives:
Organisation and evaluation of proficiency tests and follow-up on result

Description:
The EURL regularly organises 1 - 2 proficiency tests per year with 3 – 4 samples each, covering multiple analytes in different concentrations. The material usually consists of incurred matrix material produced in animal studies and controlled for homogeneity and stability at the EURL.

The evaluation is effected on the basis of a classical z-score (or z_u-score) evaluation and a point-score system. The point-score system includes an overall evaluation of the laboratories' performances with respect to residue control in general based on pre-set requirements (required analytes and required control levels).

Follow-up measures will be carried out - if necessary - in compliance with Commission draft "Protocol for management of underperformance […]" guideline of 2007. An overview of the performances per laboratory and MS in the past few years was established in 2013/2014 and is up-dated regularly.

For 2019/20 the following activities are planned:
Nitroimidazoles and avermectins in fish
Coccidiostats in egg
NSAIDs in muscle
Beta-agonists in hair or lung
Follow-up to the study on multi-residues in milk (end of 2018)

Expected Output:
Final reports on the 2019 / 2020 PTs (planned for nitroimidazoles/avermectins in fish, coccidiostats in egg, NSAIDs in muscle)
Short report on the last PT (beta-agonists) in 2020 (final report and follow-up in 2021)
Assessment of the performance of the NRLs
Assignment of values to the obtained reference materials
Follow-up (questionnaire to participants; support by provision of standard substances, materials, methods, training; provision of additional PT material on request; preparation of test material for x-lateral comparisons on request; report to COM and CA on underperformance)

Duration:
2019 / 2020 (2021)

Sub-activity 1.4 (Cooperation, collaboration and meetings with other EURLs and scientific exchange*)*

Objectives:
Cooperation, collaboration and meetings with other EURLs and scientific exchange

Description:
As a consequence of the EURL evaluation, the Commission stated that EURLs with overlapping or similar responsibilities should agree upon their work more closely. The agreement with the Commission is also indispensable. For this reason at least one meeting of the 4 EURLs for residues and a representative of the European Commission is necessary per year. Moreover, an additional exchange among the EURLs with respect to an agreed strategy, increased efficiency and exploiting synergy effects is required.

Expected Output:
- *Common PT performance criteria*
Completion of the discussion of a harmonised approach on PT evaluation and drafting of an agreed PT-protocol taking into account the individual factors of the EURLs
- *Common EURL website*
Completion of a template for a common website for the residue EURLs and start of the implementation (requirement specifications)

Duration:
2019 / 2020 (2021)

Sub-activity 1.5 *(*Development of analytical methods and validation of analytical methods*)*

Objectives:
Development of analytical methods and validation of analytical methods

Description:
All relevant methods within the scope of the EURL Berlin are available, validated and accredited. Nevertheless, validation activities due to the extension of methods (analytes, matrices), changes in the required fitness for purpose or progress in methods (new techniques, improved efficiency or accuracy) and instrumentation (changes/improvement in instruments) are permanently ongoing.

The transfer of methods to new LC-MS systems and the optimisation potential for sample preparation, enhanced analyte lists and lower decision limits are regularly checked.

In 2019/20 this will concern the following methods:
Anthelmintics in tissue (method extension, optimisation, validation)
Optimisation of a multi-method for NSAIDs in muscle
Multi-coccidiostat screening method in egg in cooperation with Randox (method optimisation, validation)
Coccidiostats in liver (optimisation, validation)
Amprolium in egg (single method optimisation)
Beta-agonists in lung (optimisation, validation if applicable)
Amitraz and metabolites in egg and tissue (single method optimisation and validation; new responsibility on request of COM)
Nitroimidazoles in fish (optimisation)
Avermectins in fish (method optimisation, validation – new instrument)
Further development of multi-screening methods with HRMS (Q-TOF, Orbitrap – data base establishment for targeted screening)
Implementation of an LC / ion mobility / MSMS system and suitability checks for the improvement of methods (e.g. coccidiostats)
Implementation of headspace-GC/MS for the determination of volatile components in standard substances (as part of purity studies)
Participation in proficiency test as part of ongoing method performance check

Based on the results of studies in earlier working periods (2015-2018), validated methods should be checked with incurred material for hydrolysis effects and for extraction efficiency.
Furthermore, validation studies for MRL substances should aim to deliver results down to approximately 0.1 * MRL, as this is the requirement foreseen at the current state of discussion with EFSA (provision of sub-MRL results). Anyhow, the requirements have not yet been fixed and may change.

Expected Output:
Method descriptions, validation reports

Duration:
2019/20 (and ongoing)

Sub-activity 1.6 *(*Analysis of official samples*)*

Objectives:
Analysis of official samples

Description:
Official samples will be analysed on request in cases of disputes between MS.

Expected Output:
Provision of definite results in cases of disputes between MS

Duration:
2019/20 and ongoing

2 TO PROVIDE SCIENTIFIC AND TECHNICAL ASSISTANCE TO NRLs

Please, provided activities related to Regulation (EU) 2017/625:
(Number of Sub-activity boxes can be adjusted by EURL)

- *Art. 94.2.d* ***Coordinating practical arrangements necessary to apply new methods of laboratory analysis, testing or diagnosis, and informing national reference laboratories of advances in this field.***
-
- *Art. 94.2.e* ***Conducting training courses for staff from national reference laboratories and, if needed, from other official laboratories, as well as of experts from third countries.***
-
- *Art. 94.2.g* ***Providing information on relevant national, Union and international research activities to national reference laboratories.***

Sub-activity 2.1 *(*Provision of technical and scientific support to NRLs*)*

Objectives:
Development of analytical methods and validation of analytical methods

Description:
Assistance to NRLs and other official laboratories for the strengthening and harmonisation of residue control (methods, SOPs, QA, QC, validation, legislation, specific practical or theoretical training, PT follow-up) is provided upon request (also see 2.3). In cases of serious underperformance, e.g. in proficiency tests, the EURL also offers a training.

Additional support to NRLs in the form of confirmatory analyses of questionable samples is provided upon request.

Expected Output:
Provision of information on analytical methods; strengthening of official control; improved food safety

Duration:
2019/20 and ongoing

Sub-activity 2.2 *(*Workshop for scientific exchange, dissemination of information and harmonisation of residue control*)*

Objectives:
Workshop for scientific exchange, dissemination of information and harmonisation of residue control

Description:

Two EURL workshop will be organised in the 2019/20 period. The following subjects (among others) will be covered:

- Discussions on revision of Decision 2002/657/EC
- Extension of methods (analytes, matrices, concentration range)
- New instruments and method developments
- Importance of sample preparation (conjugated residues, extraction)
- Evaluation of Proficiency Tests and follow-ups
- Stability testing in matrix and in solution
- ISO 17025:2017, QA measures
- NRCP evaluation and information on substance groups
- Presentations by the NRLs
- Practical training / tutorials on specific topics
- Topics according to suggestions by NRLs (collected in surveys conducted at the end of the workshops, or specific topics asked for in additional queries)

The evaluation of the annual EURL work programme as well as the forthcoming work programme will be treated and further specific questions will be discussed depending on the needs of the participants.

Expected Output:
Scientific exchange, workshop reports

Duration:
2019/20 and ongoing : annually 2-3 days

Sub-activity 2.3 *(*Organisation of training, provision of suitable methods, support in implementation and comprehensive validation*)*

Objectives:
Organisation of training, provision of suitable methods, support in implementation and comprehensive validation

Description:
- *Training courses for strengthening and harmonisation of residue control*
Information on methods, SOPs, QA, QC, validation, legislation as well as specific practical or theoretical training are provided upon request to NRLs and official routine control laboratories (also see 2.1). In cases of serious underperformance, e.g. in proficiency tests, the EURL also offers a training.

A practical training is always part of the annual workshop. Additional individual trainings are agreed at short notice with the NRLs in the framework of the EURL's possibilities and capacities (on average provision of in total 10 working days of training per year).

For 2019/20 so far, a training on HRMS / TOF has been requested.
Furthermore an NRL expert meeting on the experience of HRMS (TOF, Orbitrap) users will be organised in 2020.

Expected Output:
Training upon request; provision of information on analytical methods; strengthening of official control; improved food safety

Description:
- *Harmonisation of residue control for ß-agonists and coccidiostats*
In the 2015/16 work programme, a common method for the determination of acidic and basic NSAIDs in milk was developed, transferred to a new and more sensitive mass spectrometer and submitted to an in-house validation. Due to the interest of several NRLs in the implementation of this method, the milk method was, in addition to the in-house validation, validated in a collaborative study based on an orthogonal experimental design plan. The concept for this kind of validation was developed by the BVL and Quo data, successfully tested on the national level and then successfully transferred to an international level.

The NRLs expressed their interest in participating in this kind of studies also in future, especially beta-agonist and coccidiostat detection was of interest. Hence in the 2018 period a study for the determination of beta-agonists in liver was started and will be finalised in 2019.

Another study for the determination of coccidiostats in eggs will be started by the end of 2019.
Prior to the validation study, an introduction into the validation approach and a method demonstration are planned in the form of a two-day training for interested participants from the NRLs (limited number of participants). Afterwards, the method shall be transferred to the NRLs and pre-tested before the start of the validation study.

The expected benefits are multiple: for the participating NRLs, a complete in-house validation study will be performed, and for the method itself, robust method performance characteristics will be determined. This means that a contribution to a harmonised residue control in the EU in the form of a comprehensive multi-method for beta-agonists (according to Art. 34 (2)a of Regulation 2017/625/EC) will be achieved .

Expected Output:
Beta-agonists
2019: Implementation of the study (prepared in 2018) and evaluation of the results (individual and summary validation reports); final description of a comprehensively validated method for the determination of beta-agonists in liver and publication of the method
Coccidiostats
2019: Information of the NRLs and training; control of successful transfer of the method; preparation of the validation study
2020:
Implementation of the study and evaluation of the results (individual and summary validation reports); final description of a comprehensively validated method for the determination of coccidiostats in egg and publication of the method

Duration:
2019 / 2020 (ongoing with additional methods)

Sub-activity 2.4 *(*Supporting visits to NRLs*)*

Objectives:
Supporting visits to NRLs

Description:

In general, one to two European MS NRLs per year are visited after consultation with the Commission on necessity. Scientific information and technical support in the form of methods, SOPs etc. and/or a specific training (practical or theoretical) are provided, and specific problems like underperformance in PTs, QA, QC, validation, legislation etc. are discussed.

For 2019/20 visits to 4 NRLs are planned.

Expected Output:
Reports on NRL visits

Duration:
2019/20 (2-3 days per visit / depending on requests and performance in PTs)

Sub-activity 2.5 *(*Provision of information on new developments and relevant research activities to NRLs*)*

Objectives:
Provision of information on new developments and relevant research activities to NRLs

Description:
The EURL routinely evaluates the need for additional information with respect to the improvement and harmonisation of food control. Based on the suggestions of NRLs and third countries as well as on surveys on our own market and of scientific literature, specific research and study activities are started.

For 2019/20 the following projects are planned:

- Establishment of an ion mobility mass spectrometer (cf. 1.5)
- Establishment of a headspace GC-MS system for the detection of volatile components in pure standards (cf. 1.5)
- Participation in a pilot study for the purity assessment of standard substances (BIPM/CCQM/OAWG)
- Pharmacokinetics in egg: investigation of withdrawal periods and excretion behaviour of toltrazuril after animal study

- *Development of an online validation tool (multi-annual)*
CD 2002/657/EC offers the possibility of carrying out an efficient matrix-comprehensive validation using experimental design plans. Since this approach requires some experience, laboratories often avoid the application of this approach and use the less efficient and less robust classical validation approach instead. Given that many NRLs expressed their interest in the availability and use of a validation tool, this project shall be realised in order to support the NRLs, to harmonise validation procedures and for the sake of scientific progress.

In 2018 a feasibility study was discussed during the workshop; functional and requirement specifications were discussed with interested NRLs and a preliminary template was developed. The suggested procedures for the use of this tool will be tested with voluntary NRLs in the 2019/20 working period.

- *Follow-up on survey on salicylic acid residues in milk from 2018*
Salicylic acid residues are often present in milk samples collected and analysed in the framework of the NRCPs. These residues can be above the MRL of 9 µg/kg, even though a treatment with this drug was unlikely and not indicated. Hence the residues probably originate from a natural background (e.g. feeding conditions). In order to get an overview of possible residue levels in milk of untreated animals, a larger number of samples from different member states was analysed. The results of the measurements will be discussed with the member states. If required, additional samples will be analysed.

- *Residue levels in egg after treatment of hens (continuation from 2018, cf. 1.2)*
Started pullets can be legally treated with coccidiostats, which are not allowed for use in laying hens. It was reported by OCLs that – depending on the time span between the treatment of started pullets and the first production of eggs – elevated residue levels in eggs can occur after a legal treatment of the hens.
This finding shall be verified. The animal study described in sub-activity 1.2 is designed with regard to this issue. Egg samples from this study will be analysed and the data will be evaluated.

Expected Output:
Experiences with the use of an on-line validation tool; information on natural residue levels of salicylic acid in milk; residue levels of coccidiostats in egg after legal treatment of pullets; control of the suitability of the method for purity assessment

Duration:
2019/20 and ongoing

3 TO PROVIDE SCIENTIFIC AND TECHNICAL ASSISTANCE TO THE EUROPEAN COMMISSION AND OTHER ORGANISATIONS

Please, provided activities related to Regulation (EU) 2017/625:
(Number of Sub-activity boxes can be adjusted by EURL)

- *Art. 94.2.f* ***Providing scientific and technical assistance to the Commission within the scope of their mission.***

- *Art. 94.2.h* ***Collaborating within the scope of their mission with laboratories in third countries and with the European Food Safety Authority (EFSA), the European Medicines Agency (EMA) and the European Centre for Disease Prevention and Control (ECDC).***

- ~~*Art. 94.2.i* ***Assisting actively in the diagnosis of outbreaks in Member States of foodborne, zoonotic or animal diseases, or of pests of plants, by carrying out confirmatory diagnosis, characterisation and taxonomic or epizootic studies on pathogen isolates or pest specimens.***~~

Sub-activity 3.1 *(*Technical and scientific assistance to the European Commission*)*

Objectives:
Technical and scientific assistance to the European Commission

Description:
Support and assistance (e.g. conducting surveys, additional reports, meetings, provision of measurement capacities, etc.) will be provided to the European Commission upon request.

The following activities are fixed for the 2019/20 period:

- *Revision of Commission Decision (CD) 2002/657/EC*
At the meeting of the Expert Committee on Residues of Veterinary Medicinal Products in June 2015, the MS indicated that they considered a review of Commission Decision (CD) 2002/657/EC as necessary. Subsequently the EURLs were asked to support DG SANTE in this process. In September 2015 the EURLs carried out a survey among the NRLs on their view on required changes in this Decision. An evaluation of this survey was done and led to a working paper. A finalised agreed draft was submitted to COM by the beginning of 2018. In the course of 2018 this draft was revised based on suggestions from COM and the NRLs, which resulted in a final version by the end of 2018.
In 2019 this version will be discussed with the NRLs. A final version will be prepared in 2019 including the comments from MS and COM.

Subsequently – if needed – the preparation of practical guidance documents will be started on certain subjects such as : 1- for validation of screening methods ; 2- for validation of confirmatory methods ; 3- for extension of validated methods.

- *Analysis of national residue monitoring plans of the MS*

- *Publication of a list of the national reference laboratories designated by the Member States in accordance with Art. 100(1)*

Expected Output:
Report on NRCP evaluation; current NRL-list; working paper on Rev. of CD 2002/657/EC

Duration:
2019/20 and ongoing

Sub-activity 3.2 *(*Collaboration with European and international organisations (EFSA, EMA, JRC/IRMM, Eurachem, BIPM, CEN, ISO, …) and third countries (international networking and scientific exchange*)*

Objectives:
Collaboration with European and international organisations (EFSA, EMA, JRC/IRMM, Eurachem, BIPM, CEN, ISO, …) and third countries (international networking and scientific exchange

Description:
3.2.1
Technical and scientific support will be provided to the Commission institutions DG JRC (IRMM), EMA and EFSA. The cooperation with other international organisations is an ongoing task and will be intensified as far as possible.
At the moment the EURL is participating in EFSA VDR network meetings, directly cooperating in the Codex Alimentarius Committee CCRVDF, supporting IAEA activities (training, method data base), as well as in the CCQM working group OAWG of the BIPM. Furthermore, input to ISO working groups for standardisation, CEN working groups for standardisation and CCMAS is given via BVL representatives.

Expected Output:
Internal documents, guidance documents for and assistance to EFSA, method evaluations for EMA

Description:
3.2.2
The collaboration with official control laboratories in third countries is an important activity in order to strengthen food control in these countries and to achieve standards that offer equivalent guarantees to those applied in the European Union.

Hence the same support as to NRLs listed under 1.1, 1.2., 2.1, 2.3 and 2.5 is provided.
Furthermore, experts from third country laboratories are invited to participate in EURL workshops (2.2) and proficiency tests (1.3). Additional assistance (e.g. reference materials, standard substances) is provided upon request.

Long-standing cooperations exist among others with Albania, Serbia, Macedonia, Russia, China, Morocco, Canada and Thailand. The Veterinary Public Health Laboratory (VPHL), Bureau of Quality Control of Livestock Products (BQCLP) and Department of Livestock Development (DLD) in Thailand is the ASEAN Food Reference Laboratory for Veterinary Drug Residues. Hence it is the key contact for the food control laboratories in the ASEAN countries. In 2017 a first common training/workshop for ASEAN countries was organised under participation of the EURL Berlin, which shall be repeated in 2019.

Support (analytical methods, SOPs, QA, QC, validation, legislation, specific practical or theoretical training, PT follow-up) is provided upon request. For 2019 a common workshop with the VPHL for the ASEAN labs on validation is planned.

Expected Output:
Scientific exchange; strengthening of official control in third countries; improved safety of food entering the EU; provision of information on analytical methods; scientific support via e-mail or telephone

Duration:
2019/20 and ongoing

Sub-activity 3.3 *(*Participation in symposia, workshops and seminars for the dissemination of scientific information and scientific exchange*)*

Objectives:
Participation in symposia, workshops and seminars for the dissemination of scientific information and scientific exchange

Description:
In order to fulfil its EURL role as peak of the reference laboratory system, the regular participation in scientific conferences, symposia and seminars is mandatory. On the one hand, a scientific exchange with experienced researchers and food control experts takes place, on the other hand, the EURL's and COM's views on residue control and its implementation can be presented, discussed and shared. Especially the Symposium on Hormone and Veterinary Drug Residue Analysis, the Euroresidue Conference and the RAFA are important platforms for scientific exchange and networking.

For 2019/20 the participation in the Euroresidue Conference, the RAFA and the AOAC Europe meeting is planned.

Expected Output:
Oral presentations; poster presentations; scientific networking

Duration:
2019/20 and ongoing

Sub-activity 3.4 *(*Ensuring a sound and efficient management of the EURL funding cycle*)*

Objectives:
Ensuring a sound and efficient management of the EURL funding cycle

Description:

To ensure a sound and efficient management of the EURL/EURC funding cycle, several reports are to be issued, e.g. the technical and financial reports on the past EURL working periods as well as the cost estimate and work programme for future periods, performance indicators if applicable, etc.

The following activities are fixed for 2019/20:
Financial reports (2018, 2019); technical reports (2018, 2019)
Draft work programme 2021/2x; estimated budget 2021/2x

Expected Output:
Technical and financial reports; work programme and estimated budget

Duration:
2019/20 and ongoing

4 REAGENTS AND REFERENCE COLLECTIONS

Please, provided activities related to Regulation (EU) 2017/625:
(Number of Sub-activity boxes can be adjusted by EURL)

- *Art. 94.2.*j ***Coordinating or performing tests for the verification of the quality of reagents and lots of reagents used for the diagnosis of foodborne, zoonotic or animal diseases and pests of plants.***

- *Art. 94.2.k* ***Where relevant for their area of competence, establishing and maintaining:***
  - ***i. reference collections of pests of plants and/or reference strains of pathogenic agents;***
  - ***ii. reference collections of materials intended to come into contact with food used to calibrate analytical equipment and provide samples thereof to national reference laboratories;***
  - ***iii. up-to-date lists of available reference substances and reagents and of manufacturers and suppliers of such substances and reagents.***

Sub-activity 4.1 *(*Provision of up-to-date lists of available standard substances and matrix reference materials*)*

Objectives:
Provision of up-to-date lists of available standard substances and matrix reference materials

Description:
Suitable (pure) reference standards and incurred reference materials are the basis of a successful method development, method validation and method performance control.

Via the FIS-VL portal, the EURL provides a current list of standard reference substances and available reference materials (necessary for the control tasks within the responsibility of the EURL Berlin). Reference materials and reference standards which are in stock at the EURL are provided to the NRLs on request (see 1.2) and are continuously tested for stability.
As part of a new LIMS (to be purchased in 2019), also new web-based portals are developed to simplify the access of NRLs to the EURL's data base.

Expected Output:
Up-to-date lists of available standard substances and matrix reference materials
Test of newly developed portals

Duration:

2019/20 and ongoing

5 REQUIREMENTS RELATED TO OTHER LEGISLATION

Please specify applicable legislation: ISO 17025, ISO 17043

(Number of Sub-activity boxes can be adjusted)

Sub-activity 5.1 *(*Maintaining accreditation according to ISO 17025 and ISO 17043 (PT-provider)*)*

Objectives:
Maintaining accreditation according to ISO 17025 and ISO 17043 (PT-provider)

Description:
The QM system according to ISO 17025 is continuously maintained, developed further and was extended to an accreditation as proficiency test provider according to ISO 17043 in 2017. Costs (including fees for annual visits of the accreditation body) are not explicitly included.

Anyhow the participation in PTs by commercial providers is necessary to document and prove our proficiency outside the framework of our own proficiency tests. This is essential to fulfil the requirements of EA and of the German accreditation body (DAkkS). Furthermore, this way, PT providers can be checked for quality (to give recommendations to NRLs).

Participation depends on the range of PTs offered by commercial providers. So far the programmes for 2019/20 have been published only in parts, so that we cannot state yet in how many and in which PTs we will participate.

Expected Output:
Certificates by PT providers; successful accreditation body audits

Duration:
2019/20 and ongoing

Sub-activity 5.2 *(*Preparation for accreditation according to ISO 17034 (reference material producer)*)*

Objectives:
Preparation for accreditation according to ISO 17034 (reference material producer)

Description:
Certified reference materials are the key tool to an international comparability of measurement results. The EURL has long-term experience in the preparation of incurred reference materials (i.e. materials produced in animal studies) for proficiency testing, anyhow, so far, not with the aim of providing certified material according to ISO 17034.

Based on the existing competence, the present quality management system shall be adopted aiming at the preparation of an accreditation as reference material provider.

This would be a very useful supplement to the status of the BVL as designated institute for residues of veterinary drugs in food and its ability to provide SI-traceable reference values for these materials (based on its entries in the calibration and measurement data base of the BIPM). The accreditation could not only support the EU-wide comparability of measurement results, but also the world-wide acceptance of measurement results.

Expected Output:
Revised quality management system ready for accreditation

Duration:
2018 / 2019 / 2020

REMARKS

(if necessary)

WORK PROGRAMME OF EURL FOR GROWTHPROMOTING AGENTS, SEDATIVES AND MYCOTOXINES IN FOOD OF ANIMAL ORIGIN

PERIOD: 2019/2020

Version 2.0
(date :____20190122_____)

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SUMMARY

INTRODUCTION

Legal functions and duties
The functions and duties of the EU Reference Laboratory are described in Article 94 of Regulation (EU) 2017/625 of the European Parliament and of the Council of 7 April 2017 (Official Journal of the European Union L 95/I, 7.04.2017, pp 1-141).

The general objective of the Commission for the period 2019-2020 is "to contribute to a high level of protection for consumers and the environment while favouring competiveness and the creation of jobs[1]". This general objective is elaborated in four operation objectives which are the foundation of the EURL work programme for 2019-2020.

The EURL work programme is divided in 4 parts, linked to the five operation objectives (last objective not applicable). For each operational objective individual tasks have been formulated which are described in more detail for the two year period.

Structure Work programme EURL for residues based on OCR 2017/625 article 94

1. To ensure availability and use of high quality methods and to ensure high quality performance by NRLs.

1.1 Provide NRLs with details and guidance on the methods of laboratory analysis, testing or diagnosis, including reference methods. (a)

1.1.1 Updating the EU RL website

1.2 Follow up on requests from NRLs for providing analytical standards (b)

1.3 Organisation of proficiency tests and follow up on the results (c)'

1.3.1 Organisation of PTs

1.3.2 Follow up on and communication of the PT results

1.3.3 Preparation of incurred samples

1.4 Cooperation and meetings with other EURLs (l)

1.5 Development and validation of analytical methods (l)

1.6 Analysis of official samples (b)

2. To provide scientific and technical assistance to NRLs

2.1 Providing technical and scientific support to NRLs (d)

[1] Commission implementing decision of 24.7.2015 on the adoption of the work programme of the Commission for the years 2015 and 2016 and on the financing of the Union contribution to the European Union Reference Laboratories

2.2 Organisation of workshops (e)
2.3 Organisation of training courses (e)
2.4 Visits of NRLs (d and e)
2.5 Providing relevant information on national, Union and international research activities to NRLs (g)
2.6 Updating and publication of the list of NRLs

3. To ensure scientific and technical assistance to the European Commission and other organisations

3.1 Technical and scientific assistance to the Commission (f)

e.g. 3.1.1 Analysis of National residue monitoring plans of the MS (f)

e.g. 3.1.2 Conducting surveys at the request of COM(f)

3.2 Collaboration with European and international organisations (EFSA, EMA, Eurachem, CEN, ISO, …) and Third Countries (h)

3.3 Participation in symposiums, workshops and seminars for the dissemination of scientific information. (h)

3.4 To ensure a sound and efficient management of the EURL/EURC funding cycle.

3.4.1 EURL work programmes

3.4.2.EURL reports

3.4.3 EURL performance indicators

4. Reagents and reference collections

4.1 Up to date lists of available reference substances and reagents and of manufacturers and suppliers of such substances and reagents (k)

Regulation (EU) 2017/625 Art 94(2):
European Union reference laboratories designated in accordance with Article 93(1) shall be responsible for the following tasks insofar as they are included in the reference laboratories' annual or multiannual work programmes that have been established in conformity with the objectives and priorities of the relevant work programmes adopted by the Commission in accordance with Article 36 of Regulation (EU) 652/2014:
(taking into account Art 147 of (EU) 2017/625)

1 TO ENSURE AVAILABILITY AND USE OF HIGH QUALITY METHODS AND TO ENSURE HIGH QUALITY PERFORMANCE BY NRLs.

Please, provided activities related to Regulation (EU) 2017/625:
(Number of Sub-activity boxes can be adjusted by EURL)

- *Art. 94.2.a* ***Providing national reference laboratories with details and guidance on the methods of laboratory analysis, testing or diagnosis, including reference methods.***

- *Art. 94.2.b* ***Providing reference materials to national reference laboratories***

- *Art. 94.2.c* ***Coordinating the application by the national reference laboratories and, if necessary, by other official laboratories of the methods referred to in point (a), in particular, by organising regular inter-laboratory comparative testing or proficiency tests and by ensuring appropriate follow-up of such comparative testing or proficiency tests in accordance, where available, with internationally accepted protocols, and informing the Commission and the Member States of the results and follow-up to the inter-laboratory comparative testing or proficiency tests.***

- *Art. 94.2.l* ***Where relevant for their area of competence, cooperate among themselves and with the Commission, as appropriate, to develop methods of analysis, testing or diagnosis of high standards.***

Introduction

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 in analytical methods and new technologies will have to be implemented. Based on the results of research activities within the EURL-NRL network, and/or outcome of the risk-based surveillance studies of memberstates methods will have to be re-evaluated on specific aspects. Adequately validated methods for all analyte-matrix combinations included in the list of Recommended Concentrations for Control (CRL Guidance paper 2007), or for new MRPLs or the RPA-values to be set will be maintained and made available on request. The EFSA document with regard to toxicological limits on veterinary medicinal products in food of animal origin will also be included in setting

priorities. Priorities are set on the basis of input by the Commission, discussions with the NRLs, e.g. during annual workshops and the EURLs view on important scientific and technical trends and innovations.

New methods will be developed for new classes of compounds, not yet included in the CRL-guidance paper or current monitoring plans, or for analytes for which methods have proven to be inadequate. Developing and implementing efficient strategies for the control on natural hormones will remain an important research topic during the coming years. This includes four different classes of compounds: the classic natural hormones, the so-called minor androgens that can be present or formed in biological samples, protein hormones and substances that can be foodborne or stress related (e.g. corticosteroids). This part of the work programme is partly based on the EURL Reflection paper from 2014 and the foreseen update of the Reflection paper in 2018.

Sub-activity 1.1 *Provide NRLs with details and guidance on the methods of laboratory analysis, testing or diagnosis, including reference methods. (a)*

1.1.1 *Updating the EU RL website*

Objective: To have a customer friendly informative website for NRLs and the EC.
In 2018 the RIKILT EU RL website was renewed. Standard Operating Procedures for methods of analysis were placed on the public part of the website for a number of analyte-matrix combinations. The website will be updated with new analytical methods. SOPs will be translated in English (request of NRLs) and placed on website. The EURL website will also be updated with current legislation and EFSA and Commission documents.

Expected output: Publication of, legislation and documents, analytical methods and research reports on the public EURL website.

Duration: 2019 and 2020 ongoing whole year

Sub-activity 1.2 *Follow up on requests from NRLs for providing analytical standards (b)*

1.2.1 *Collection of standard substances and deuterated internal standards*

Objectives: Provision of standard substances including storage, administration, documentation and shipment.
Description: Acquiring essential standards and internal standards and metabolites. When necessary and possible, selected compounds will be purchased or (custom) synthesised. Critical consumables such as antibodies eg. will be made available for NRLs.

Expected Output: Ampoulated reference (internal) standards, antibodies (in 2019 production and making available of antibodies for rBST analysis) and reference materials available through EU RL webshop

Duration: 2019 and 2020 ongoing whole year

Sub-activity 1.3 *Organisation of proficiency tests and follow up on the results (c)*

1.3.1 *Organisation of PTs*

Objectives: Organisation of PTs for routinely used method and organisation of research study for new analyte or new analyte-matrix combinations
Description:
2019:

a. Research study Continuation A3 and A4 compounds in muscle started October 2018
b. PT Thiouracil (A2) in urine (bovine and/or sheep)
c. PT Zeranol (RALs) in urine (bovine)

2020: Proposed depending on outcome of consultation with NRLs in 2019

a. PT Methyltestosterone in urine
b. PT Nortestosterone(ester) in hair and/or urine
c. PT Trenbolone in urine

Expected Output:
PT reports
Duration: 2019 and 2020

1.3.2 Follow up on and communication of the PT results to NRLs and if needed to European Commission

Objective: The follow up protocol of the EU DG Santé for proficiency testing is implemented in 2018. This protocol is followed for every PT. The 3 EU RLs for residues will prepare a harmonised protocol for assessing PT performance of NRLs. And a template to inform the EC will be prepared.

1.3.3 Preparation of incurred samples

Objectives: To produce incurred sample materials for PT and research studies.
Description: Perform animal experiment and collect sample materials to be used
Expected Output: Incurred materials for use in PTs and research studies
Materials as Quality Control sets for NRL to be used for ongoing method evaluation
Duration: 2019 and 2020

1.4 Cooperation and meetings with other EU RLs (1)

Objective: To attend meeting with other EURL. Either organised by DG Santé or organised by 3 EU RLs for residues. To coordinate, harmonize the work of the EU RL and to work on revision of legislation and guidance documents.

1.4.1 Establishing a web portal for the 3 EU RLs for residues. Filling this with the appropriate information. To be implemented in 2019. Further filling and maintenance in 2020

1.4.*2 Harmonisation of proficiency test protocols for assessing PT performance of NRLs*: a common protocol for the residues EU RLs. Developing and testing in 2019. Further implementation 2020.

1.4.3 Attend workshops of EURLs in Fougères and Berlin and meetings organised by DG Santé
Both 2019 and 2020 1x workshop Berlin and 1x workshop Fougères. Attend 3 meetings in Brussels organised by DG Santé.

1.5 Development and validation of analytical methods

1.5.1 Method development

Objectives: To develop methods for new emerging risk compounds for known compounds in different matrices and species.

Description:

a. For a number of naturally occurring compounds there is still no possibility to distinguish between exogenous or endogenous origin, eg. zeranol, prednisolone, thiouracil and BST. These compounds are difficult to analyse using gas chromatography coupled to IRMS, the approach used for testosterone and oestradiol. Liquid chromatography is the separation technique of choice for these compounds. Coupling LC to IRMS could be the solution to this problem. 2018 the pre-work involved in the separation of compounds using liquid chromatography was done. However, due to delays at the supplier no interface was tested. In 2019 the interface for LC-RMS for coupling LC to IRMS will be tested and if fulfils the criteria and suitability tests will be acquired. Method development for eg. zeranol and thiouracil and other synthetic natural growth promoters in urine will be implemented.

   In 2020 further method development will be done for more natural occurring compounds..

b. In 2017 research into the use of new state of the art full scan high resolution GC-mass spectrometry for multi analyte steroid detection and untargeted analysis was started. The preliminary studies into the feasibility of this technique for steroid analysis showed good results. In 2018 the high resolution method for the detection of steroids in urine was extended. A libraries was built for GC-Q-orbitrap MS analysis. In 2019 a workflow for untargeted analysis will be developed. The new workflow/method aims at detecting forbidden substances at low levels using an untargeted approach. The possibility of quantification of the compounds will also be studied.

c. Sampling on farm of live animals is difficult. For a number of compounds this is the best time (risk based sampling) to test animals. Inspectors have to wait for animals to produce urine and for blood sampling veterinarians are needed. Sampling of blood droplets is easier to perform, quick and can also be done by inspectors. Bloodspot cards can be archived and stored easily and do not take up much space. In 2018 the proof of principle for the steroid-esters (four testosterone esters in blood was developed and validated. In 2019 this method will be extended with more steroid esters and other growthpromoters. In 2020 this method will be validated.

d. For several years growth hormone and peptides are being used to increase muscle mass in humans. Farmers “learn” from athletes and these compounds can potentially be misused in animal husbandry. Some peptides have anabolic properties (GHRP’s) others inhibit the growth inhibition (myostatine inhibition).

   On the black market there are peptides available who claim to inhibit growth inhibition. At the moment there are no methods available to detect these peptides. On the basis of literature research into the mechanism of these peptides in 2018 a start was made to develop methods and strategies to detect misuse of these peptides. In 2019 the focus will be on the myostatine axis(inhibiting growth inhibition). In 2020 depending on research outcome in 2019 validation will be performed on the developed method.

e. A number of laboratories use ligand binding assay approaches for residue testing. These tests are the method of choice when performing on-site (on farm or at the slaughterhouse) testing. Although these tests are cheap and fast they are not able to detect all required compounds and therefore there is a realistic risk in producing false negative results. For the analysis of multiple compounds at regulatory levels mass spectrometry (MS) should be the method of choice. Thanks to recent developments in miniaturization of mass analysers, (trans)portable mass spectrometry can be used to replace ligand binding assay and can be used for on-site testing. In 2020 GC-MS methods using (trans)portable MS will be developed for residue analysis.

Expected output:
2019:
LC-IRMS method for natural occurring compound, zeranol eg.
GC-Q-Orbitrap workflow for untargeted screening of steroids
Extended dried bloodspot method for more testosterone, nortestosterone and boldenone esters in blood.
Method development for myostatine inhibition compounds
2020:
LC-IRMS validation of method for zeranol
Further method development for more natural occurring compounds
Continuation of method development for peptide/protein growthpromoters depending on outcome and progress 2019.
Mobile MS pilot at point of care, first applications for detection of residues using (trans)portable mass spectrometry.

1.5.2 Maintenance or extension of existing analytical methods
Objectives: Analytical methods need re-validation or extension with new compounds when MRPL or RPA changes or in view of the EFSA guideline or in view of more quantitative data collection for EFSA. In 2019 the methods below will be either (re)validated or extended.

Description:
2019:

a. In 2017 a profiling analytical method for screening of thiouracil in bovine urine was developed using a biomarker approach. In 2018 this method was biologically validated with urine samples. This to check the hypothesis of the biomarker. In 2019 . the method will be validated according to EU 2002/657 CD in porcine urine.
b. In 2018 the method was validated for natural occurring IGF-1 forms. Validation of synthetic forms of IGF-1 using LC-MS/MS will be done in 2019.
c. Validation of SOP 1242 for steroids in bovine for different species, eg. poultry, fish, rabbit, horse, sheep.

2020:

a. Multiclass LC-MS/MS method for A1-A6 Directive 96/23/EC). NRLs more and more combine different groups of analytes. To assist the NRLs existing methods will be extended with compounds from A1-A6 (if possible) to make possible to do one analysis for these combined groups.
b. Validation of DBS method from 2019
c. GC-Q-Orbitrap validation

Expected Output:
2019:

Validated SOP for thiouracil discrimination and validation file

Validation file different forms of synthetic IGF-1 in serum
Extended SOP1242 for meat of different species

2020:

Extended SOP for multi group analytical method using LC-MS/MS
Validated DBS method
GC-Q-Orbitrap validation

Duration: 2019 and 2020

1.6 Analysis of official samples
Objective: To help NRLs with confirmatory analysis on individual sample basis. Performing arbitration analysis in case of dispute.
Description: Analysis of samples of NRLs for confirmation when technical problems arise in an NRL and/or when there is a dispute on sample analysis results or in case of arbitration.
Expected Output:
Analysis report
Duration: Ongoing 2019 and 2020, AdHoc depending on request of NRL.

2 TO PROVIDE SCIENTIFIC AND TECHNICAL ASSISTANCE TO NRLs

Please, provided activities related to Regulation (EU) 2017/625:
(Number of Sub-activity boxes can be adjusted by EURL)

- *Art. 94.2.d* ***Coordinating practical arrangements necessary to apply new methods of laboratory analysis, testing or diagnosis, and informing national reference laboratories of advances in this field.***
-
- *Art. 94.2.e* ***Conducting training courses for staff from national reference laboratories and, if needed, from other official laboratories, as well as of experts from third countries.***
-
- *Art. 94.2.g* ***Providing information on relevant national, Union and international research activities to national reference laboratories.***

2.1 Providing technical and scientific support to NRLs (d)

2.1.1 Studies to detect abuse of (semi)- natural hormones

Objective: Based on the EURL Reflection Paper (2014), priorities for research are set together with the NRLs.
Description: In 2018 the reflection paper was extended with chapter on IGF-1 and updated for chapter of (r)BST. In 2019 the whole paper will be revised and updated with relevant new scientific research and peer reviewed articles. This new reflection paper will be used to set research priorities for 2020 amongst others.
Expected output: Update Reflection Paper report
Duration:1 year

2.1.2 Trends in growthpromoter use.

Objective: To have insight in new risks and trends in growthpromoter use.
Description: The field of growthpromoter is constantly changing. Laboratories need to be prepared for new compounds being used eg. designer steroids, protein growthpromoters and ecdysteroids. The prepare for this a literature research also including internet search will be performed in which also human steroid/doping use will be searched to come to having a view on new trends and compounds. It is also known that growthpromotors are present in plant products and in insects Ecdysteroids), literature search into these compounds and possible misuse will be included.
Expected output: 2020 report on new risks and trend in growthpromoter use.

2.1.3 Identification of new compounds

Objectives: Identification of new growthpromoting compounds in preparations and/or supplements and feed (using analytical techniques).
Description: When preparations are found or new information is gathered on new compounds being misused the identity of such compounds can be elucidated within this activity.
Expected Output: identification of new compounds, illegally used as growth which is published on the EURL website and which is communicated to the NRLs.
Duration: 2019 and 2020 ongoing on ad hoc basis

2.1.4 Analytical support
Objective: to help the NRLs and OFL with technical problems on the analysis.
Expected output: 2019 and 2020 upon request by NRLs. Advice and/or analysis (for analysis see 1.6)

2.15 Documentation and information services
Objectives: 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.
Description: The EU-RL-website is maintained. The EU-RL website will be maintained with continued efforts to further implement its use within the EU-NRL/OFL network.
The database with EURL literature inclusive scientific reports, will be maintained as a source of information for EU RLs and NRLs .
Extension and promoting use of EU-RL web forum for information exchange.
Expected Output: Available information on website
Duration: ongoing 2019 and 2020

2.2 Organisation of workshops (e)

Objectives: Organisation of an annual workshop to inform NRLs on new methods, new legislation ao and discuss work programmes and PTs. To have information exchange between the NRLs.
Description: Memberstates and a selected number of third countries come to RIKILT for information exchange and discussion on new topics in the growthpromoter field
Expected Output: 2019 and 2020
Information exchange, Workshop report
Duration: 2-3 days

2.3 Organisation of training courses (e)

2.3.1 Individual based training

Objective: Two or three short visits from NRL scientists to EURL RIKILT to be trained in an analytical method.

2.3.2 Organisation of an additional group training for NRLs or OFLs on analysis of growthpromoters. This training will be organised if a minimum of 5 participants is interested and if subjects are available for which the NRLs want to receive more in depth training.

2019: rBST in serum with LC-MS/MS

2020: thiouracil markers in urine with LC-MS/MS

2.3.3 Training on method validation for DG Santé (former FVO) in 2019

Objective: To train auditors from DG Santé (former FVO) on laboratory validation.

Expected output: 2.5 day training course for 8 auditors

2.4 Visits of NRLs (d and e)
Objective: Missions to NRLs, visit to NRLs in member states, 2 per year. 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, or analytical support. In 2019 Estonia will be visited as the laboratory moved to a different place and staff changes have occurred. Also the NRL of Italy will be visited. In 2020 Portugal will be visited as there is a new laboratory and Greece.
Expected Output:
- visit reports

2.5 Providing relevant information on national, Union and international research activities to NRLs (g)
Objective: This objective is already discussed in 1.1.1., EU-RL website and 2.1.5 Documentation and information service.
Expected Output: Up to date website with SOPs, Legislation, Guidance documents, documentation etc.

2.6 Updating and publication of the list of NRLs
Objective: To have an updated list of NRLs in the competence field of our EURL. This list will be published on the website. Changes in institutes, contact names etc. will be updated when received by EURL. Annually during the workshop the NRL are requested to check and if necessary update the information.

3 TO PROVIDE SCIENTIFIC AND TECHNICAL ASSISTANCE TO THE EUROPEAN COMMISSION AND OTHER ORGANISATIONS

Please, provided activities related to Regulation (EU) 2017/625:
(Number of Sub-activity boxes can be adjusted by EURL)

- *Art. 94.2.f* ***Providing scientific and technical assistance to the Commission within the scope of their mission.***

- *Art. 94.2.h* ***Collaborating within the scope of their mission with laboratories in third countries and with the European Food Safety Authority (EFSA), the European Medicines Agency (EMA) and the European Centre for Disease Prevention and Control (ECDC).***

- *Art. 94.2.i* ***Assisting actively in the diagnosis of outbreaks in Member States of foodborne, zoonotic or animal diseases, or of pests of plants, by carrying out confirmatory diagnosis, characterisation and taxonomic or epizootic studies on pathogen isolates or pest specimens.***

3.1 Technical and scientific assistance to the Commission (f)

3.1.1 *Objective: Revision Commission Decision 2002/657 EC*

The process of revising Commission Decision 2002\657 has started in 2016. Under the 2016-2017 work program a first draft revised version of CD. 2002/657/EC was prepared. The first draft was prepared in 2018. In 2019 this will be discussed with the NRLs. A final version will be prepared in 2019 including the comments from MS and COM. Subsequently – if needed – the preparation of practical guidance documents will be started on certain subjects such as : 1- for validation of screening methods ; 2- for validation of confirmatory methods ; 3- for extension of validated methods.

Expected output: In 2019 the final draft of the new proposal will be prepared together with EURLs in Berlin and Fougères.
For 2020 a small amount of hours is budgeted for finalising the revision and in case new criteria are challenged to conduct experiments to determine if these challenges are rightful or false .

3.1.2 Analysis of National residue monitoring plans of the MS (f)

Objective: To evaluate the NRCP of the memberstates.
Evaluation of the annual national control plans for the member states.
Expected output: Combined report with FVO and EURLs for residues in 2019 and 2020

3.1.3 Upon request of the Commission support through information on analytical methods or through surveys among NRLs.

3.2 Collaboration with European and international organisations (EFSA, EMA, Eurachem, CEN, ISO, …) and Third Countries (h)

EC/EURL related co-operation with International Bodies (e.g. AOAC international, Eurachem, Codex, CVMP, TAIEX, EMA, EFSA, JRCs, IRMM, FVO and IAEA) on method validation, analytical methodology, reference materials and performance quality criteria (communication, co-ordination, and harmonisation).

Example given:

3.2.1 When requested, assist FVO as laboratory expert in audits for third countries.

3.2.2 Cooperate in IAEA coordinate research projects as advisor to third countries.

2019 Coordinated research meeting in Botswana

2019: request for support NRCP plan Uganda

3.2.3 Assist EMA with evaluation of analytical methods in registration files.

3.3 Participation in symposiums, workshops and seminars for the dissemination of scientific information. (h)
2019 and 2020: Participation in organising and Scientific Committee of Euroresidue IX congress, May 2020.
2019 and 2020: Presenting oral and poster on scientific research performed within the EURL.

3.4 To ensure a sound and efficient management of the EU RL/EURC funding cycle.

3.4.1 EU RL work programmes
Compilation of an annual work programme and budget forecast

3.4.2.EU RL reports
Compilation of an annual report and cost statement

4 REAGENTS AND REFERENCE COLLECTIONS

Please, provided activities related to Regulation (EU) 2017/625:
(Number of Sub-activity boxes can be adjusted by EURL)

- *Art. 94.2.*j ***Coordinating or performing tests for the verification of the quality of reagents and lots of reagents used for the diagnosis of foodborne, zoonotic or animal diseases and pests of plants.***

- *Art. 94.2.k* ***Where relevant for their area of competence, establishing and maintaining:***
  - ***i. reference collections of pests of plants and/or reference strains of pathogenic agents;***
  - ***ii. reference collections of materials intended to come into contact with food used to calibrate analytical equipment and provide samples thereof to national reference laboratories;***
  - ***iii. up-to-date lists of available reference substances and reagents and of manufacturers and suppliers of such substances and reagents.***

4.1 Up to date lists of available reference substances and reagents and of manufacturers and suppliers of such substances and reagents (k)
Objective: To provide the NRLs with information on available standards and providers
Expected output: A list of reference standard suppliers on the website in 2019
To be updated in 2020.

5 REQUIREMENTS RELATED TO OTHER LEGISLATION

Please specify applicable legislation:
(Number of Sub-activity boxes can be adjusted)

Not applicable

REMARKS