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WORK PROGRAMME of the EU-RL for

ANTIMICROBIAL AND DYE RESIDUES IN FOOD FROM ANIMAL ORIGIN

GROUP SUBSTANCES: B1, A6, B2f, B3e

CONTRACT PERIOD: 01/01/2021-31/12/2022

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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 Veterinary Medicinal Product Residues (VMPRs)

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 in combination with the project 1.4.6 of the VMPR cluster of the 3 EURLs

Over the year 2021: Sub-activity 1.1.1.a
Over the year 2022: 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 to be made available to NRLs and DG-SANTE posted onto the EU-RL website *(http://eurl-fougeres-veterinaryresidues.anses.fr)* (**Output 1**)
Duration: 2021 and on-going in 2022.
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 2021: Sub-activity 1.1.2.a
Over the year 2022: 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 due to improvements of 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 EU-NRLs, for Third Country Official Laboratories (**Output 1**) and Survey of Documentation provided through the years 2021-2022 (**Output 2**)
Duration: 2021 and on-going in 2022
EU-RL staff considered for the task: Scientists + Secretary

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

Over the year 2021: Sub-activity 1.1.3.a
Over the year 2022: Sub-activity 1.1.3.b

Objectives: Follow-up and update of the EU-RL Website in regard to analytical method publication on the Home Page
Description: As a follow-up of a request from the Commission DG-SANTE, publication of technical notices of our EU-RL developed analytical methods will be posted on the public part of our EU-RL website: http://eurl-fougeres-veterinaryresidues.anses.fr together with a table enlisting the available EU-RL methods
Expected Output: Provision of information on analytical methods; update on the publication of the list of EU-RL available analytical methods via the EU-RL website (**Output 1**)
Duration: 2021 and on-going in 2022
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 2021: Sub-activity 1.2.1.a
Over the year 2022: 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: 2021 and on-going in 2022
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 2021: Sub-activity 1.2.2.a
Over the year 2022: 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 upon request
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: 2021 and on-going in 2022
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

Sub-activity 1.3.1.a. / 1.3.2.a. - Provision of Proficiency or Collaborative Testing Studies for MULTI-SCREENING and CONFIRMATION of Authorized and/or Prohibited substances from Group A6, B1, B2f and/or B3e (1 large or 2 reduced PT round each year in a different species/matrix) **for the year 2021**

Sub-activity 1.3.1.a. / 1.3.2.a.

Objectives: Providing to the EU-MS 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 PT organization launched during the program 2019-2020, the substances of choice might be a combination of either the non-authorized substances chosen among the groups A6 (antimicrobials), B2f (quinoxalines) and B3e (dyes) or of the authorized substances of group B1 (MRL substances non-authorized in certain species/products). 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 large PT with including the possible 2-step strategy of analysis (screening + confirmation) where applicable will primarily be considered for evaluation during this PT round**. For**

2021, a multi-Screening and Confirmation of Chloramphenicol Residues in Meat in line with new RPA of 0.15 µg/kg (*Reg 2019-1871*) will be delivered. Additionally, will be delivered either a second PT for Multi-Screening and Confirmation of Group B1 Authorized Antimicrobial Residues in Milk or a Collaborative Study dedicated specifically to LC-MSMS / LC-HRMS(MS) instruments for Multi-Screening of Group B1-B2 Authorized VMP Residues in Extracts of Milk and of Meat

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 (or Collab Study) rounds 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**). For PTs, 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 (or Collab Study) 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 large or 2 reduced PT round each year in a different species/matrix) **for the year 2022**

Sub-activity 1.3.1.b. / 1.3.2.b.

Objectives: Providing to the EU-MS 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 PT organization launched during the program 2019-2020, the substances of choice might be a combination of either the non-authorized substances chosen among the groups A6 (antimicrobials), B2f (quinoxalines) and B3e (dyes) or of the authorized substances of group B1 (MRL substances non-authorized in certain species/products). 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 large PT with including the possible 2-step strategy of analysis (screening + confirmation) where applicable will primarily be considered for evaluation during this PT round. F**or 2022,** a multi-Screening and Confirmation of Dye Residues in Seafood Meat in line with new RPA of 0.5 µg/kg (*Reg 2019-1871*) will be delivered. Additionally, will be delivered either a second PT for Multi-Screening and Confirmation of Group B1 Authorized Antimicrobial Residues in Meat or in Eggs or a Collaborative Study dedicated specifically to LC-MSMS / LC-HRMS(MS) instruments for Multi-Screening of Group B1-B2 Authorized VMP Residues in Extracts of Milk and of Meat (if project is not delivered in 2021).

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 (or Collab Study) rounds 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**). For PTs, 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 (or Collab Study) 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 Projects as mentioned here-above in 1.3.1a and 1.3.1.b

Sub-activity 1.3.3.a: over the year 2021 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 2022 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 (Quinoxalines) and/or B3e (Dyes)
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 2021 (**Output 1**) and also for year 2022 (**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 2021: Sub-activity 1.3.4.a
Over the year 2022: 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 (Quinoxalines) and/or B3e (Dyes)
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 NRL destinations each year
Duration: 2021 and on-going in 2022
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 *(up to 5 meetings of 2 days per year except for 2021 with only 2 in-person meetings forecast due to Covid19 restrictions as sub-activity 1.4.1.a and 5 meetings in 2022 as sub-activity 1.4.1.b) and some additional virtual webconference-like meetings*

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 + virtual webconference-like meetings at least once every 2 months
Duration: In-person meetings over 2 days per mission
EU-RL staff considered for the task: Scientists

Sub-activity 1.4.2. – On going support and assistance as regards the implementation of the new draft Regulation SANTE 2018-11188 and its attached EURL guidelines to be carried out over 2021 (sub-activity 1.4.2.a) and 2022 (sub-activity 1.4.2.b)

Objectives: Drafting together with the Cluster of 3 EU-RLs and together 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 repealed Decision (EC) No 2002/657 replaced by Regulation still to be enforced in 2021 as from the draft document SANTE 2018-11188.
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 forecast to update/replace the Decision (EC) No 2002/657 including all technical guidances for validation of screening and confirmatory VMP residue analytical methods, i.e. replacing the current Document SANCO/2004/2726 rev4 and the CRL Guidelines of 10/1/2010 for validation of the VMPR screening methods. The first draft of SANTE 2018-11188 was created end of 2018. In the period of 2019 and 2020 this draft was discussed together with the NRLs. A finalised version being presented to SCPAFF by end 2020 with taking into account the comments from Member States and COM. Subsequently, the preparation of practical guidance documents have also been started in the period 2019-2020 on subjects such as: 1- guidance for validation of screening methods; 2- guidance for validation of confirmatory methods; 3- guidance for extension of validated methods and 4- guidance for on-going performance of validated methods. They all will have to be finalised during the programme 2021-2022.
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 have to be posted onto our EU-RL website (http://eurl-fougeres-veterinaryresidues.anses.fr) and/or onto the brand-new VMPR cluster portal (https://eurl-residues.eu/) (Output 3).
Duration: Over the years 2021 and on-going in 2022
EU-RL staff considered for the task: Scientists

Sub-activity 1.4.3. – On going support and maintenance of a common portal for facilitated access to the 3 websites of the "VMPR" EURLs to be carried out over 2021 (sub-activity 1.4.3.a) and 2022 (sub-activity 1.4.3.b)

Objectives: Follow-up of the organisation and scientific and technical maintenance 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 the 3 VMPR EU-RLs to check technical feasibility for implementing a better coverage of the links toward the EU-RL websites. This issue was further advanced during the programme 2019-2020 where it was finally proposed the BVL-EURL would be the one EURL purchasing and installing the portal. The project will have to be finalized by the 3 EU-RLs and together with links to the COMMISSION DG-SANTE website by end 2021. Future maintenance of the portal will be addressed by teams within the 3 EU-RLs.
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). Future maintenance of the portal by teams within the 3 EU-RLs (Output 3).
Duration: Over the year 2021 and on-going in 2022
EU-RL staff considered for the task: Scientists

Sub-activity 1.4.4. – Advances in harmonisation of PT performance criteria within the "VMPR" EURLs to be carried out over 2021 (sub-activity 1.4.4.a)

Objectives: To follow-up with the harmonized protocol for assessing the PT performance of NRLs for VMP residue testing in order to cover screening methods as well as confirmatory ones.
Description: Discussions started during the previous programme within the cluster of VMPR EU-RLs and specifically between BVL and WFSR to try implementing a harmonised approach on PT-Evaluation via an agreed upon PT-protocol but taking into account the individual factors of the 2 EU-RLs of BVL and WFSR for essentially confirmatory methods. A further discussion including the EU-RL Anses will be started during this programme to try better including if possible the individual factors dedicated to screening methods. This second-step project will be carried out to be presented to the network of EU-MS NRLs by end 2021.
Expected Output: Common PT performance criteria drafted in a EU-RL cluster's protocol delivered to the network of NRLs (Output 1) and posted onto the EU-RL website (Output 2).
Duration: Over the year 2021
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 2021 (sub-activity 1.4.5.a) and 2022 (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 scheme 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 2021-2022
EU-RL staff considered for the task: Scientists

Sub-activity 1.4.6. – Development of a common EU-RL cluster VMP-database to be carried out over 2021 (sub-activity 1.4.5.a) and 2022 (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: A database with information on the substances within the responsibility of the 3 EU-RLs for VMP residues shall be developed; the database will contain information on details for analysis of VMP residues (exact masses, characteristic mass transitions, ionisation parameter, etc.) and additional practical information (e.g. stability data, standard provider, etc.). A draft will be prepared and contents are to be discussed with the NRLs in order to meet their needs.
Expected Output: Database hosted by the EURL websites (Output 1) and the Cluster portal website (Output 2).
Duration: Over the year 2021 and on-going in 2022
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 our LC-HRMS screening method of Group B1 antimicrobial residues in Meat to a confirmatory method

Over the year 2021: Sub-activity 1.5.1.a
Over the year 2022: Sub-activity 1.5.1.b

Objectives: To demonstrate the adaptation for future surveillance plans of a Full-Scan High Resolution MS analytical method for a large scope of VMPRs and through a workflow of "Screen + Confirm" process.
Description: Further to the evolution of screening strategies by means of LC-HRMS analytical systems demonstrated in meat and in milk during our 2019-2020 programme by means of a Q-EXACTIVE^{+} equipment and in eggs during the 2020 and 2021 programmes by means of a LC-QTOF equipment, it is now intended to start building a complete workflow for screening/identifying VMPRs at large and confirming their presence in meat in an accurate quantified confirmation. This project will address the future official plans for surveillance of VMPRs to be set up after enforcement of the new delegated act SANTE 11987-2017 to be replacing after 2022 the Annexes of repealed Directive 96/23.
Expected Output: In 2021, development of the workflow for VMPRs in meat including antibiotics (Output 1), followed in 2022 by a validation of the workflow (Output 2), an hands-on training dedicated to the workflow LC-HRMS strategy (Output 3) will be presented to the network of EU-NRLs during the next annual workshop of 2022 together with the release of a Standard Operating Procedure (Output 4).
Presentations together with SOP and summary of validation report to be posted in due times by end of 2022 on our EU-RL website to the attention of the network of NRLs (Output 5); 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 2022 (Output 6).
Duration: Over 2021-2022
EU-RL staff considered for the task: Scientists + Technicians + Secretary+ Doctoral or Postdoctoral fellowship

Sub-activity 1.5.2. - Development and Validation of Analytical Methods – A collaborative evaluation of the state-of-the-art in EU-MS NRLs analytical instrumentation as of their advanced analytical strategies for implementing a Multi-Antimicrobial and other group B2 VMP Method using suitable LC-MSMS and/or LC-HRMS instruments

Over the year 2021: Sub-activity 1.5.2.a
Over the year 2022: Sub-activity 1.5.2.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 and milk 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 recent 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 in 2021 to further investigate the outcomes and benefits of these multi-screening methods whatever Low Resolution or High Resolution mass spectrometric detection.

For this purpose this new collaborative study will be carried out possibly enlarged to the whole NRLs network LC-LRMS and LC-HRMS systems provided they are used for a large screening of VMPR analytes. 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 2021-2022

EU-RL staff considered for the task: Scientists + Technicians + Secretary + Doctoral or Postdoctoral fellowship

Sub-activity 1.5.3 - 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 2021: Sub-activity 1.5.3.a
Over the year 2022: Sub-activity 1.5.3.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. A first presentation of this restarting project after the 2020 Covid-19 period was made to the EU-MS NRLs network during the workshop of October 2020.

Expected Output: In 2021, will be continued the development of the egg product LC-HRMS screening method (Output 1). As a follow-up of the validation of the method to occur in the course of 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 or of 2022 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 by 2022 (Output 5).

Duration: Over 2021-2022

EU-RL staff considered for the task: Scientists + Technicians + Secretary+ Doctoral or Postdoctoral fellowship

Sub-activity 1.5.4. - Development and Validation of Analytical Methods - Confirmatory LC-MS/MS monitoring of group A6 VMP substance residues in meat and also in casings as of follow-up on new rules for entry into the EU *(this project is in fact a '2020-programme-postponed-topic' to 2021 subsequent to January-2020 accepted change of project in the 2019-2020 programme)*

Over the year 2021: Sub-activity 1.5.4.a
Over the year 2022: Sub-activity 1.5.4.b

Objectives: 1 - To develop a LC-MS/MS method capable of including low Reference Point for Action (RPA) level of control for prohibited antimicrobials (chloramphenicol and all nitrofuran metabolites) and prohibited nitroimidazoles in meat products and also in casings as a follow-up on new rules for their entry into the EU; the production of first choice would be the porcine production. 2 - To validate the performance of the method in line with the new regulation for monitoring of unauthorised substances (Reg 201-1871) and the new standardized criteria for performance of official control methods according to the 2021-forecast revised Decision (EC) No. 657/2002 (currently doc SANTE 2018-11188).

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 27 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. The specific case of the casings will be evaluated together with porcine meat in order to speed-up the implementation of the new control plans for casings forecast in 2022.

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: Over 2021-2022

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

Sub-activity 1.5.5. - Development and Validation of Analytical Methods - Confirmatory LC-MS/MS monitoring of fumagillin residues in Honey (*prog2020 delayed project partly shifted to 2021 for COVID-19 reason)*

Over the year 2021: Sub-activity 1.5.5.a

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. A complete bibliography review (use, chemical properties, stability, analytical method, marker residues, stability) was acted in 2020 during the 2020 Covid-19 period. A technical development of an analytical method will be started in 2021 and after the 2020 Covid-19 period 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: 2021

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 florfenicol and florfenicol amine residues in Meat and Aquaculture products (*prog2020 delayed project partly shifted to 2021 for COVID-19 reason)*

Over the year 2021: Sub-activity 1.5.6.a

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 complete bibliography review (use, chemical properties, stability, analytical method, marker residues, stability) was acted in 2020 during the 2020 Covid-19 period. A specific method for accurate measurement of FF and its metabolites as FFA will be developed in 2021, 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); SOP and validation report to be posted in due times on our EU-RL website to the attention of the network of NRLs (Output 3); a communication to the International Scientific Community to be delivered in a Symposium (Output 4).
Duration: 2021
EU-RL staff considered for the task: Scientists + Technicians + Secretary

BIOLOGICAL-BIOCHEMICAL METHODS

Sub-activity 1.5.7. - Evaluation of new bio rapid methods for testing residues of antibiotics in eggs by means of immunological techniques

Over the year 2021: Sub-activity 1.5.7.a

Objectives: The objective of this project is to evaluate an immunological-based rapid method for testing residues of antibiotics in eggs, to give technical 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. The Evidence Investigator (Randox) is an innovative multiplex system based on chemiluminescence detection which allows the detection of multiple analytes simultaneously. The kit AM II® was validated in 2015 for the detection of 6 families of antimicrobial residues in eggs. A new multiplex kit named InfiniPlex® for milk (IPM) developed by Randox was evaluated in 2016 for the screening of at least 77 antibiotics (authorized and banned substances) in milk. The encouraging results allow us now to consider this kit for its applicability in eggs. This tool for control will be evaluated in eggs according to the decision EC/2002/657 and to the European guideline for the validation of screening methods (2010).
Expected Output: An evaluation report will be delivered by end of 2021 (Output 1). The evaluation report will be then posted on our EU-RL website to the attention of the network of NRLs by end of 2021 (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: 2021
EU-RL staff considered for the task: Scientists + Technicians + Secretary

Sub-activity 1.5.8. - Development and Validation of Analytical Methods - Evaluation of innovative technologies for rapid screening of veterinary antimicrobial residues in Foodstuffs (Milk, Honey, Aquaculture products) - Electrochemical biosensors (Potentiometric– Amperometric – Voltammetric devices) for unique or multiplex screening of **non-authorised antimicrobial substances**

Over the year 2021: Sub-activity 1.5.8.a
Over the year 2022: Sub-activity 1.5.8.b

Objectives: 1 - Our first action in 2021 will be to go on with the evaluation of amperometric and voltametric biosensors in order to develop new multiplex methods applicable to the screening of non-authorised antimicrobial substances (eg. Chloramphenicol, Nitrofuran metabolites, Dyes) in honey. A method will be developed, optimised and validated for the screening of a range of one to three antibiotic families below their RPA in honey. 2 - The second combined objective is to continue to test capacities of nanoparticles (ie. carbon-based, metal-based and/or uncommon nanomaterials: nanohorns, fullerenes) to try improving the sensitivity of the electrochemical biosensors which were first tested during the 2019/2020 programme. 3- The third objective in 2021-2022 will be to test different bioreceptors (when available) (eg. antibodies and aptamers). 4- The fourth objective in 2022 will be to develop one new multiplex method for these 2 to 3 families in honey first. Afterwards we will try to adapt the new multiplex method for non-authorised substances in other matrices (eg. milk, aquaculture products).

Description: One type of electrochemical biosensor has been identified during the programs for 2015 & 2016-2017 & 2018 which is able to perform multiplex screening of antibiotics:

- An amperometric biosensor has been developed by a Spanish research team. The detection relies on the use of a mixture of target-specific modified magnetic beads and implementation 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. A specific amperometric method for chloramphenicol detection in milk was developed. Other electrochemical detection systems are available and fitted to the screening of contaminants in foodstuffs (eg. voltammetry). The development of specific amperometric and voltametric methods for chloramphenicol in honey started in our programme 2019-2020. The first objective in the 2021-2022 period will be to go on with chloramphenicol in milk and honey, two complex matrices for electrochemical detection. We will compare the performances of amperometric and voltametric biosensors, based on different bioreceptors (antibodies, aptamers) and using different nanomaterials. The second objective in 2021-2022 will be to enlarge with the development of new single methods first and then in 2022 to develop one new multiplex method of non-authorized substances (*e.g.* chloramphenicol and 5 nitrofuran metabolites) in honey first, and then in milk, and in aquaculture products if possible with including also the dyes (*malachite green, crystal violet and brilliant green*).

Expected Output: An intermediate report of the advances in the project will be delivered by end of 2021 (Output 1). It will contain the advances on the single compounds methods for non-authorised substances that will be developed and validated in 2021. A presentation of the advances on the project will be delivered during the EU-RL workshop of 2021 (Output 2) and/or during an international congress in 2021 (Output 3).

In 2022, a multiplex method for several non-authorised substances will be developed and validated. The evaluation report will be delivered by the end of 2022 to the network of NRLs (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 2022 to the attention of the NRLs experts (Output 6). Then publications in peer-reviewed scientific journals might be also considered (Output 7).

Duration: 2021-2022

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

Sub-activity 1.5.9. - Evaluation of sensitivities of ELISA testing kits for residues of group A6 prohibited antibiotics at and below their new RPAs according to Reg 2019-1871

Over the year 2021: Sub-activity 1.5.10.a
Over the year 2022: Sub-activity 1.5.10.b

Objectives: 1 - Evaluation of the performance of several commercially available ELISA kits (Europroxima, The Netherlands and r-Biopharm, Germany) aimed at screening the group A6 prohibited substances (chloramphenicol, nitrofuran metabolites, dyes) in meat products and aquaculture products at and below their new RPAs according to new Reg 2019-1871.

Description: The screening of chloramphenicol, nitrofuran metabolites and dyes with immunoassays is an interesting alternative to LC-MS/MS methods because of a lower investment in equipment. In the period 2010-2018, the evaluation of the performance of several commercially available kits from r-Biopharm (Germany) and from Europroxima (The Netherlands) was performed at the concentration levels of interest: the 2003 and 2005 set regulatory MRPLs. Now the Regulation 2019-1871 requires to control these prohibited substances at lower RPA levels. Several EU-NRLs for the network requested these past 2 years to have assessed the capacities of the ELISA kits as regards to new RPAs. Each ELISA kit targeting one analyte : chloramphenicol, single nitrofuran metabolite., single dye will be evaluated in the course of the 2021-2022 years of our programme. These kits will be evaluated according to the revised decision EC/2002/657 and to the revised European guideline for the validation of screening methods.

Expected Output: One evaluation report per kit will be delivered 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 each year (Output 3). A scientific publication in a peer-reviewed journal and communication in international symposia could be also further considered (Output 4).

Duration: 2021-2022

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 2021: Sub-activity 1.6.1.a
Over the year 2022: 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) 2017/625 and the Annex V of the Directive (EC) 96/23. Only the analyses to discriminate MS disputes and in the form of third-part EU reference analysis will be eligible after a specific DG-SANTE request to the EURL.

Expected Output: From 2 and up to 10 different requests for one sample each may be considered over a year

Duration: Requests' admissibility/acceptability evaluated and analysis carried out within 1 month over the 2021-2022 programme

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 2021: Sub-activity 2.1.1.a
Over the year 2022: 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: 2021 and on-going in 2022
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 2021 and from 2022

Over the year 2021: Sub-activity 2.2.1.a
Over the year 2022: 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.
Remark: After the year 2020 COVID-19 sanitary restrictions, in case similar restrictions for travelling and distanciation apply in 2021 and 2022, the organisation of the workshop will be reconsidered according to a virtual approach and funding of the event will be devoted to other relevant EU-RL tasks related to the preparation of the virtual event (production of videos, interacting tools, …).
Expected Output: Announced at the beginning of the year 2021 (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 6 months for preparation-dissemination and over a 3-4 day venue for 2 workshops in 2021 and in 2022
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 2021: Sub-activity 2.3.1.a
Over the year 2022: 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 lacking in 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.
Remark: After the year 2020 COVID-19 sanitary restrictions, in case similar restrictions for travelling and distanciation apply in 2021 and 2022, the organisation of the trainings will be reconsidered according to a virtual approach and funding of the event will be devoted to other relevant EU-RL tasks related to the preparation of the virtual event (production of videos, interacting tools, …).
Expected Output: A set of maximum 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 2021-2022
Duration: Organised over max 40 days across the 24 months of the 2021-2022 WP and in separate sets of 1-week session (5-day) for up to 8 analysts or 2-week session (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 2021 and 2 visits in 2022) of EU-RL delegates to EU-NRLs from the Member States or from the Candidate Countries

Over the year 2021: Sub-activity 2.4.1.a
Over the year 2022: 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
Remark: After the year 2020 COVID-19 sanitary restrictions, in case similar restrictions for travelling and distanciation apply in 2021 and 2022, the organisation of the visits will be reconsidered according to a virtual approach and funding of the event will be devoted to other relevant EU-RL tasks related to the preparation of the virtual event.

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 2021 Sub-activity 2.5.1.a
Over the year 2022: 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: 2021 and on-going in 2022
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 2021: Sub-activity 2.5.2.a
Over the year 2022: 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 opportunity to interact externally in our field of expertise on 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: 2021 and on-going in 2022 several missions scheduled on a 3 to 5 day travel basis for each
EU-RL staff considered for the task: Scientists
Remark: After the year 2020 COVID-19 sanitary restrictions, in case similar restrictions for travelling and distanciation apply in 2021 and 2022, the organisation of the missions will be reconsidered according to a virtual approach and funding of the event will be devoted to other relevant EU-RL tasks related to the preparation of the virtual event.

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 2021: Sub-activity 2.6.1.a
Over the year 2022: 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) and/or onto the brand-new VMPR cluster portal (https://eurl-residues.eu/) (Output 2)
Duration: 2021 and on-going in 2022
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 EU-MS for 2021 (f)**

Objectives: For the year 2021, an evaluation of the National Residue Monitoring Plans of the 27 Member States + 2 EFTA Countries (Norway, Iceland) 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 after the first step of a final report to the Commission DG-SANTE (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 after the second step 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 6 months for step 1 (April-July for Ouputs 1-2) and 3 months for step 2 (August-October for Output 3)
EU-RL staff considered for the task: Scientists (4)

Sub-activity 3.1.1.b - **Analysis of National residue monitoring plans of the EU-MS for 2022 (f)**

Objectives: For the year 2022, an evaluation of the National Residue Monitoring Plans of the 27 Member States + 2 EFTA Countries 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 6 months for step 1 (April-July for Ouputs 1-2) and 3 months for step 2 (August-October for Output 3)
EU-RL staff considered for the task: Scientists

Sub-activity 3.1.2.a – **Support to Commission on specific items upon request in 2021 (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 2021 of the WP 2021-2022
Duration: Over the 12 months of 2021
EU-RL staff considered for the task: Scientists

Sub-activity 3.1.2.b – **Support to Commission on specific items upon request in 2022 (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 2022 of the WP 2021-2022
Duration: Over the 12 months of 2022
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 2021: Sub-activity 3.2.1.a
Over the year 2022: 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 are every year several solicitations at the European or International levels requesting our EU-RL expertise
Expected Output: Exchange and release of reports for expertised data or advices delivered to these European or International Food Safety Official Entities
Duration: 2021 and on-going in 2022
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 2021: Sub-activity 3.2.2.a
Over the year 2022: 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: 2021 and on-going in 2022
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 2021: Sub-activity 3.2.3.a
Over the year 2022: Sub-activity 3.2.3.b

Objectives: Delivering to the EU-MS NRLs upon requests from European and international organisations and Third Countries 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 European and international organisations and Third Countries released to EU-MS NRLs by the continuous line of communication cited above.
Duration: 2021 and on-going in 2022
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 2021 ***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 2022 ***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 for dissemination of information to be released at EU-RL workshops and posted onto the EU-RL website: (http://eurl-fougeres-veterinaryresidues.anses.fr)
Duration: 2021 and on-going in 2022 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 2021

Sub-activity 3.4.1.b - Compilation of provisional programme, final term biannual reports and cost estimates of the combined years 2021-2022

Objectives: Documents to be released to the Commission-DG-Santé in due time according to the contracted agreement.

Description: One programme for 2021-2022 including the scientific & technical tasks, a proposed 2-year budget for the proposed tasks. One final report for 2019-2020 biannual program including scientific & technical issues and budget execution.

Expected Output: By end of November 2020, the provisional Programme 2021-2022 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 2021, the Final Technical report of the programme for the period 2019-2020 (Output 3) + Postage onto the EURL website to the exclusive attention of COMM (Output 4)

By March 2022, the mid-term biannual Technical report and year 2021-budget of programme 2021-2022 (Output 5) + Postage onto the EURL website to the exclusive attention of COMM (Output 6) (http://eurl-veterinaryresidues.anses.fr)

By March 2023, the Final Technical report of programme 2021-2022 (Output 7) + Postage onto the EURL website to the exclusive attention of COMM (Output 8) (http://eurl-veterinaryresidues.anses.fr)

Duration: 2021 and on-going in 2022 and up to March 2023

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 2021
Sub-activity 4.1.1.b - Follow-up of the database of the analytical standards for 2022

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 years 2021-2022
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 2021
Sub-activity 4.1.2.b - Follow-up of the database for the reference materials for 2022

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 years 2021-2022
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 RESIDUES OF VETERINARY MEDICINES AND CONTAMINANTS IN FOOD OF ANIMAL ORIGIN (BVL BERLIN)

PERIOD: 2021/22

Version 1.0
(date 14/09/2021)

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.

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

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 Member States' official control laboratories as well as to official control laboratories in third countries. The (non-confidential)

information is made available on the common EURL website (www.eurl-residues.eu). Confidential information is published via the FIS-VL (a permanently up-dated restricted-access website of the EURL Berlin; https://fis-vl.bvl.bund.de/share/page/site/eurl-veterinary-drug/dashboard). On these platforms all relevant information on validated methods, standard substances, reference materials, workshops, stability studies, and much more can be found. 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 and legislation; publication of methods via the EURL website (following the procedure of the pesticide EURLs); scientific support via e-mail or telephone

Duration:
2021/22 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 possesses a large stock of incurred matrix reference materials, which are continuously controlled for stability, as well as of standard substances. Nevertheless, several reference materials are still lacking, 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 and stock depletion 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 novel and emerging 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 reasonable. In addition, the EURL Berlin purchases substances, metabolites or internal standards which are presumed 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 2020 amended for reference materials provided to the OCLs via the FIS-VL).

Based on the above-mentioned considerations, annual plans for animal studies for the production of incurred matrix materials are established.

However, the plans for 2021/22 are associated with an element of uncertainty due to the unpredictable situation with COVID 19 on the one hand, and with regard to cases of infectious animal diseases, which are presentely spreading in Germany, on the other hand. In addition, the realisation of animal experiments requires the reliable availability of suitable staff (for animal keeping, slaughtering, etc.), which can presently not be guaranteed, especially for longer lasting studies and if animals are to be slaughtered at the end of the animal study.

Hence in 2021/22 besides of the finalisation of experiments which were originally planned for 2020 only a few additional studies shall take place. The following materials shall be produced accordingly:

1 coccidiostat in turkey tissue (from 2020)
1 anthelmintic in porcine tissue (from 2020)
Nitroimidazoles in porcine plasma, serum and whole blood (from 2020)
Nitroimdazoles in porcine casings
Finalisation of the multiannual study on beta-agonists in bovine hair (1 beta-agonist)

The production of the materials comprises the treatment of the animals, the collection of the materials (if necessary, this may include the slaughtering of the animals) 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) and tests on extraction efficiency (if applicable).

The following materials will be produced and characterised in 2021/22 (cf. 1.3):

Nitroimidazoles in plasma (2+1 materials) and milk (1 material /finalisation)
Coccidiostats in egg and tissue (2 egg materials with 2 analytes each ; 2-3 tissue materials with 3 chemical coccidiostats)
Beta-agonists in urine, liver and lung (3+1 materials urine (5-6 analytes) ; 1 liver material (4 analytes); 1 lung materials (3 analytes)
nitroimidazoles in muscle (1-2 materials, 2 analytes, OAWG study)
Anthelmintics in milk and muscle (one analyte + metabolites, 1 milk + 1 muscle material)
Fluralaner in egg

Expected output:
Pre-tested incurred matrix materials for proficiency tests and for scientific purposes; candidate reference materials: coccidiostats in egg and tissue (overall 5-6 materials), nitroimidazoles in plasma and milk (overall 4 materials), beta-agonists in urine, liver and lung (overall 6 materials); nitroimidazoles in muscle (1 – 2 materials), anthelmintics in milk and muscle (2 materials)
support to NRLs/OCLs; cooperation with synthesis laboratories; synthesis of new standards; literature reviews on new substances, purity of selected important standard substances

Duration:
2021/2022 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 Berlin 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 which is controlled for homogeneity and stability at the EURL.

The proficiency assessment is usually based on classical z-score (or z_u-score) evaluation and on top of that 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 taking into account false positive and false negative results).

Follow-up measures will be carried out - if necessary - in compliance with the Commission draft "Protocol for management of underperformance […]" guideline of 2007, substantiated in the "Common EURL Protocol for Proficiency Testing in the Field of Veterinary Drug Residues" (2020). An overview of the performances per laboratory and per MS in the past years was established in 2013/2014, is up-dated regularly and submitted to COM once per year.

For 2021/22 the following activities are planned:
- Follow-up to PT BETA0320 (beta-agonists in bovine hair)
- Final report and follow-up to PT NSAI1120 (NSAIDs in bovine and equine muscle)
- PT on nitroimidazoles in plasma and milk (NIIM1021)
- Final report and follow-up to PT NIIM1021
- PT on precision and accuracy in the analysis of standard solutions (STRD0521)
- Final report and follow-up to PT STRD0521
- PT on beta-agonists in urine (BETAXX22)
- Final report and follow-up to PT BETAXX22
- PT on coccidiostats in tissue (COCCxx22)
- Final report and follow-up to COCCxx22

The accuary of standard solutions used for the quantification of drug residues is essential for the successful participation in proficiency tests. So far, the measurement of standard solutions has only been applied as a follow-up measure in case of underperformance in proficiency tests. In such cases standard solutions supplied by the EURL were reanalysed by participants and often the analysis proved that the reason for failure was a standard solution with an incorrect analyte content. In addition, NRLs suggested that standard solutions should generally be provided by the EURL. Since this is not feasible (and sensible), the planned proficiency test shall give the participants the possibility to test their quantification (i.e. the content of their standard solutions) for a variety of substance groups (2-3 standard mixes with a focus on MRL substances) without the added difficulty of sample preparation and matrix effects. It is planned to prepare the standard mixes gravimetrically and to derive the assigned values based on this procedure. If available, certified standards will be used for the preparation of the test items.

Expected output:
Final reports on the 2020/2021/2022 PTs (NSAIDs in muscle [2020 study], nitroimidazoles in plasma and milk, precision and accuracy in the analysis of standard solutions, beta-agonists in urine; short report on PT coccidiostats in tissue; assessment of the performance of the NRLs; assignment of values

to the in-house 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; submission of annual update of long-term overview of NRL performance to COM)

Duration:
2021/22 and ongoing

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 3 EURLs for residues of VMP and a representative of the European Commission takes place per year. Moreover, an additional exchange among the EURLs with respect to an agreed strategy, increased efficiency and synergy effects is required.

Expected output:
- *Common PT performance criteria*
Continuous improvement of the existing document taking into account NRL feedback and new developments regarding relevant standards
- *Common EURL website*
Continued development of the joint EURL website
- *Common EURL guidance documents on implementation of CIR (EU) 2021/808*
Drafts of guidance documents for the validation of confirmation and screening methods and method extensions were provided and shall be further discussed and finalised as far as possible; additional guidance documents are developed/updated upon request (e.g. on HRMS method validation).
- *Development of a common EURL VMP database*
A database with information on the substances within the responsibility of the EURLs for VMP residues shall be developed; the database shall contain information on analytical details (exact masses, characteristic mass transitions, ionisation parameters, etc.) and additional practical information (e.g. stability data, standard provider, etc.). A draft will be prepared and the contents are to be discussed with the NRLs in order to meet their needs.

Duration:
2021/22 and ongoing

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

Objectives:
Development 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 methodology (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, extended analytical scopes and lower decision limits are checked regularly.

In 2021/22 this will concern the following methods:
Anthelmintics in liver (method extension, optimisation, validation)
Coccidiostats in liver (extension of method scope - extension to other species in addition to poultry)
Amprolium in muscle (extension of method scope)
Beta-agonists in urine (optimisation, revalidation)
Development and validation of multi-screening methods for B-substances in tissue or egg with HRMS (Orbitrap or Q-TOF)
Inclusion of the LC / ion mobility / MSMS system into the validation of coccidiostats in liver
Ionophores (Coccidiostats) in poultry liver (method optimisation and validation)
NSAIDs in egg (development and validation)
Salicylic acid in feed (development)
nitroimidazoles in honey (re-validation)
Participation in proficiency test as part of ongoing method performance control

Based on the results of studies carried out in earlier working periods, validated methods should be checked with incurred material for hydrolysis effects and for extraction efficiency.
Furthermore, validation studies for MRL and ML substances should aim to deliver results down to approximately 0.1 * MRL/ML (cf. CIR (EU) 2021/808, Annex 2.2). This requirement is also the current state of discussion with EFSA with regard to the provision of sub-MRL results.

Expected output:
Method descriptions, validation reports

Duration:
2021/22 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:
2021/22 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:
Provision of technical and scientific support to NRLs

Description:
Assistance to NRLs and other official laboratories for the strengthening and harmonisation of residue control (methods, SOPs, QA, QC, validation, information on 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 individual trainings.

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

Method data base
The method performance characteristics of the analytical methods applied by the NRLs shall be updated and introduced into a newly developed data base. Method data shall be made available to the NRLs in order to contribute to method harmonisation and further development. The data base shall be made available for use of the other EURLs for VMP residues if the applicability proved to be appropriate.

Expected output:
Provision of information on analytical methods; provision and maintaining of a method data base; plausibility check of NRL data; strengthening of official control; improved food safety

Duration:
2021/22 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:
Annual EURL workshops will be organised in 2021 and 2022. The meetings should preferably be planned as face-to-face meetings, but may be rescheduled as web-meetings, if necessary. The following subjects (among others) will be covered:

- Discussions on implementation of CIR (EU) 2021/808
- Discussion on guidance documents supplementing CIR (EU) 2021/808, including method validation, method extension, screening methods and MMPR values
- New instruments and method developments
- News on substance groups and EURL projects
- Importance of sample preparation (conjugated residues, extraction)
- Evaluation of proficiency tests and follow-up activities
- Stability testing in matrix and in solution
- ISO 17025:2017, QA measures
- MANCP/NRCP evaluations
- Presentations by NRLs
- Practical training / tutorials on specific topics
- Topics according to suggestions by NRLs (collected in surveys conducted at the end of previous 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 addressed and further specific questions will be discussed depending on the needs of the participants.

Expected output:
Scientific exchange, workshop report

Duration:
2021/22 and ongoing : 2-3 days per year

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

Objectives:
Organisation of training, provision of suitable methods, support in implementation of methods 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 usually part of the annual workshop. Additional individual training courses are agreed on 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).

It is planned to initiate a follow-up meeting to the 2020 seminar on HRMS/TOF within the 2021/22 working period.

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

Description:
- *Harmonisation of residue control*
With the 2015/16 work programme, a concept for an in-house validation as part of a collaborative method validation study was developed and introduced. Following this concept, collaborative studies based on an orthogonal experimental design plan for methods which were of interest for several NRLs were offered. The concept was applied successfully on the national level and has meanwhile been successfully transferred to an international level with method validations for NSAIDs in milk, beta-agonists in muscle, as well as coccidiostats in egg.
The resulting benefits were multiple: for the participating NRLs, a complete in-house validation study was performed, and for the method itself, robust method performance characteristics were determined. With this a contribution to a harmonised residue control in the EU in the form of comprehensive multi-methods for beta-agonists, NSAIDs and coccidiostats (according to Art. 34 (2)a of Regulation 2017/625/EC) was achieved. This approach shall be followed for additional studies.

Plans for 2021/22:
The study for the determination of coccidiostats in egg was started in the end of 2019. The participating laboratories provided results by the end of 2020. Primary evaluations have been made, individual validation reports will be finalised in 2021, and a final summary report will be released 2022.

For 2021, preparations for an additional study (e.g. nitroimidazoles in honey) are planned. Given the interest of the NRLs, a study will be prepared and will start in 2022. If the NRLs have different priorities, another method may be selected.
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 implemented by the NRLs and pre-tested before the start of the validation study.

Expected output:
Final evaluation of the coccidiostat study 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; initiation / start of an additional study (working period 2021/22)

Duration:
2021 and ongoing

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 2021/22 on-site visits to 1-3 NRLs are planned (depending on the possibilities with regard to travelling).

Expected output:
Reports on NRL visits

Duration:
2021/22 (2-3 days per visit / depending on request 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 regard to the improvement and harmonisation of food control. Based on suggestions by 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 2021/22 the following projects are planned:

Suitability check of ion mobility mass spectrometer / QTOF system for reliable screening (cf.1.5)

Additional in vitro study for metabolisation of amitraz (additional species, follow-up to 2019/20)

Comparison of residues of nitroimidazoles in plasma, serum and whole blood

Identification of metabolisation products of morantel in incurred pig samples

Additional in vitro study for metabolisation of morantel in pig (counter-check of incurred sample results)

Carry-over of salicylic acid residues from feed to egg

Participation in a purity study for standard substances of the OAWG (cf. 3.2)

Expected Output:
Experiences with the application of IMS/QTOF systems and recommendations for residue control; information on metabolisation; recommendations for sampling of nitroimidazoles; information on the origin of salicylic acid residues in eggs

Duration:
2021/22 (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 2021 period:

- Assistance in implementation of CIR (EU) 2021/808 (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 carried out and resulted in a working paper. A finalised agreed draft was submitted to COM in the beginning of 2018. In the course of 2019/20 this draft was revised several times based on suggestions from COM and the NRLs, which resulted in a final version at the end of 2020. This version was presented as SANTE 11188 at the Standing Committee on Plants, Animals, Food and Feed (Novel Food and Toxicological Safety of the Food Chain) in November and is to be discussed further in 2021.

In addition EURL Guidance Documents on the implementation of CIR (EU) 2021/808 were requested by COM (cf. 1.4).

- Analysis of national residue monitoring plans of the MS / adaptation to new rules in agreement with DG SANTE (F)

- 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; support in implementation of CIR (EU) 2021/808

Duration:
2021/22 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 participating in the CCQM working group OAWG of the BIPM and in world wide key comparisons organised by this group. Furthermore, input to ISO working groups for standardisation, CEN working groups for standardisation and CCMAS is provided upon request or if necessary within the EURL tasks.

Expected output:
Internal documents, guidance documents for and assistance to EFSA, method evaluations for EMA, maintenance and expansion/confirmation of CMC (calibration and measurement capabilities) entries in the database of the BIPM

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 (cf. 2.2) and proficiency tests (cf. 1.3). Additional assistance (e.g. reference materials, standard substances) is provided upon request (as requested e.g. by Albania for 2021).

Long-standing cooperations exist among others with Albania, Serbia, Northern 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 and 2019 trainings/workshops for ASEAN countries were organised by the VPHL with participation of the EURL Berlin. This joint activity shall be continued in future.

Support (analytical methods, SOPs, QA, QC, validation, legislation, specific practical or theoretical training, PT follow-up) is provided upon request.

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:
2021 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.

In 2022, the participation in the Euroresidue Conference (postponed from 2020) and RAFA (2021) is planned, but participation in other appropriate conferences like the AOAC meeting or the International Proficiency Testing Conference (postponed from 2020), and Eurachem workshops is also considered.

Expected output:
Oral presentations; poster presentations; scientific networking

Duration:
2021/22 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 2021/22:
Financial report (2019/20); technical report (2019/20)
Work programme 2021/22; estimated budget 2021/22
Interim report 2021
Draft work programme 2023/2x; estimated budget 2023/2x

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

Duration:
2021/22 (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 Berlin provides an up to date list of standard reference substances and available reference materials (necessary for 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 and are continuously tested for stability (cf. 1.2).
As part of a new LIMS (to be put in operation in the course of the present working period), also new web-based portals are to be developed to simplify the access of the NRLs to the EURL's data base.

Expected output:
Up-to-date lists of available standard substances and matrix reference materials;
testing of newly developed portals

Duration:
2021/22 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 and further developed. In 2017, it was extended to an accreditation as proficiency testing provider in accordance with ISO 17043. 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 2021 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:
2021 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 Berlin has long-standing experience in the preparation of incurred reference materials (i.e. materials produced in animal studies) for proficiency testing, but, 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 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:
2021 / 2022 / ongoing

REMARKS

(if necessary)

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

(EURL GP WFSR in short notation)

PERIOD: 2021-2022

Version 1.0
(date 09/08/2021

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SUMMARY

INTRODUCTION

In this workprogramme 2021-2022 the full name of " EURL for growthpromoting agents, sedatives and mycotoxines in food of animal origin" is abbreviated into EURL-GP WFSR. This also to distinguish the EURL for growthpromoters from the other EURL at WFSR for mycotoxines and panttoxines.

Starting 2022 the EURL-GP WFSR has officially also the mandate for anti-viral substances and peptide and protein hormones.

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 2021-2022 is "to contribute to a high level of protection for consumers and the environment while favouring competitiveness 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 2021-2022.

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.

[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

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)
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 member-states methods will have to be re-evaluated on specific aspects. Adequately validated methods for all analyte-matrix combinations included in the EURL Guidance on Minimum Method Performance

Requirements (MMPRs) for specific pharmacologically active substances in specific animal matrices, or for new MMPRs or the RPA-values 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 EURL Guidance on MMPRs 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, other compounds that can be of semi-natural origin, 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 2020-2021.

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 EURL-GP WFSR website*

Objective: To have a customer friendly informative website for NRLs and the EC DG SANTE.
The renewed website contains amongst others Standard Operating Procedures for methods of analysis, legislation, guidance documents, news on training and workshops and literature.
The website will be updated regularly with new analytical methods. SOPs will be translated in English (request of NRLs) and placed on website.
Upon request by the Dutch Competent Authority, through their experience in court cases, it was proposed to DG SANTE to not make the SOPs publicly available.
The titles of the SOPs are published on the website. The SOPs can be downloaded by NRLs after login.
On the website a button is present for requesting a copy.
The EURL-GP WFSR 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) WFSR EURL website.

Duration: 2021, 2022 ongoing whole

1.1.2 *Establishing an NRL methods database*

Objective: Establishing a harmonised database together with EURL BVL and EURL ANSES on methods used by NRLs. Method characteristics, validation status and contact

information amongst others will be collected. The database will be web-based. A prototype is developed by EURL BVL. NRLs can update the information via a login.
Expected output: Interactive web-based database for NRL methods
Duration: 2021 establishing format and in 2022 further filling of the database and maintaining database

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 quality control, storage, administration, documentation and shipment.
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 for rBST analysis and reference materials available through EURL-GP WFSR webshop.

Duration: 2021, 2022 ongoing whole period

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/or organisation of research study for new analyte or new analyte-matrix combinations
2021:
a. Finalising report A3 steroids in bovine and porcine urine
b. Research study to be finished started in 2020 for steroid-esters in hair
c. PT corticosteroids and steroids in bovine and porcine urine
d. Sedatives in porcine kidney

2022:
a. Finalising report corticosteroids in bovine and porcine urine
b. Finalising report on sedatives in porcine kidney
c. A3 steroids in bovine and porcine urine (Chlorotestosterone, ethynyloestradiol, nortestosterone, trenbolone)

Expected Output:
Research study and PT reports
Duration: 2021 and 2022

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 SANTE for proficiency testing is implemented since 2018. This protocol is followed for every PT.

1.3.3 Preparation of incurred samples

Objectives: To produce incurred sample materials for PT and research studies. 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 2021 and 2022

Sub activity 1.4 *Cooperation and meetings with other EURLs (1)*

Objective: To attend meeting with other EURL online and/or physical meetings. Either organised by DG SANTE or organised by 3 EURLs for VMPR. To coordinate, harmonize the work of the EURL and to work guidance documents.

1.4.1 Web portal for the 3 EURLs for residues.

Objective: In 2020 a web-portal was built. The portal is hosted by EURL BVL . In 2021 this will be filled with the appropriate information of EURL-GP WFSR. Further filling and maintenance in 2022.
Expected output: Web-portal with information on EURLs for residues.
Duration: 2021 and ongoing

1.4.*2 Harmonisation of proficiency test protocols for assessing PT performance of NRLs*

Objective: In 2020 EURL BVL and EURL-GP WFSR prepared a harmonised protocol for assessing PT performance of NRLs. In 2021 harmonisation with EURL ANSES is foreseen.
A common protocol for the residues EURLs. Developing and testing in 2021-2022. Further implementation 2022.

1.4.3 Attend workshops of EURLs in Fougères and Berlin and meetings organised by DG SANTE

Objective: In 2021 1x workshop in Berlin at EURL BVL and 1x workshop in Fougères at EURL ANSES. Attend 3 meetings in Brussels organised by DG SANTE. In 2021 as long as the situation due to Covid-19 Pandemic is not cleared workshops will be hosted on-line and attendance will be on-line.
In 2022 attendence EURL workshop in Berlin and Fougeres and 3 meetings at DG SANTE.

1.4.4 Cooperation, collaboration and meetings with other EURLs and scientific exchange

Objective: Development of a common EURL VMP database. A database with information on the substances within the responsibility of the EURLs for VMP residues shall be developed; the database shall contain information on details for analysis (exact masses, characteristic mass transitions, ionisation parameter, etc.) and additional practical information (e.g. stability data, standard provider, etc.). A draft will be prepared and contents are to be discussed with the NRLs in order to meet their needs in 2021.
In 2022 the database will be filled with data by EURLs and NRLs
Duration: 2021 and 2022

Sub activity 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. In 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 2020 the interface for LC-RMS for coupling LC to IRMS was purchased after testing. Method development for thiouracil started in 2020. In 2021 the method will be finalised and validated (can go on into 2022). Data will be collected on delta values of thiouracil of pharmaceutical compounds and in samples. NRLs are requested to send in thiouracil non-compliant samples. A proposal will be made for a strategy for Thiouracil involving also biomarker analysis combined with LC-IRMS.

   In 2022 further method development will be done for more natural occurring compounds.

b. In 2020 a GC-Q-orbitrap MS analysis was developed and validated. A library was built for GC-Q-orbitrap MS analysis. In 2021 the possibility of quantification of the compounds will be studied. Extension of the library is foreseen.

   In 2022 the method will be extended to porcine urine.

c. For several years growth hormones 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 (myostatin 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 2020 the focus was on the myostatin axis (inhibiting growth inhibition). In 2021 depending on research outcome in 2020 validation will be performed on the developed method.
   2022: inventarisation of peptide and protein analysis amongst NRLs.
   Literature search on possible peptide and protein hormones which can be abused.

d. 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 were developed (proof of principle). In 2021 these methods will be further optimised for onsite use.

e. Ecdysteroids are steroids derived from plants and/or insects. These steroids are marketed as growth promoting compounds in fitness scene and are readily available from the internet. A method will be developed for the most common ecdysteroids in urine. In vitro and in vivo metabolism will be studied in 2021.
   In 2022 the method will be validated.
f. Antiviral substances: In 2022 an inventory will be held amongst NRLs with regard to antiviral methods of analysis. This because this group of compounds in new in the revision of 96/23 EU. The status of knowledge and practice in the NRLs will be investigated.
g. Literature overview of anti-viral substances, methods of analysis and issues in this field will be made as a starting point for the further workplan in 2023.

Expected output:
2021:
LC-IRMS validated method for discrimination of illegally used Thiouracil and endogenously formed Thiouracil.
GC-Q-Orbitrap MS method also for quantification. Extension of library for steroids.
Further method development for myostatin inhibition compounds
Mobile MS pilot at point of care, first applications for detection of residues using (trans)portable mass spectrometry.
Method for ecdysteroids in urine.
2022:
LCIRMS for other endogenous compounds
Extension of GC-Q-Orbitrap method to porcine urine
Validation of method for ecdysteroids
Inventory anti-viral substances
Literature oveview antiviral substances and methods of analysis

1.5.2 Maintenance or extension of existing analytical methods
Objectives: Analytical methods need re-validation or extension with new compounds when MMPR or RPA changes or in view of the EFSA guideline or in view of more quantitative data collection for EFSA. In 2021 the methods below will be either (re)validated or extended.

Description:
2021:

a. In 2021 the method to be validated for synthetic IGF-forms.

b. Re-validation for the method of gestagens in kidney fat from different species.

c. Update Thyyreostatics in feed, serum and meat

d. Update oestradiol in liver

e. Maintenance A1160 SOP steroids in liver

2022:

a. For A4, Resorcylic acid lactones in the late 1990's a excel sheet was build using data on bovine urine concentrations of RALs. This is used to make a decision on the origin of Zeranol findings.

This spreadsheet will be applied to porcine urine data. Validation will be done using real life samples and animal experiment with porcine animals. Data from member-states national residue control plans will be used.

b. Extension of sedative method for horses. New compounds new matrix

c. Adapting the Resval soreadsheet for validation to the revision of CD 2002/657, 2021/808 (EU)

Expected Output:

2021:

Validation file different forms of synthetic IGF in serum
Validation report re-validation gestagens in kidney fat and new SOP
Updated SOP Thyreostats feed, serum and meat
Updated SOP A1160 steroids in liver

2022:

A4 excel decision sheet for pig urine
Extended method for sedatives in horse
New version of Resval spreadsheet

Duration: 2021 - 2022

Sub activity 1.6: *Analysis of official samples*
Objective: To help NRLs with confirmatory analysis on individual sample basis. Performing arbitration analysis in case of dispute.
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 results and reports
Duration: Ongoing 2021 and 2022, Ad-Hoc 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.***

Sub activity 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 2019-2020 the whole paper was revised and updated with relevant new scientific research and peer reviewed articles. This new reflection paper will be used to set research priorities for 2021 amongst others.
Expected output: Research of specific subjects identified in updated reflection paper. E.G. LC-IRMS in 1.5.1 for natural occuring compounds and zeranol contamination in porcine urine in 1.5.2.
In 2022 the reflection paper will be updated
Duration: 2021-2022
Output:
2022 updated reflection paper

2.1.2 Identification of new compounds

Objectives: Identification of new growth promoting 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: 2021 to 2022 ongoing on ad hoc basis

2.1.3 *Identification of new compounds using data-mining, twitter-monitoring and other tools*
Objectives: To use data mining tools to detect new possible compounds to be abused as growth promoters. Tools already developed at WFSR for data-mining and mining the internet will be used to pro-actively search the world wide web for new compounds which can be abused as growth promotors. In 2021 a European Media Monitoring tool will be made. In 2022 EMM will be implemented. Compounds found will be incorporated in existing methods if possible.
Expected output:
2021: EMM tool build
2022: report on twitter monitoring and EMM

2.1.4 Analytical support
Objective: to help the NRLs and OFL with technical problems on the analysis.
Expected output: 2021 and 2022 upon request by NRLs. Advice and/or analysis (for analysis see 1.6)

2.1.5 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 EURL-GP WFSR website.
The EURL-GP WFSR-website is maintained. The EURL-GP WFSR website will be maintained with continued efforts to further implement its use within the EU-NRL/OFL network.
Literature searches will be made available on the website as Endnote files to be downloaded. These files will be updated regularly with new publications.
Once to twice a year a newsletter will be send to NRLs.
Expected Output: Available information on website
Literature endnote files on website
Newsletters to NRLs
Duration: ongoing 2021 and 2022

2.2 Organisation of workshops (e)

Objectives: Organisation of an annual workshop to inform NRLs on new methods, new legislation and discuss work programmes and PTs. To have information exchange between the NRLs.
Description: Member-states and a selected number of third countries come to WFSR for information exchange and discussion on new topics in the growth promoter field.
Expected Output: 2021 online workshop. 2022 workshop at location WFSR
Information exchange, Workshop report
Duration: 2-3 days

Sub activity 2.3: *Organisation of training courses (e)*

2.3.1 Individual based training

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

2.3.2 Organisation of an additional group training for NRLs or OFLs on analysis of growth promoters. 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.

2021: Thiouracil markers in urine with LC-MS/MS was planned. However due to Covid restrictions this is postponed to 2022.

Sub activity 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 2021 depending on Covid Pandemic the NRL of Italy will be visited. In 2021 Portugal will be visited as there is a new laboratory.
Due to Covid situation these visits will be postponed to 2022
Expected Output:
- visit reports

Sub activity 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., EURL-GP WFSR website and 2.1.5 Documentation and information service.
Expected Output: Up to date website with SOPs, Legislation, Guidance documents, documentation etc.

Sub activity 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-GP WFSR 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.
Ongoing in 2021 and 2022

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 Commission (f)
3.1.1 *- Finalizing of EURLs guidance documents to updated Commission Decision 2002/657/EC*
Objective The process of revising Commission Decision 2002\657 has started in 2016 and was finalized in 2021. The work on practical EURLs guidance documents (with other EURLs in the field of residues of veterinary medicinal products) on certain subjects such as: 1- for validation of

screening methods ; 2- for validation of confirmatory methods ; 3- for extension of validated methods, 4- for ongoing method validation will continue.

Expected output: In 2021 guidance document on extension of methods will be finalised. The guidance document on screening and confirmatory validation will be sent for consultation to MS.
For 2021 also the MMPR Guidance document will be updated if needed.
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 .
2022: finalisation of Guidances on confirmation and screening

3.1.2 Analysis of National residue monitoring plans of the MS (f)
Objective: To evaluate the NRCP of the member states.
Evaluation of the annual national control plans of the Member States. Together with DG SANTE a new template for evaluation will be developed and used in 2021.
Expected output: Combined report with unit F4 of DG SANTE and EURLs for residues in 2021 and 2022

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

Sub activity 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).

3.2.1 When requested, assist unit F4 of DG SANTE as laboratory expert in audits for third countries.

2021 Due to Covid Pandemic not clear if audits will be resumed.

2022 depending on Covid situation

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

2021 Third Coordinated research meeting to be organised. Location not yet known

2021 On-line training course for Food Safety system in central and Latin America. IAEA, RLA5081 Programa de Monitoreo para el mejoramiento de los programas de monitoreo de residuos de medicamentos veterinarios, online training on NRCP planning and analytical capabilities.

2022: Online training for african countries. Similar to south american training.

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

2021 and 2022 upon request

Sub activity 3.3: *Participation in symposiums, workshops and seminars for the dissemination of scientific information. (h*)
2021: Organisation of postponed Euroresidue IX congress to be held in May 2022.Participation in organising and Scientific Committee of Euroresidue IX congress, May 2022.
2022: Presenting oral and poster on scientific research performed within the EURL.

Sub activity 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.***

Sub activity 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 2021
To be updated in 2021 and 2022.

5 REQUIREMENTS RELATED TO OTHER LEGISLATION

Please specify applicable legislation:
(Number of Sub-activity boxes can be adjusted)
Not applicable

REMARKS