EUROPEAN HEALTH AND DIGITAL EXECUTIVE AGENCY (HADEA)
Department A Health and Food Unit A2 EU4Health/SMP

Single Market Programme (SMP Food)

SMP-FOOD-2023-EURL-EURC-AG-IBA
Activities of the EU reference laboratories and EU reference centres in 2023-2024

SUBMISSION FORM: DESCRIPTION OF THE ACTION
(Annex 1 – Description of the action (part B))

SMP-FOOD-2023-EURL-EURC-AG-IBA

Activities of the EU reference laboratories and EU reference centres in 2023-2024

Applicant shall provide information on each question contained in the Form. The information filled in the Form, shall be clear, concise, consistent and complete.

For questions on the information requested in this Form, please contact: please contact: HADEA-EURL@ec.europa.eu.

For questions on the eGRANTS Portal Submission System, please contact the IT Helpdesk.

Applicant - COORDINATOR (Name of EU-RL)	AGENCE NATIONALE DE SECURITE SANITAIRE DE L'ALIMENTATION, DE L'ENVIRONNEMENT ET DU TRAVAIL - LABORATOIRE DE FOUGERES (European Union Reference Laboratory for ANTIMICROBIAL AND DYE RESIDUES IN FOOD FROM ANIMAL ORIGIN GROUP SUBSTANCES: B1a), A2a)b)d), A3a)c))
Topic	**Veterinary Medicinal Product Residues in Food**
Implementation period	**01/01/2023 – 31/12/2024**

CONTACT PERSON for the programme:

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History of changes

Version (date)	Changes
22/01/2024	Correct template of DoA – part B

Contents

1. LIST OF ABBREVIATIONS AND KEY WORDS

EU	European Union
MS	Member States
EURL	European Union Reference Laboratory
NRL	National Reference Laboratory
PT	Proficiency Test
SOP	Standard Operating Procedure
ISO	International Organization for Standardization

2. 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).

3. ACTIVITIES

3.1. WP1: METHODS

WP1 Objectives: To ensure availability and use of high-quality methods and to ensure high quality performance by NRLs.

- *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)

This WP is divided in **23 sub-activities**, as follows:

A) Provide NRLs with details and guidance on the methods of laboratory analysis, testing or diagnosis, including reference methods

Sub-activity 1.1: To provide an updated survey of available EU-NRL network analytical methods in combination with the project 1.4.7 of the VMPR cluster of the 3 EURLs

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 and of accreditation (still not accredited or under fixed or flexible scopes).

Expected Output: Database to be made available to NRLs and DG-SANTE posted onto the EU-RL website (http://eurl-fougeres-veterinaryresidues.anses.fr) and/or (http://eurl-residues.eu)

Duration: 2023-2024

Sub-activity 1.2: Follow-up and update of the EURL Websites

Objectives: Follow-up and update of the EURL Websites

Description: Follow-up and improvement of the EU-RL Websites 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 and including the VMPR EURLs cluster website http://eurl-residues.eu

Expected Output: Update of webpages and Postage of Documentation for COMM, for EU-MS NRLs, for Third Country Official Laboratories and Survey of Documentation provided through the years 2023-2024

Duration: 2023-2024

Sub-activity 1.3: Publication of the list of EURL analytical methods on the public EU-RL website

Objectives: Follow-up and update of the EURL Website in regard to analytical method publication on the public Home Page

Description: As a follow-up of a request from the Commission DG-SANTE, publication of the list of our EU-RL developed analytical methods will be posted and yearly updated on the public part of our EU-RL website: http://eurl-fougeres-veterinaryresidues.anses.fr together with links to technical notices when appropriate.

Expected output: Provision of information on analytical methods; update on the publication of the list of EU-RL available analytical methods via the EURL website

Duration: 2023-2024

B) Follow up on requests from NRLs for providing analytical standards

Sub-activity 1.4: Procurement of reference analytical standards to the network of EU-NRLs

Objectives: Procurement of reference analytical standards to the network of EUMS-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 standard 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) 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.

Duration: 2023-2024

Sub-activity 1.5: Procurement of reference tissue sample materials to the network of EU-NRLs

Objectives: Procurement of reference tissue sample materials to the network of EU-NRLs

Description: The PT materials placed 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: The EU-RL PT materials will be made available enlisted in the appropriate web page of the EU-RL website (http://eurl-fougeres-veterinaryresidues.anses.fr) and prepared for shipment to the EU-MS NRLs upon their specific request through our EU-RL website procedure

Duration: 2023 - 2024

C) Organisation of proficiency tests and follow up on the results

Sub-activity 1.6: Organisation of PTs and Follow up on and communication of the PT results

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 previous program of the period 2021-2022, the substances of choice might be a combination of either the non-authorized substances chosen among the groups A2ab (chloramphenicol, nitrofurans), A3a (dyes) and A3c (quinoxalines) or of the MRL-authorized substances of group B1a (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 corresponding issues raised in 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 2023, a Confirmatory PT for Chloramphenicol Residues in Casings in line with new RPA of 0.15 µg/kg (Reg 2019-1871) will be delivered.

For 2024, a Confirmatory PT for Nitrofuran Residues in Casings in line with new RPA of 0.5 µg/kg (Reg 2019-1871) will be delivered. This PT might be provided partially outsourced (materials preparation and sending of the round samples) with an external recognized PT provider. Additionally, will be delivered a second PT for Multi-Screening and Confirmation of Group B1a Authorized Antimicrobial Residues in Farmed Fish and followed by a Collaborative Study Round 2 dedicated specifically to LC-MSMS / LC-HRMS(MS) instruments for Multi-Screening of all Group B MRL-Authorized VMP Residues in Extracts of Fish and/or Honey.

Expected Output: Provision of Proficiency Testing Studies for MULTI-SCREENING and CONFIRMATION of Authorized and/or Prohibited substances from Group A2ab, A3ac, or B1a (by means of either 1 large or 2 reduced PT round each year in selected species/matrices) for year 2023 and for year 2024.

A final report on the results obtained by the participating laboratories will be delivered by the EURL to the participants and to the DG-SANTE desk officer within the 6 months following the end of the PT round(s) of analyses carried out by EU-MS NRLs.

The report will also be posted in due time on our EU-RL website to the attention of the DG-SANTE exclusively. For PTs, a specific follow-up by the EU-RL of corrective actions after non-compliant results of NRL participant(s) will also be undertaken in line with Commission requirements. Specific information will be attached to the final report posted to the attention of the DG-SANTE exclusively and to the relevant Competent Authority(ies).

Duration: 8 to 9 months from the organisation and delivery of the PT round to the release of final report + 2 to 3 more months for the follow-up of possible corrective actions handled by specifically designated NRLs after the final report delivery.

Sub-activity 1.7: Production of incurred materials for PT testing

Objectives: Production of incurred sample materials for the Proficiency Testing task and relevant for authorized and /or non-authorized substances from Groups A2a, A2b, A3a, A3c, or B1a

Description: According to the sub-activity 1.6 here-above for testing relevant authorized and/or non-authorized substances from Groups B1 (MRL-antimicrobials), A2ab (CAP, NIFU), A3a (FISH-FARMING DYES), and/or A3c (QUINOXALINES) the requested reference sample materials (as far as possible being prepared naturally incurred materials) will be produced at one of the experimental farms of Anses laboratories and prepared in accordance with the ISO standards of PT testing material preparation (homogeneity and stability studies) and under our recognized quality assurance scheme (accreditation N° 1 – 2294 - www.cofrac.fr). Additionally, the preparation of the materials for the PT on nitrofurans in casings might be prepared outsourced with an external recognized PT provider.

Expected Output: Production of at least 3 new Testing Materials per PT round for year 2023 and also for year 2024

Duration: 2023-2024

Sub-activity 1.8: Preparation for transfer of incurred samples

Objectives: Maintenance and testing of incurred sample materials prepared for previous Proficiency Testing task and relevant for authorised and /or non-authorised substances from Groups A2a, A2b, A3a, A3c, or B1a

Description: According to the here-above sub-activity 1.3 for testing relevant authorized and/or non-authorized substances from Groups B1a (MRL-antimicrobials), A2ab (CAP, NIFU non-authorised antimicrobials) and/or A3a (FISH-FARMING DYES) and/or A3c (QUINOXALINES), 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. Transfer of the produced reference materials to convenient storage, stability control and use for the EU-MS-NRLs network.

Duration: 2023-2024

D) Cooperation, collaboration and meetings with other EURLs and scientific exchange

Sub-activity 1.9: Meeting of the cluster of EU-RLs, EU-RLs residues management

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. Up to 5 meetings of 1 or 2 days for year 2023 and also 5 meetings in 2024. Probably some additional on-line web conference-like meetings.

Expected Output: Up to 5 missions per year for one EU-RL delegate including the annual general meeting of the EU-RLs Directors + virtual webconference-like meetings at least once every 2 months.

Duration: 2023-2024; In-person meetings over 2 days per mission

Sub-activity 1.10: On going support and assistance as regards the implementation of the new Regulation (EU) 2021/808 and its attached EURL guidelines to be carried out over 2023 and 2024

Objectives: Follow-up by the Cluster of the 3 EU-RLs (ANSES, BVL, WFSR) on the implementation of the Regulation 2021/808 for the validation of performance of VMPR analytical methods and of its attached EURL Technical Guidelines that will need to be from time to time technically updated.

Description: The regulation (EU) 2021/808 entered into force in June 2021 and is intended to require a 5-year period to be completely implemented in the EU-MS official control laboratories by June 2026 (see Reg (EU) 2021/808).
Subsequently, four relevant practical guidance documents have also been proposed to the network of official laboratories to clarify the implementation of the regulation.
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. Finalised during the programme 2021-2022, they will probably need updates during the programme 2023-2024.

Expected Output: Revised version of updated Technical Guidelines for Validation of VMPR Analytical Methods complementing the foreseen Regulation. All revised documentation and its follow-up versions will be posted onto our EU-RL website (http://eurl-fougeres-veterinaryresidues.anses.fr) and onto the VMPR cluster portal (https://eurl-residues.eu/)

Duration: 2023-2024

Sub-activity 1.11: 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 2023 and 2024

Objectives: Follow-up of the organisation and scientific and technical maintenance for a common Internet approach to disseminate VMPR information throughout the cluster of 3 "EURLs" to the attention of the network of NRLs and further outside the EU.

Description: The project of VMPR Portal Website was finalized by the 3 EURLs in Feb 2021 and together with links to the COMMISSION DG-SANTE Website. Future maintenance of the Portal and update of the VMPR news will be addressed by habilitated staff from each of the 3 EURLs.

Expected Output: Maintenance/improvement of a website portal able to give enough visibility for the different EU-RL websites already in place and Linkage between EU-RL websites of the VMPR cluster and the Portal possibly supported by the DG-SANTE website platform. Update of the portal webpages by habilitated staff from the 3 EURLs.

Duration: 2023-2024

Sub-activity 1.12: Advances in harmonisation of PT performance criteria within the "VMPR" EURLs to be carried out over 2023-2024

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 was started in 2022 to try better including if possible the individual factors dedicated to evaluate screening methods. This second-step project will be carried out to be presented to the network of EU-MS NRLs during the programme 2023-2024.

Expected Output: Common PT performance criteria drafted in a EU-RL cluster's protocol delivered to the network of NRLs and posted onto the EU-RL website.

Duration: 2023-2024

Sub-activity 1.13: Development of a common EURL cluster VMP-database for Mass Spectrometric data to be carried out over 2023 and 2024

Objectives: Development of a common EURL cluster VMP-database dedicated to Mass Spectrometric aspects.

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.). A draft will be prepared and contents are to be discussed with the NRLs in order to meet their needs.

Expected Output: Database to be hosted by the EURL and/or the Cluster portal website.
Duration: 2023-2024

Sub-activity 1.14: Development of a common EURL cluster VMP-database for collecting VMPR stability studies to be carried out over 2023 and 2024

Objectives: Development of a common EU-RL cluster VMP-database dedicated to Stability aspects

Description: A database with information on the stability issues, and on standard providers, etc. A draft will be prepared and contents will be discussed with the NRLs in order to meet their needs

Expected Output: Database to be hosted by the EURL websites and/or the Cluster portal website.
Duration: 2023-2024

Sub-activity 1.15: Development of a common EURL cluster VMP-database for EURL/EU-NRL VMPR Analytical Methods to be carried out over 2023 and 2024

Objectives: Development of a common EU-RL cluster VMP-database dedicated to share analytical methods for VMPR.

Description: A database will be built under the scope of the 3 EURL and yearly updated by the NRLs from the 27 EU-MS with the aim to disseminate the information and parameters on the VMPR analytical methods developed and validated across the EU reference laboratories (EURLs + EU-NRLs).

Expected Output: Database hosted by the EURL BVL-Berlin and with links posted in the 3 EURL websites and in the VMPR-EURL Cluster portal website.

Duration: 2023-2024

E) Development and validation of analytical methods

Sub-activity 1.16: Development and Validation of Analytical Methods - Extending our LC-HRMS Q-Orbitrap screening/identifying method developed in Meat and Milk for Group B1a antimicrobial residues and for other Group B1bcde and B2 (about 200 substances) to cover also analysis in Eggs

Objectives: To demonstrate the adaptation for future surveillance plans of a Full-Scan High Resolution MS analytical method based on a LC-Q-Orbitrap system for a large scope of VMPRs and through a workflow of "Screen + Confirm" process.

Description: The context of the evolution of screening strategies put the new LC-HRMS analytical systems at the top 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 and including as many relevant Group B1a antibiotic residues as possible and also including some other relevant classes B1bcde and B2 of VMP residues (Benzimidazoles, Avermectins, Anticoccidials, NSAIDs, …) within a single Full Scan High Resolution Mass Spectrometric instrument: an LC-QOrbitrap-MS instrument. Further to the evolution of screening strategies by means of considering LC-HRMS analytical systems demonstrated during our 2019-2020 programme in meat and during our 2021-2022 programme in milk by means of a LC-Q-Orbitrap equipment, it is now intended to enlarge these extensions to eggs by starting building a complete Q-Orbitrap workflow demonstrating the screening/identifying/confirming VMPRs at large in all 3 major commodities (meat/milk/eggs). This project will address the need for these enlarge scope methods for the surveillance of targeted and non-targeted VMPRs to be set up after enforcement of the new Commission regulations (EU) 2022/1644 and 2022/1646.

Expected Output: In 2023, extending the development of the workflow for about 200 VMPRs in Eggs including the about 80 antibiotics to be transferred from the LC-QTOF strategy to the LC-Q-Orbitrap strategy, followed in 2024 by a validation of the workflow, an hands-on training dedicated to the workflow LC-HRMS strategy will be presented to the network of EU-NRLs during the annual workshop of 2024 together with the release of a Standard Operating Procedure.
Presentations together with SOP and summary of validation report to be posted in due times on our EU-RL website to the attention of the network of NRLs; communication to the international scientific community should be delivered in a symposium and/or through an article in an international peer-reviewed scientific journal.

Duration: 2023-2024

Sub-activity 1.17: Development and Validation of Analytical Methods - Extending our LC-HRMS Q-TOF screening/identifying method on Group B1a antimicrobial residues in Eggs to cover other Groups of VMPR from B1bcde and B2 and extending the scope of analysis from Eggs to Meat and Milk commodities

Objectives: To demonstrate the adaptation for future surveillance plans of a Full-Scan High Resolution MS analytical method based on LC-Q-TOF systems for a large scope of VMPRs and through a workflow of "Screen + Confirm" process.

Description: : The context of the evolution of screening strategies put the new LC-HRMS analytical systems at the top 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 and including as many relevant Group B1a antibiotic residues as possible and also including some other relevant classes B1bcde and B2 of VMP residues (Benzimidazoles, Avermectins, Anticoccidials, NSAIDs, …) within a single Full Scan High Resolution Mass Spectrometric instrument: an LC-QTOF-MS instrument. Further to the evolution of screening strategies by means of considering LC-HRMS analytical systems demonstrated during our 2019-2020 programme in meat and during our 2021-2022 programme in milk by means of a LC-Q-Orbitrap equipment, it is now intended to transfer and enlarge these extensions to the LC-QTOF-MS system by starting building a complete QTOF detection workflow demonstrating the screening/identifying/confirming VMPRs at large in all 3 major commodities (meat/milk/eggs). This project will address the need for these enlarge scope methods for the surveillance of targeted and non-targeted VMPRs to be set up after enforcement of the new Commission regulations (EU) 2022/1644 and 2022/1646.

Expected Output: In 2023, will be started the transfer of the meat and milk VMPR screening method developed on LC-Q-Orbitrap to the LC-Q-TOF screening method. As a follow-up the validation of the enlarged transferred method will occur in the course of 2024, an hands-on training dedicated to this LC-HRMS method will be presented to the network of EU-NRLs during the next annual workshop of 2024 together with the release of a Standard Operating Procedure; also the report of validation according to Reg (EU) No 2021/808 and the SOP will be posted into the EU-RL Website.
Communications to the international scientific community should be delivered in a symposium and/or through an article in an international peer-reviewed scientific journal.

Duration: 2023-2024

Sub-activity 1.18: Development and Validation of Analytical Methods – Follow-up on a collaborative evaluation of the state-of-the-art in EU-MS NRLs analytical instrumentation as of their advanced analytical strategies for implementing Method(s) dedicated to B1a Multi-Antimicrobial and other group B1bcde and B2 VMP using suitable LC-MSMS and/or LC-HRMS instruments

Objectives: 1 - To demonstrate the current state-of-art of the EU-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 extending to several food commodities.

Description: Considering the advances in mass spectrometric high resolution technologies (i.e. time-of-flight and orbital trap instruments) and the current level of instrumental acquisition by EU-MS NRLs

of such systems over the very 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 HRMS instrumentation. This sub-activity corresponds to an additional stage in the previous project carried out during our 2021-2022 programme which was to further investigate the outcomes and benefits of these multi-screening methods whatever employing Low Resolution or High Resolution mass spectrometric detection in meat and milk VMPR contaminated extracts. This new stage of the collaborative study will be enlarged to the whole NRLs network using LC-LRMS and LC-HRMS systems provided they are used their methods for a large screening of Group B VMPR analytes in food commodities other than Meat and Milk, ie. in Eggs, Liver, Kidney, Fish and Honey. 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; the report of the collaborative inter-laboratory study; these reports will also be presented thoroughly during one of our EU-RL workshops and also posted onto our EU-RL website to the attention of the network of NRLs. A scientific presentation will be delivered in at least one international scientific symposium. A publication might be further submitted to a peer-reviewed international scientific journal.

Duration: 2023-2024

Sub-activity 1.19: Development and Validation of Analytical Methods - Confirmatory LC-MS/MS monitoring of group A2 prohibited VMP substance residues in porcine/ovine meat and casings and gelatine manufactured products as of follow-up of new rules for their entry into the EU

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 possibly prohibited nitroimidazoles in porcine/ovine meat products and also in manufactured porcine/ovine casings and gelatine products 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 2019-1871) and the new standardized criteria for performance of official control methods according to the 2021-808.

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 EU-MS. In order to reduce 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 prohibited antimicrobial substances (Table 2 of Reg 2010/37) as possible within the very same unique routine official 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. The specific case of the gelatines and possibly other similar products will also be evaluated in order to demonstrate the applicability of the method to these manufactured products in line with new version of Regulation 2019/1871.

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

validation according to Regulation (EU) No 2021/808 will be drafted; a hands-on training will be delivered during the next annual workshop; SOP and validation report to be posted in due times on our EU-RL website to the attention of the network of NRLs; a communication to the International Scientific Community to be delivered in Symposium and/or through an International Peer-review Scientific Journal.

Duration: 2023-2024

Sub-activity 1.20: Development and Validation of Analytical Methods – Search for new Marker Residue of the Nitrofurazone intended to replacing the Semicarbazide

Objectives: To search for new metabolite markers of nitrofurazone illegal therapeutic treatments in aquaculture and also in manufactured food products like gelatin.

Description: Nitrofurazone is a medicinal active principle belonging to the class of antibacterials. It has been prohibited throughout the European Union for almost 30 years (Community decision n ° 2003/181/EC of March 13, 2003). This ban also applies to all its congeners of the same family namely the nitrofurans for all of their previous usage in animal husbandry veterinary treatments. These molecules bear proven toxicity (carcinogenic, mutagenic) and therefore represent a risk for the consumer. Nitrofurans and nitrofurazone are also substances assigned by the European Commission DG-SANTE and by the French Ministry of Food & Agriculture to the National Reference Laboratory at ANSES-Fougères for its methodological control. Currently, their detection in foodstuffs is based on the control of persistent marker residues, mainly derived from metabolized substances which bind to proteins in animal tissues (Hoogenboom, 1992; Rupp, 1993; McCracken, 2000). The current metabolic marker of nitrofurazone treatment, which is also considered toxic, corresponds to a molecule called semicarbazide whose internationally accepted acronym is SEM. However, it has been shown that under certain thermal and biochemical conditions applied in the food processing industries, this compound can also appear in certain food products of animal origin without any veterinary treatment based on the nitrofurazone active drug. This indicates that testing for nitrofurazone treatment using SEM may lead to some false positive test results. This marker is not unambiguous and generate a concern when veterinary inspection checks in animal-derived food (Pereira et al, 2004; Saari et al, 2004; McCracken et al, 2010; Van Poucke et al, 2011). Finding a new way to control the illegal use of nitrofurazone in food-producing animals is the objective of our project. The phases of the project consist in i) re-investigating with recent analytical means the metabolism of nitrofurazone in targeted aquaculture species (farmed fish and shrimp) ii) detecting one or more new marker(s) able to discriminate illegal treatment with nitrofurazone in aquaculture from environmental contamination by native SEM; and iii) developing suitable analytical control methods for the foodstuffs of concern. Over a 2-year study, the applied approaches will be as follows:

• Approach 1 on NF marker: Pharmacokinetics study of bound and unbound NF and SEM in the trout Oncorhynchus mykiss and in the Penaeus Monodon-type shrimp or similar aquaculture products (fish).
• Approach 2 on other relevant metabolite(s): suspected and unsuspected non-targeted search for new metabolites,
• Approach 3: non-targeted search for markers of treatment (metabolomics approach).

In parallel will be investigated the relevance of new marker of nitrofurazone to be replacing SEM for findings of nitrofurazone in gelatine and other food-producing animal derived manufactured products.

Expected Output: Synthesis of the DNPH derivative of 5-Nitro-2-furaldehyde (DNPH-NF) and development and validation of analytical method(s) for confirming DNPH-NF in biological matrices (shrimp and farmed fish) by chromatographic analyses of the LC-MS/MS and LC-HRMS type with relevant SOP and validation report deliverables. Treatment of shrimp in experimental farm with nitrofurazone and targeted depletion study (NP-SEM, DNPH-NF) and non-targeted search for other metabolites. Research and determination of SEM and NF in the shrimps resulting from the experiment

after respective derivations by LC-MS/MS. Advances and deliverables will be transferred to the attention of the network of NRLs during the appropriate annual workshop. SOP and validation report to be posted in due times on our EU-RL website to the attention of the network of NRLs. Communication to the International Scientific Community to be delivered in Symposium and/or through an International Peer-reviewed Scientific Journal. Dissemination of information on relevance of new marker of nitrofurazone in gelatine and other food-producing animal derived manufactured products

Duration: 2023-2024

Sub-activity 1.21: 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 – Voltametric devices) for unique or multiplex screening of non-authorised antimicrobial substances

Objectives: 1 - Our first action in 2023 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 milk and meat products. A method will be developed, optimised and validated for the screening of a range of one to three antibiotic families below their RPA in milk and meat products. 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 2023-2024 will be to test different bioreceptors (when available) (eg. antibodies and aptamers). 4- The fourth objective in 2024 will be to develop one new multiplex method for these 2 to 3 families in milk and meat products. Afterwards we will try to adapt the new multiplex method for non-authorised substances in other matrices (eg. 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 based on Screen printed carbon electrodes (SPCE) is low. Moreover, the development of methods is manageable, using antibodies and antibiotic-enzyme conjugates. In 2017, a technical evaluation of the system was performed in our laboratory. A specific amperometric method for chloramphenicol detection in milk was developed but the detection capability was much higher than the RPA. The development of specific amperometric and voltametric methods for chloramphenicol in honey started in our programme 2019-2020. However again the sensitivity of the developed sensor was not enough low, especially due to high matrix effects related to the different botanical origin of honey matrix. Therefore, in 2021-2022, the development of new biosensors called aptasensors for the detection of chloramphenicol in milk started. The use of aptamers (ie. DNA) as biorecognition elements instead of antibodies is a major trend in the development of biosensors for clinical purposes and in food safety developments. Preliminary results obtained in 2022 on aptasensors for the detection of chloramphenicol in milk were very promising. Therefore, the first objective in the 2023-2024 period will be to go on with the development of aptasensors for chloramphenicol in milk and meat products, two complex matrices for electrochemical detection. Then the second objective is to compare the performances of the different aptasensors combined with different voltametric techniques, and using different nanomaterials for signal amplification purposes. The third objective in 2023-2024 will be to enlarge with the development of new single methods first and then in 2024 to develop one new multiplex method of non-authorized substances (e.g. chloramphenicol and 5

nitrofuran metabolites) in milk and meat products, 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. It will contain the advances on the single compounds methods for non-authorised substances that will be developed and validated in 2023. A presentation of the advances on the project will be delivered during the EU-RL workshop of 2023 and/or during an international congress in 2023.
In 2024, a multiplex method for several non-authorised substances will be developed and validated. The evaluation report will be delivered by the end of 2024 to the network of NRLs. The evaluation reports will be then posted on our EU-RL website to the attention of the network of NRLs. A formal presentation of the final advances on the project will be delivered during the workshop organised in 2024 to the attention of the NRLs experts. Then publications in peer-reviewed scientific journals might be also considered.

Duration: 2023-2024

Sub-activity 1.22: Evaluation of sensitivities of ELISA testing kits for residues of groups A2 & A3a prohibited antibiotics at and below their new RPAs according to Reg 2019-1871

Objectives: 1 - Evaluation of the performance of several commercially available ELISA kits (BIOREX, Randox, Creative Diagnostics, TECNA, ….) 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. Each ELISA kit is targeting one analyte: chloramphenicol, single nitrofuran metabolite, single dye. 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. ELISA kits for these banned substances, especially chloramphenicol and nitrofurans metabolites, are commercialised by many different manufacturers, with different analytical protocols and different performance characteristics. Some ELISA kits (Europroxima, r-Biopharm) were evaluated in the course of the 2021-2022 years of our programme according to the new regulation EC/2021/808 and to the European guideline for the validation of screening methods (2010). The objective in the programme 2023-2024 is to continue the evaluation of ELISA kits from other manufacturers (eg. BIOREX, Randox, Creative Diagnostics, TECNA, ….).

Expected Output: One evaluation report will be delivered to the network of NRLs. The evaluation report will then be posted on our EU-RL website to the attention of the network of NRLs. 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. A scientific publication in a peer-reviewed journal and communication in international symposia could be also further considered.

Duration: 2023-2024

Sub-activity 1.23: Analysis of official samples in case of dispute or as third-part evaluation

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: 2023-2024

WP1 List of indicators:

- Number of laboratory methods for which details and guidance as regards their techniques, validation and interpretation are available in the EURL website
- Number of new laboratory methods developed in the reporting period
- Number of laboratory methods improved in the reporting period
- Number of Proficiency Tests (PTs) organised by the EURL for national reference laboratories/NRLs (indicate for each year – 2023 & 2024)
- Cost of PTs
- Number of Comparative Tests (CTs) organised by the EURL for NRLs (indicate for each year – 2023 & 2024)
- Cost of CPs
- Success rate of Member States NRLs/OLs in PTs/CTs and, if necessary, corrective action
- Number of corrective actions undertaken (aggregated data on corrective actions for all NRLs)

3.2. WP2: SCIENTIFIC AND TECHNICAL ASSISTANCE TO NRLs

WP2 objectives: To provide scientific and technical assistance to NRLs

- *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. (including for instance GLOBAL TRAININGS DURING ANNUAL WORKSHOPS)*
- *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. (including for instance 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. (at ANNUAL WORKSHOP / at INTERNATIONAL SYMPOSIA / onto EU-RL WEBSITE / at any relevant NRL request / …)*

This WP is divided in **five sub-activities**, as follows:

Sub-activity 2.1: Continuous technical and scientific communication with the network of EU-MS NRLs

Objectives: Delivering upon requests from the EU-MS-NRLs any technical and scientific advices and information related to the field of VMPR groups A2abd-A3ac-B1a

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 can be reported upon request.

Duration: 2023-2024.

Sub-activity 2.2: Organisation of the annual workshop to the attention of the network of EU-MS NRLs from 2023 and from 2024

Objectives: Organisation of the annual workshop to the attention of EU-MS NRLs

Description: A 2-day or 3-day workshop to the attention of the experts from the network of EU-MS NRLs and EU-CC-NRLs in charge of antimicrobial residue control in food will be organised in conformity with requirements of current enforced Regulation (EU) for Union financial aid to the EU reference laboratories. This annual workshop may also include when necessary a technical training session. The venue and a preliminary agenda will be announced at the beginning of the year and prepared according to main regulatory, scientific and technical issues to be exchanged with the EU-MS NRL network.

Expected Output: Announced at the beginning of the year 2023 and of the year 2024; Postage onto the EU-RL website; Release of the programme and list of participants to the workshop; Dissemination of all documents delivered during the workshop by posting onto the EU-RL website.

Duration: 2023-2024.

Sub-activity 2.3: Analytical support and technical TRAININGS at the specific request of EU-NRLs or Official Laboratories of Candidate Countries

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

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, …) are foreseen for the period 2023-2024.

Duration: 2023-2024.

Sub-activity 2.4: Continuous technical and scientific communication with the network of EU-MS NRLs by phone, email and any other type of communication

Objectives: Delivering upon requests from the EU-MS-NRLs any technical and scientific advices and information related to the field of VMPR groups A2abd-A3ac-B1a

Description: Over the year, a continuous line of communication is carried out by any means like phone call, emails, EU-RL website, …. can be reported upon request

Expected Output: Listing of the issues exchanged with the EU-MS NRLs by the continuous line of communication.

Duration: 2023-2024.

Sub-activity 2.5: Update of the LIST of EU-MS NRLs in charge of VMPR Control in Food

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: A2abd, A3ac, B1a.

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) and/or onto the new VMPR cluster portal (https://eurl-residues.eu/)

Duration: 2023-2024.

WP2 List of indicators:

- Number of enquires requested from national support networks and bodies and competent authorities
- Number and quality of replies provided to enquiries of national support networks and bodies and competent authorities
- Number of training and collaboration activities with national support networks and bodies and competent authorities
- Number of workshops & meetings organised
- Cost for workshops & meetings and average cost for participant
- Number of technical assistance provided by the EURL to NRLs enquiries

3.3. WP3: ASSISTANCE TO THE EUROPEAN COMMISSION AND OTHER ORGANISATIONS

WP3 Objective: To provide scientific and technical assistance to the European Commission and other organisations.

- *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.*

This WP is divided in **eight sub-activities**, as follows:

A) Scientific and technical assistance to the Commission (94.2.f)

Sub-activity 3.1: Analysis of National residue monitoring plans of the EU-MS for 2023

Objectives: For the year 2023, an evaluation of the National Residue Monitoring Plans of the 27 Member States + 3 EFTA Countries (Norway, Iceland, Northern Ireland) + 1 CC (North Macedonia) in terms of analytical methods in use for VMPR substances of Groups A2abd (CAP, NIFU, DAP), A3ac (Dyes, CBX, OQX), B1a (MRL-antimicrobials)

Description: The evaluation of the National Residue Monitoring Plans is operated under the recommendations and in collaboration with DG-SANTE-F4 and with the EFSA Chemical Monitoring IDATA Unit. The main period of evaluation occurs from April-May to July-August of the Year. Additional steps in the evaluation may be carried out in the September-November period when requested by DG-SANTE-F4.

Expected Output: Release of the evaluation after the first step to the Commission DG-SANTE-F4 and after the second step afterwards comments from and technical exchange with the MS-CAs and MS-NRLs if needed.

Duration: 2023.

Sub-activity 3.2: Analysis of National residue monitoring plans of the EU-MS for 2024

Objectives: For the year 2024, an evaluation of the National Residue Monitoring Plans of the 27 Member States + 3 EFTA Countries (Norway, Iceland, Northern Ireland) + 1 CC (North Macedonia) in terms of analytical methods in use for VMPR substances of Groups A2abd (CAP, NIFU, DAP), A3abc (Dyes, CBX, OQX), B1a (MRL-antimicrobials).

Description: The evaluation of the National Residue Monitoring Plans is operated under the recommendations and in collaboration with DG-SANTE-F4 and the EFSA ChemMon Unit. The main period of evaluation occurs from April-May to July-August of the Year. Additional steps in the evaluation may be carried out in the September-October period when requested by DG-SANTE-F4.

Expected Output: Release of the evaluation after the first step to the Commission DG-SANTE-F4 and after the second step afterwards comments from and technical exchange with the MS-CAs and MS-NRLs if needed.

Duration: 2024.

Sub-activity 3.3: Support to Commission on specific items upon request in 2023

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.

Description: -

Expected Output: 2 or 3 medium-large requests over the year 2023 of the WP 2023-2024

Duration: 2023.

Sub-activity 3.4: Support to Commission on specific items upon request in 2024

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.

Description: -

Expected Output: 2 or 3 medium-large requests over the year 2024 of the WP 2023-2024

Duration: 2024.

B) Collaboration with European and international organisations and Third Countries

Sub-activity 3.5: Co-operation with European / International organisations: DG-SANTE/FVO, EMA, EFSA, EURACHEM, AOACI, FAO-AIEA, ISO, CEN, FIL-IDF, IUPAC, …

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 expertise data or advices delivered to these European or International Official Entities

Duration: 2023-2024

Sub-activity 3.6: Participation to advanced schools for Third Countries Laboratories like SARAF or BTSF training courses upon request

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: 2023-2024

Sub-activity 3.7: International missions of EURL 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 programs 2023 and 2024

Objectives: International missions of EURL 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: 2023-2024

Sub-activity 3.8: Continuous reporting of staff activities in our 'PROJEO' tool time-sheets of the years 2023 and 2024

Objectives: Mandatory reporting of staff activities related to the EURL programme and according to the contracted agreement.

Description: A reporting of the time dedicated to EURL projects will be reporting monthly per each staff under prescribed sub-activities. The staff time-sheets will be validated by the Direction of the laboratory and will be made available to the Commission upon request at the end of the program together with the final report for 2023-2024 biannual program.

Expected Output: Monthly reported time-sheets per EURL staff

Duration: 2023-2024

WP3 List of indicators:

- Number of technical and scientific feedback provided by the EURL based on European Commission enquiries
- Number of collaboration activities with other organisations

3.4. WP4: REAGENTS AND REFERENCE COLLECTIONS

WP4 objectives:

- *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.*

EU-RL not concerned

- *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;
  EU-RL 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 our 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 Materials from our PTs

This WP is divided in **two sub-activities**, as follows:

Sub-activity 4.1 Up to date lists of available reference substances and reagents and of manufacturers and suppliers of such substances and reagents

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 EURL 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)

Duration: Over the years 2023-2024

Sub-activity 4.2 Database for reference materials

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. 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.

Duration: Over the years 2023-2024

3.5. REQUIREMENTS RELATED TO OTHER LEGISLATION

Not applicable.

4. REMARKS

Not applicable

EUROPEAN HEALTH AND DIGITAL EXECUTIVE
AGENCY (HADEA)
Department A Health and Food Unit A2 EU4Health/SMP

Single Market Programme (SMP Food)

SMP-FOOD-2023-EURL-EURC-AG-IBA
Activities of the EU reference laboratories and EU reference centres in 2023-2024

SUBMISSION FORM: DESCRIPTION OF THE ACTION
(Annex 1 – Description of the action (part B))

SMP-FOOD-2023-EURL-EURC-AG-IBA

Activities of the EU reference laboratories and EU reference centres in 2023-2024

Applicant shall provide information on each question contained in the Form. The information filled in the Form, shall be clear, concise, consistent and complete.

For questions on the information requested in this Form, please contact: please contact: HADEA-EURL@ec.europa.eu.

For questions on the eGRANTS Portal Submission System, please contact the IT Helpdesk.

Applicant - COORDINATOR (Name of EURL)	EURL for Residues of veterinary medicines and contaminants in food of animal origin at the German Federal Office of Consumer Protection and Food Safety (BVL), "EURL Berlin"
Topic	**Residues of veterinary medicines and contaminants in food**
Implementation period	**1/1/2023 – 31/12/2024**

CONTACT PERSON for the programme :

Name	Joachim Polzer
Function	Director of EURL Berlin
e-mail	eurlvetdrug@bvl.bund.de

ASSOCIATED PARTNER 1 (Name)	
Contact person :	
e-mail :	

Contents

1. LIST OF ABBREVIATIONS AND KEY WORDS

BIPM	Bureau International de Poids et Mesure
FIS-VL	Restricted access information platform of the EURL Berlin for NRLs
HRMS	High resolution mass spectrometry
IMS	Ion mobility spectrometry
NSAID	Non-steroidal anti-inflammatory drugs
MMPR	Minimum method performance requirements
OAWG	Organic analysis working group
PT	Proficiency test
QTOF	Time-of-flight mass spectrometry
RM	Reference materials

2. INTRODUCTION

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 16 of Regulation (EU) No 2021/690:

(taking into account Art 147 of (EU) 625/2017)

The following program for the 2023/24 work period was presented to the Member States on December 9, 2022, during the meeting of the Working Group on Residues of Veterinary Medicinal Products in Food of Animal Origin of the Toxicological Section of the Standing Committee on Plants, Animals, Food and Feed (SCPAFF). The program was approved by the responsible desk officers of DG SANTE.

3. ACTIVITIES

3.1. WP 1 - METHODS

Objective: TO ENSURE AVAILABILITY AND USE OF HIGH QUALITY METHODS AND TO ENSURE HIGH QUALITY PERFORMANCE BY NRLs

- *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 *3.*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. According to the request of COM, the provided information is restricted to specific groups with special access rights for each group (MS-NRLs, candidate country NRLs, EFTA country NRLs, third country NRLs, COM).

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: 2023/24

Sub-activity 3.1.2 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 and standard substances 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 materials to official control laboratories (OCL) for scientific purposes.

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. Furthermore, it is an ongoing task to investigate possible novel and emerging veterinary drugs, their metabolisation or degradation products.

Reference standards ("standard substances") and incurred reference materials are provided to NRLs as well as to official control laboratories in third countries upon request (regularly updated order forms for standard substances and for reference materials are made available 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 2023/24 are associated with an element of uncertainty due to the still unpredictable situation with COVID 19 on the one hand, and with regard to cases of infectious animal diseases, which are presently spreading in Germany, on the other hand. In addition, the realisation of animal experiments gets more and more complicated due to the changed animal welfare rules and requirements set by the competent regulatory authority. This is especially the case for the treatment of animals with banned or unauthorised substances, and if animals are to be slaughtered at the end of the animal study.

In 2023/24 the following materials shall be produced:

Avermectins in milk (2-3 analytes)

NSAIDs in milk (2-3 analytes)

NSAIDs in egg (1-2 analytes)

Fipronil in egg

Pesticides in animal matrix (1-2 analytes)

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 2023/24 (cf. 3.1.3):

Avermectins in milk (2-3 analytes)

NSAIDs in milk (2-3 analytes)

NSAIDs in egg (1-2 analytes)

Coccidiostats in liver (2 analytes)

Anthelmintics in milk and muscle (1 analyte + metabolites, 1 milk + 1 muscle material)

Beta-agonists in urine (2-3 analytes)

Expected Output:

Pre-tested incurred matrix materials for proficiency tests and for scientific purposes; candidate reference materials: avermectins in milk (overall 2-3 materials), NSAIDs in milk and egg (overall 3-4 materials), beta-agonists in urine (overall 2-3 materials), coccidiostats in 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:

2023/2024

Sub-activity 3.1.3 *Organisation and evaluation of proficiency tests and follow-up on results*

Objectives:

Organisation and evaluation of proficiency tests and follow-up on results

Description:

The EURL Berlin regularly organises 1 - 2 proficiency tests a 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 are 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 a year.

For 2023/24 the following activities are planned:

- Follow-up to PT on nitroimidazoles in plasma and milk (NIIM1021)

- Final report and follow-up to PT BETA0622

- Final report and follow-up to NIIM1122

- PT on precision and accuracy in the analysis of standard solutions (2023)

- Final report and follow-up to PT on standard solutions (2023/24)

- PT on coccidiostats in tissue (2023)

- Final report and follow-up to PT on coccidiostats in tissue (2023/24)

- PT on beta-agonists in tissue (2024, final report and follow-up if feasible in 2024)

- Avermectins in milk (2024, final report and follow-up if feasible in 2024)

The accuracy 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 usually been done 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. Therefore, NRLs suggested that standard solutions be generally provided by the EURL. Since this is not feasible (and sensible), PT STRD0521 allowed participants 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. As the NRLs' feedback on the suitability on this type of PT was positive, it is planned to repeat this kind of study with relevant analytes every couple of years. As with STRD0521 it is envisaged to prepare the standard mixes gravimetrically and to derive the assigned values based on this procedure, if feasible. If available, certified standards will be used for the preparation of the test items.

Expected Output:

Final reports on the 2022/2023 PTs (BETA0622 on beta-agonists in bovine urine, NIIM1122 on nitroimidazoles in porcine muscle, standard solutions, coccidiostats in tissue); short report on either PT on beta-agonists in tissue or avermectins in milk; 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:

2023/24

Sub-activity 3.1.4 *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 every year. Moreover, an additional exchange among the EURLs with respect to an agreed strategy, emerging problems, increased efficiency and synergy effects is required and takes place several times a year.

For the 2023/24 working period the following common activities are planned:

- Extension and maintenance of a cluster EURL VMP method performance database for EURLs/EU-NRLs network (Almanac), update of database to the revised substance group assignment

- Harmonisation of the “Common EURL Protocol for Proficiency Testing in the Field of Veterinary Drug Residues” with regard to the scoring for the evaluation of screening methods

- Continuation of a cluster EURL VMP database for the EURL/EU-NRL network with provision of VMPR mass spectrometric data and other substance information (initiated in 2021/22)

- Provision of a common NRL contact list in FIS-VL for the regular update of NRL information (only accessible to the 3 VMP EURLs); annual provision of generic contact information on EURL cluster portal

- Ongoing support and assistance to NRLs, COM and EFSA with regard to the implementation of CIR 2021/808 and the EURL guidance documents:

    - Discussion and update (if necessary) of existing guidances

    - Guidance on standard addition (to be finalised in early 2023)

- Screening guidance (to be finalised in early 2023)

- Evaluation of the requirements for a guidance on the application of HRMS methods with the objective of clarifying ion ratios in identification and levels of quantification

- Discussion on the possible design and future ways for the implementation of a database for VMPR stability

- Revision of the list of minimum required, recommended and optional substance - inclusion of a risk-based evaluation

- Revised procedure for the annual evaluation of the NRCPs of the MS in agreement with F4 (DG SANTE) taking into account the possibilities of the new EFSA data base

- Maintenance and updating of the common EURL VMPR cluster website

Expected Output:

Agreed guidance documents, data bases as service for NRLs

Duration: 2023/24

Sub-activity 3.1.5 *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 2023/24 this will concern the following methods:

- Revalidation of all methods with regard to the new requirements laid down in CIR 2021/808 (to be finalised end of 2025)

- Development of methods for new substance-group responsibilities

- Beta-agonists in urine (re-optimisation, re-validation)

- Morantel in tissue and milk (validation)

- Validation of a multi-screening method for B-substances in milk with HRMS and LC-MS/MS

The participation in proficiency tests serves as part of the 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 at delivering 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:

2023/24

Sub-activity 3.1.6 *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:

2023/24

Sub-activity 3.1.7 *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 in the cost estimate.

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 2023/24 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:

2023/24

Sub-activity 3.1.8 *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 many years of 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 promote 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:

2023/24

List of Indicators WP1:

- Number of laboratory methods for which details and guidance as regards their techniques, validation and interpretation are available in the EURL website

- Number of new laboratory methods developed in the reporting period

- Number of laboratory methods improved in the reporting period

- Number of Proficiency Tests (PTs) organised by the EURL for national reference laboratories/NRLs (indicate for each year – 2023 & 2024)

- Cost of PTs

- Number of Comparative Tests (CTs) organised by the EURL for NRLs (indicate for each year – 2023 & 2024)

- Cost of CTs

- Success rate of Member States NRLs/OLs in PTs/CTs and, if necessary, corrective action

- Number of corrective actions undertaken (aggregated data on corrective actions for all NRLs)

3.2. WP 2 - ASSISTANCE TO NRLs

Objective: TO PROVIDE SCIENTIFIC AND TECHNICAL ASSISTANCE TO NRLs

- *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 3.2.1 *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 3.2.3). 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 for substance groups within the responsibility of the EURL Berlin were introduced into a newly developed data base. This data base is available to the NRLs in order to contribute to method harmonisation and further development. The data base has to be updated according to the new legislation (2022/1644) and shall be made available also for use of the other EURLs for VMP residues (cf. 3.1.4).

Expected Output:

Provision of information on analytical methods; provision and maintaining of a method data base; plausibility checks of NRL data; support to other EURLs in terms of data collection and import; strengthening of official control; improved food safety

Duration:

2023/24

Sub-activity 3.2.2 *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 2023 and 2024. The meetings should preferably be planned as face-to-face meetings, but may be rescheduled as web-meetings or amended by web-meetings, if necessary. The following subjects (among others) will be covered:

- Discussions on implementation of CIR (EU) 2021/808
- Discussions on guidance documents supplementing CIR (EU) 2021/808, including method validation, method extension, screening methods, standard addition 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:

2023/24: 2-3 days per year

Sub-activity 3.2.3 *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

- *Training courses for strengthening and harmonisation of residue control*

Description:

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.

Moreover, a practical training is usually part of the annual workshop. Additional individual training courses are agreed upon with the NRLs at short notice 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 in conjunction with the planned collaborative trial.

Expected output:

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

- *Harmonisation of residue control*

Description:

As part of 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 of interest to 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 and 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. Thus 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 made. This approach shall be continued for additional studies.

In the 2021/2022 working period, preliminary experiments for a collaborative trial focussing on a multi-method for selected A and B-substances (> 100 individual analytes) in milk were carried out. The NRLs were invited to participate in this study in 2022, the study itself will start in 2023. Prior to the validation study, an introduction into the validation approach and a method demonstration are planned in the form of an on-site 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; start of a collaborative study focussing on the analysis of A- and B-substances in milk (working period 2023/24)

Duration:

2023/24

Sub-activity 3.2.4 *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 addressed.

For 2023/24 on-site visits to 3-4 NRLs are planned (depending on the possibilities with regard to travelling).

Expected Output:

Reports on NRL visits

Duration:

2023/24: 2-3 days per visit / depending on request and performance in PTs

Sub-activity 3.2.5 *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, on surveys conducted on our own market as well as on scientific literature, specific topics for research and study are identified.

For 2023/24 the following projects are planned:

- Data base HRMS and collision cross section for screening methods (IMS-QTOF)

- Comparison of IMS (ion mobility) / QTOF screening method specificity against HRMS- and LCMSMS-based screening methods (cf.3.1.5)

- Participation in a key comparison (purity study) for standard substances of the OAWG (cf. 3.3.2)

- Organisation and evaluation of a BIPM OAWG key comparison study on nitroimidazoles in tissue

Expected Output:

Experiences in the application of IMS/QTOF systems and recommendations for residue control; increase in performance of HRMS/IMS-methods; proof that the EURL approach is capable to determine standard substance purity and to carry out the associated purity calculations; provision of SI traceable reference values for standard substances and to participants of the EURL PT on nitroimidazoles

Duration:

2023/24

List of Indicators WP2:

- Number of enquires requested from national support networks and bodies and competent authorities

- Number and quality of replies provided to enquiries of national support networks and bodies and competent authorities

- Number of training and collaboration activities with national support networks and bodies and competent authorities

- Number of workshops & meetings organised

- Cost for workshops & meetings and average cost for participant

- Number of technical assistance provided by the EURL to NRLs enquiries

3.3. WP 3 – ASSISTANCE TO THE EUROPEAN COMMISSION AND OTHER ORGANISATIONS

Objective: TO PROVIDE SCIENTIFIC AND TECHNICAL ASSISTANCE TO THE EUROPEAN COMMISSION AND OTHER ORGANISATIONS

- *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 3.3.1 *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 2023/24 period:

- Assistance in interpretation of CIR (EU) 2021/808 (Revision of Commission Decision (CD) 2002/657/EC) by provision of EURL guidance documents for implementation and clarification of open questions

- 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:

2023/24

Sub-activity 3.3.2 *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

3.*3.2.1*

Description:

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 present the EURL participates in EFSA VDR network meetings*,* directly cooperates in the Codex Alimentarius Committee CCRVDF, supports IAEA activities (training, method data base), and participates in the CCQM working group OAWG of the BIPM and in world-wide key comparisons organised by this group (cf. 2.5). 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 in order to provide universally accepted calibration certificates for standard substances and reference materials.

3.3.2.2

Description:

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 3.1.1, 3.1.2., 3.2.1, 2.3 and 3.2.5 is provided.

Furthermore - depending on the approval of COM - experts from third country laboratories are invited to participate in EURL workshops (cf. 3.2.2) and proficiency tests (cf. 3.1.3). Additional assistance (e.g. reference materials, standard substances) is provided upon request (as requested e.g. by Albania in 2021).

Long-standing cooperation exist among others with Albania, Serbia, North Macedonia, 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 the participation of the EURL Berlin. These joint activities shall be continued in future.

Support (analytical methods, SOPs, QA, QC, validation, legislation, specific practical or theoretical training, PT follow-up) is provided upon individual request and through presentations in conferences for an international audience (ITS-Food, SARAF meetings).

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:

2023/24

Sub-activity 3.3.3 *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 can take place, and 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.

The participation in RAFA (2024) and a possible follow-up conference to the Euroresidue conference is planned, but a participation in other suitable conferences like the AOAC meeting or the International Proficiency Testing Conference, BERM and Eurachem workshops is also considered.

Expected Output:

Oral presentations; poster presentations; scientific networking

Duration:

2023/24

List of Indicators WP3:

- Number of technical and scientific feedbacks provided by the EURL based on European Commission enquiries
- Number of collaboration activities with other organisations

3.4. WP 4 - REFERENCE COLLECTIONS

Objective: TO PROVIDE UP-TO-DATE LISTS OF AVAILABLE STANDARD SUBSTANCES AND MATRIX REFERENCE MATERIALS

- *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 3.4.1 *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 (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. 3.1.2).

As part of a new LIMS (to be put in operation in the course of the working period 2023/24), 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:

2023/24

4. REMARKS

(if applicable)

EUROPEAN HEALTH AND DIGITAL EXECUTIVE
AGENCY (HADEA)
Department A Health and Food Unit A2 EU4Health/SMP

Single Market Programme (SMP Food)

SMP-FOOD-2023-EURL-EURC-AG-IBA
Activities of the EU reference laboratories and EU reference centres in 2023-2024

SUBMISSION FORM: DESCRIPTION OF THE ACTION
(Annex 1 – Description of the action (part B))

SMP-FOOD-2023-EURL-EURC-AG-IBA

Activities of the EU reference laboratories and EU reference centres in 2023-2024

Applicant shall provide information on each question contained in the Form. The information filled in the Form, shall be clear, concise, consistent and complete.

For questions on the information requested in this Form, please contact: please contact: HADEA-EURL@ec.europa.eu.

For questions on the eGRANTS Portal Submission System, please contact the IT Helpdesk.

Applicant - COORDINATOR (Name of EURL)	EURL for Growthpromoters Wageningen Food Safety Research
Topic	**Growth promoters, sedatives, anti-viral compounds and peptide and protein hormones**
Implementation period	**1/1/2023 – 31/12/2024**

CONTACT PERSON for the programme :

Name	Drs. Saskia S. Sterk
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ASSOCIATED PARTNER 1 (Name)	Not applicable
Contact person :	
e-mail :	

Contents

1. LIST OF ABBREVIATIONS AND KEY WORDS

WFSR	Wageningen Food Safety Research
WUR	Wageningen University & Research
GP	Growthpromoters
EURL	European Union Reference Laboratory
NRL	National Reference Laboratory
OL	Official Laboratory
PT	Proficiency Test
GC-c-IRMS	Gas Chromatography combustion Isotope Ratio Mass Spectrometry
GC-HRMS	Gas Chromatography High Resolution Mass Spectrometry
LC-MS/MS	Liquid Chromatography tandem mass spectrometry
LC-IRMS	Liquid Chromatography Isotope Ratio Mass Spectrometry
GHRP	Growth Hormone Releasing peptides
MMPR	Minimum Method Performance Requirements
RPA	Reference Point for Action
QA/QC	Quality Assurance / Quality Control
EFSA	European Food Safety Authority
EMA	European Medicinal Agency
IAEA	International Atomic Energy Agency

2. INTRODUCTION

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 16 of Regulation (EU) No 2021/690:

(taking into account Art 147 of (EU) 625/2017)

In this work programme 2023-2024 the full name of "EURL for Growthpromoting agents, sedatives and antivirals 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 Mycotoxins and Plant toxins.

Starting 2022 the EURL-GP WFSR has officially also the mandate for antiviral substances and peptide and protein hormones (Commission Delegated Regulation (EU) 2022/1644).

3. Work Package 1 – GP 2023-2024 WORK PROGRAMME

3.1. Objectives: TO ENSURE AVAILABILITY AND USE OF HIGH QUALITY METHODS AND TO ENSURE HIGH QUALITY PERFORMANCE BY NRLs

- *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-labora tory 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 **3.1.1*Provide NRLs with details and guidance on the methods of laboratory analysis, testing or diagnosis, including reference methods***

3.1.1.1 *: Updating the EURL-GP WFSR website*

Objectives: To have a customer friendly informative website for NRLs and the EC DG SANTE.
Description: The website contains amongst others Standard Operating Procedures for methods of analysis (restricted access), 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.
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, literature and research reports on the (public) EURL-GP WFSR EURL website.
Duration: 2023, 2024 ongoing during whole project

3.1.1.2: *Establishing a NRL methods database ALMANAC*

Objectives: Establishing a harmonised database together with EURL BVL and EURL ANSES on methods used by NRLs.
Description: 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. In 2022 NRLs were requested to fill the database with their methods. In 2023 and 2024 the database needs to be kept up-to-date and overviews can be generated.
Expected output: An up to date web-based database for NRL methods.
Duration: 2023 and 2024 Further filling of the database and maintaining database. Generating overviews per compound class for workshops and DG SANTE

Sub-activity **3.1.2: Follow up on requests from NRLs for providing analytical standards**

3.*1.2.1 Collection of standard substances and deuterated internal standards*

Objective: Provision of standard substances including quality control, storage, administration, documentation and shipment.
Description: Acquiring essential standards and internal standards and metabolites. If standards are easily commercially available this will not be made available from EURL-GP WFSR. 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 recombinant Bovine Somatotropine analysis and reference materials available through EURL-GP WFSR webshop.
Duration: 2023, 2024 ongoing whole project

Sub-activity **3.1.3: Organisation of proficiency tests and follow up on the results**

3.1.3.1 *Organisation of Proficiency tests*

Objective: Organisation of PTs for routinely used method and/or organisation of research study for new analyte or new analyte-matrix combinations
Description:
2023:
a. Finalising report A3 steroids in bovine and porcine urine (Chlorotestosterone, ethynyloestradiol, nortestosterone, trenbolone)
b. PT for Gestagens in kidney fat
c. PT for Thyrostats in porcine and / or bovine urine
2024:
a. Finalising report gestagens in kidney fat
b. Finalising report on thyrostats in porcine and bovine urine
c. Antivirals in poultry muscle
d. A3 steroids in urine
Expected output: PT reports
Duration: 2023 and 2024

3.1.3.2 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.
Description: Contact NRLs with false positive, false negative results or questionable z-scores to ask for corrective measures and give support in corrective measures in means of training, methods, standards amongst others.
Expected output: Better trained NRLs and harmonised overview for DG SANTE on performance of NRLs.
Duration: 2023 and 2024

3.*1.3.3 Preparation of incurred samples (Animal experiment)*

Objectives: To produce incurred sample materials for PT and research studies and for reference materials and QC samples.
Description: Animal experiments can be used to get incurred materials to do research into in-vivo metabolism of Growthpromoters. Perform animal experiments 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 2023 and 2024

Sub-activity **3.1.4: Cooperation and meetings with other EURLs**

3.*1.4.1 Webportal for the 3 EURLs for residues*

Objective: Host a portal for NRLs and OL and DG SANTE and stakeholders where all information on EURLs, residues, legislation etc can be found.
Description: In 2020 a web-portal was built. The portal is hosted by EURL BVL. In 2021 content was added with the appropriate information of EURL-GP WFSR. Further filling and maintenance in 2023 and 2024.
Expected output: Web-portal with information on EURLs for residues.
Duration: 2023 and 2024 ongoing

3.*1.4.2 Harmonisation of proficiency test protocols for assessing PT performance of NRLs*

Objective: To score PTs amongst EURLs for residues in the same way**.** To have a harmonised overview for DG SANTE per Memberstate.
Description: In 2020 EURL BVL and EURL-GP WFSR prepared a harmonised protocol for assessing PT performance of NRLs. In 2022 harmonisation with EURL ANSES was foreseen. However, this was delayed. In 2023 the Guidance for Harmonisation of PT performance criteria within the "VMPR" EURLs cluster with Follow-up on the harmonisation of scoring for evaluation of screening methods will be finalised.
Expected output: A common protocol for the residues EURLs. Developing and testing in 2023 to be used in the coming years.
Duration: 2023

3.*1.4.3 Attend workshops of EURLs in Fougères and Berlin and meetings organised by DG SANTE*

Objective: Attend workshops of other EURLs for residues. Keep informed and meet the network.
Description: In 2023 and 2024 1x workshop in Berlin at EURL BVL and 1x workshop in Fougères at EURL ANSES. Attend 3 meetings in Brussels organised by DG SANTE (either online, hybrid or life format
Expected output: Network and information
Duration: 2023 and 2024

3.1.4.4. Cooperation, collaboration and meetings with other EURLs and scientific exchange

Objective: Development of a common EURL VMP database.
Description: 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 was prepared in 2022 and contents are to be discussed with the NRLs in order to meet their needs in 2023. In 2023 the database will be filled with data by EURLs and NRLs. In 2024 maintenance and extension of the database is foreseen.
Expected output: Online database for HRMS analysis
Duration: 2023 and 2024

Sub-activity **3.1.5 Development and validation of analytical methods**

3.1.5.1. Method development

Objective: 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, e.g. 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. Method development for thiouracil, which was chosen as a priority compound, was done in 2021 and 2022. In 2022 it was concluded that LC-IRMS was not suitable to detect low concentrations of Thiouracil and discriminate using Carbon isotope footprint to distinguish the origin.
In 2023 method development will be done for more natural occurring compounds. The focus will be on prednisolone in 2023 and 2024.
b. 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. In 2023 the focus will be on GHRP method development. In 2024 depending on the outcome a new group will be developed or GHRP method development will continue
2023: Inventory of peptide and protein analysis amongst NRLs.
c. Ecdysteroids are steroids derived from plants and/or insects. These steroids are marketed as growth promoting compounds in the fitness scene and are readily available from the internet. In 2022 a method was developed to analyse in vitro media for metabolites formed from ecdysterone. The in vivo metabolism will be researched in 2023 using animal experiment materials. The method will be further developed and validated in 2023 and 2024.
d. Anti-viral substances: In 2022 an inventory was held amongst NRLs with regard to antiviral methods of analysis. Only one NRL had methods for antiviral compounds. Based on the outcome of the literature overview for antivirals performed in 2022, priority matrix chicken muscle meat and compounds will be selected and method development will be performed in 2023. Validation of the antiviral method in 2024
e. Method development for insects. Insects are mentioned in CDR 2022/1644 as a new group to be controlled. As now it is not mandatory to control insects for A1 group, this could happen in the future. Study on natural levels of ecdysteroids in insects will be done in 2024 and method development for steroids in insects will be started in 2024.

Expected output:
2023:
a. LC-IRMS method development for discrimination of illegally used prednisolone and endogenously formed prednisolone.
b. Method for GHRPs in urine
c. report or draft SOP.
d. In vivo metabolism experiments and method development for ecdysterone and metabolites. Report or draft SOP.
e. Anti-viral substances' method development. Report and/or draft SOP.

2024:
a. LC-IRMS method development for discrimination of illegally used prednisolone and endogenously formed prednisolone
b. Validation of GHRP method. Validation report.
c. Validation of method for ecdysteroids.
d. Validation of anti-viral substances' method. Validation report.
e. Report on occurrence of ecdysteroids in insects. Report on methods for analysis of steroids in insects.
Duration: 2023 and 2024

3.1.5.2. 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 2023-2024 the methods below will be either (re)validated or extended.
Description:
2023:
a. GC-c-IRMS method will be updated with new QA/QC materials form animal experiment.
b. A GC-Q-orbitrap MS analysis was developed and validated. A library was built for GC-Q-orbitrap MS analysis. The method was validated for porcine and bovine urine as a screening method. Maintenance, extension of library and validation for minor species will be done, if needed.
c. Resorcylic acid lactones (RAL) method validation according to CIR 2021/808
d. Finalisation and publication of new sedative method
e. Maintenance A1160 SOP steroids in liver
f. Factsheet nortestosterone
g. Paper on steroids in soil

2024:
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 was applied to porcine urine data. Research form 2022 showed that it could be used for porcine. The work will be published in 2023.
The spreadsheet will be tested for minor species when sample materials are available.
b. Update corticosteroid method in urine
c. Factsheet RALs
Expected Output:
2023:
a. GC-c-IRMS updated method
b. GC-HRMS for steroids updated sop

c. Validation report RALs
d. Finalised SOP for thyrostats
e. Updated SOP A1160 steroids in liver
f. Factsheet to be published on the EURL-GP website

2024:

a. A4 excel decision sheet for minor species urine
   Publication RALs decision sheet in porcine urine
b. Update SOP for corticosteroids in urine
c. Factsheet to be published on the EURL-GP website

Duration: 2023 - 2024

Sub-activity **3.1.6 Analysis of official samples**

Objective: To help NRLs with confirmatory analysis on individual sample basis. Performing arbitration analysis in case of dispute.
Description: Analysis of samples of NRLs for confirmation when technical problems arise in an NRL and/or when there is a dispute on sample analysis results or in case of arbitration.
Expected Output: Analysis results and reports
Duration: Ongoing 2023 and 2024, Ad-Hoc depending on request of NRL.

3.2. Objectives: TO PROVIDE SCIENTIFIC AND TECHNICAL ASSISTANCE TO NRLs

- *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 3.2.1: ***Providing technical and scientific support to NRLs***

3.2.1.1 Studies to detect abuse of (semi)- natural hormones
Objective: Updated Reflection paper on detecting of abuse of semi natural hormones and compounds.
Description: Based on the updated EURL Reflection Paper (beginning 2023), priorities for research are set together with the NRLs.
This new updated reflection paper will be used to set priorities for scientific research and peer reviewed articles.
Expected output: Research of specific subjects identified in updated reflection paper.
In 2023 and 2024 the reflection paper will be maintained with new information and research.
Duration: 2023-2024

3.2.1.2 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 growthpromoters which will be published on the EURL website and which will be communicated to the NRLs.
Duration: 2023 to 2024 ongoing on ad hoc basis

3.2.1.3 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.
Description: 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 promoters. In 2022 a European Media Monitoring tool was made. In 2023 EMM will be implemented. Compounds found will be incorporated in existing methods if possible.
Expected output:
2023: Implementation of EMM tool
2023 and 2024: report on twitter monitoring and EMM
Duration: 2023 and 2024

3.2.1.4 Analytical support

Objective: to help the NRLs and OFL with technical problems on the analysis.
Description: When needed EURL can help NRLs with technical analytical report. In the form of SOPs, dedicated information, stability data etc.
Expected output: 2023 and 2024 upon request by NRLs. Advice and/or analysis (for analysis see 1.6)
Duration: 2023 and 2024

3.2.1.5 Documentation and information services

Objectives: To provide NRLs with recent scientific documentation.
Description: 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 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 and 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 2023 and 2024

Sub-activity **3.2.2: Organisation of an annual workshop for NRLs**

Objectives: Organisation of an annual workshop.
Description: To inform NRLs on new methods, new legislation and discuss work programmes and PTs. To have information exchange between the NRLs.
Member-states and a selected number of third countries come to WFSR for information exchange and discussion on new topics in the growthpromoter field.
Expected Output: 2023 and 2024 workshop at location WFSR
Information exchange, Workshop report
Duration: 2023 and 2024, 2-3 days per workshop

Sub-activity **3.2.3: Organisation of training course for NRLs**

3.2.3.1: Organisation of individual based training courses
Objective: Two or three short visits from NRL scientists to EURL-GP WFSR to be trained in an analytical method.
Description: Tailor made training in methods needed in Memberstate
Expected Output: Trained scientific staff able to implement methods in own laboratory
Duration: Training of maximum 1 week. Request from NRLs in 2023 and 2024

3.2.3.2 Organisation of an additional group training for NRLs on analysis of growth promoters

Objective: Group training on a specific new method.
Description: 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.
2023: Thiouracil markers in urine with LC-MS/MS.
2024: Antivirals in priority matrix are planned
Expected outcome: Trained scientific staff able to implement methods in own laboratory
Duration: Training of maximum 1 week. Topic selected by EURL for NRLs in 2023 and 2024

Sub-activity **3.2.4 Visits to NRLs**

Objective: Missions to NRLs, visit to NRLs in Member States, 2 per year.
Description: 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 2023 the NRL of Bulgaria and Greece will be visited. In 2024 Spain and the Czech Republic.
Expected Output:- visit reports
Duration: 2-3 days per visit in 2023 and 2024

Sub-activity **3.2.5 Providing relevant information on National, Union and international research activities to NRLs**

Objective: This objective is already discussed in 3.1.1.1., EURL-GP WFSR website and 3.2.1.5 Documentation and information service.

Expected Output: Up to date website with SOPs, Legislation, Guidance documents, documentation etc.

Sub-activity **3.2.6 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.
Description: This list will be published on the EURL-PG-WFSR website. Changes in institutes, contact names etc. will be updated when received by EURL. A harmonised format will be used as of 2023, database by BVL. All information will be available to EURLs and the generic info will be published on cluster portal. Annually during the workshop the NRLs are requested to check and if necessary update the information. In the new portal NRLs can update their own information.
Expected Output: Up to date database with contact information
Duration: Ongoing in 2023 change to harmonised format and 2024 maintenance.

3.3. Objectives: TO PROVIDE SCIENTIFIC AND TECHNICAL ASSISTANCE TO THE EUROPEAN COMMISSION AND OTHER ORGANISATIONS

- *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 **3.3.1 Technical and scientific assistance to the Commission**

3.3.1.1 Finalizing of EURLs guidance documents to CIR 2021/808

Objective: The in 2021 published CIR 2021/808 will be supported with guidance documents for the laboratories to have a practical interpretation for their work.
Description: The past years the guidance on validation of confirmatory methods, guidance on extension of validated methods and the guidance on ongoing method validation was finalised.
Expected output: In 2023 and 2024 ongoing support and assistance as regard to the implementation of the CIR 2021/808 and follow-up of its Technical Guidances will be given:
Standard Addition Guidance to be finalised early 2023
Screening Guidance to be finalised early 2023

HRMS Guidance to be started or HRMS info to be included in guidance for confirmatory methods. Working group to be set for 2023. asking NRLs who can participate - HRMS guidance with objectives to clarifying amongst others ion ratios in identification and level of quantification for surveillance plans in 2023
For 2023 also the MMPR Guidance document will be updated.
In 2024 a guidance on HRMS will be finalised.
Duration: 2023 and 2024

3.3.1.2 Analysis of National residue monitoring plans of the Member states

Objective: To evaluate the NRCP of the member states.
Description: Evaluation of the annual national control plans of the Member States. Together with DG SANTE, F4, a new template for evaluation will be developed together with F4 incorporating the risk-based principle and used in 2023. In 2023 a "light" version of the evaluating will be performed.
Expected output: Combined report with unit F4 of DG SANTE and EURLs for residues or individual evaluations per Member State in 2023 and 2024
Duration: 2023 and 2024

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

Objective: overviews of analytical technology for DG SANTE
Description: Upon request of EC DG SANTE provide overview of analytical technology from NRLs. Either by survey or from NRL method database.
Expected output: Overviews
2023 and 2024

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

Objective: On request of DG SANTE assisting F4 during audits as a laboratory expert.
Description: In 2023 and 2024 depending on audit scheme DG SANTE F4. In 2023 assisting in audit to United Kingdom.
2024 not yet known.
Expected Output: Contribution to audit report F4.
Duration: 2023 and 2024 upon request.

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

Objective: 2023 The final Coordination research meeting of an IAEA project will be organised in Vienna, Austria. Other cooperations, in 2023 and 2024 training to third countries upon request of IAEA, TAIEX and/or EC.
Description: Advisory role for residues in food for final report..
Expected Output: report IAEA
Duration: 1 week meeting

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

Objective: Evaluation of veterinary drug registration files.
Description: Evaluation of registration files for fit for purposeness of residue methods
Expected output: Evaluation report
Duration: 2023 and 2024 upon request

3.3.1.7 Participation in symposiums, workshops and seminars for the dissemination of scientific information.

Objective: To present the scientific work of the EURL.
Description: 2023: and 2024 attending symposia to present the EURL work.
Expected Output: Knowledge dissemination and presentations.
Duration: 2023 and 2024

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

Objective: To manage the EURL workplan and the finances
Description: Compilation of an annual work programme and budget forecast.
Compilation of an annual report and cost statement for 2023 and 2024.
Expected output: Annual workplan and report and budget forecast and financial reporting
Duration: 2023 and 2024

3.4. Objectives: REAGENTS AND REFERENCE COLLECTIONS

- *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

Objective: To **p**rovide the NRLs with information on available standards and providers
Description: Every year an update is made of suppliers of standards, chemicals and critical reagents.
Expected output: A list of reference standard suppliers on the website in 2023 and 2024
Duration:To be updated ongoing in 2023 and 2024.

List of indicators WP1:

- Number of laboratory methods for which details and guidance as regards their techniques, validation and interpretation are available in the EURL website

- Number of new laboratory methods developed in the reporting period

- Number of laboratory methods improved in the reporting period

- Number of Proficiency Tests (PTs) organised by the EURL for national reference laboratories/NRLs (indicate for each year – 2023 & 2024)

- Cost of PTs

- Number of Comparative Tests (CTs) organised by the EURL for NRLs (indicate for each year – 2023 & 2024)

- Cost of CTs

- Success rate of Member States NRLs/OLs in PTs/CTs and, if necessary, corrective action

- Number of corrective actions undertaken (aggregated data on corrective actions for all NRLs)

- Number of enquires requested from national support networks and bodies and competent authorities

- Number and quality of replies provided to enquiries of national support networks and bodies and competent authorities

- Number of training and collaboration activities with national support networks and bodies and competent authorities

- Number of workshops & meetings organised

- Cost for workshops & meetings and average cost for participant

- Number of technical assistance provided by the EURL to NRLs enquiries

- Number of technical and scientific feedback provided by the EURL based on European Commission enquiries

- Number of collaboration activities with other organisations

3.5. REQUIREMENTS RELATED TO OTHER LEGISLATION

Not applicable

4. REMARKS

(if applicable)