WORK PROGRAMME of EURL for BOVINE TUBERCULOSIS

PERIOD: 2018

Version 2.0
date 30/11/2017

CONTACT DETAILS

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SUMMARY

INTRODUCTION

(Regarding relevant regulations and functions)

The purpose of the work programme is to cover the objectives (general, specific and operational) and the priorities defined in the Annex to the Commission Implementing decision of 17th November 2017 on the adoption of the work programmes of the Commission for the year 2018, 2019 and 2020. Moreover, the responsibilities and tasks defined in the article 94 Regulation (EU) 2017/625 and Annex II to the Commission Regulation (EC) No 415/2013 regarding the EU-RL for Bovine Tuberculosis will be also taken into account in the work-programme.

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

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

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

- *Art. 94.2.a* ***Providing national reference laboratories with details and guidance on the methods of laboratory analysis, testing or diagnosis, including reference methods.***
  Sub-activity 1.1. Database with recommended protocols.
- *Art. 94.2.b* ***Providing reference materials to national reference laboratories***
  Sub-activity 1.2. Reference material for culture and/or the molecular detection of members of the Mycobacterium tuberculosis complex (MTBC) *in animal tissues.*
  Sub-activity 1.3. Reference material for DVR-Spoligotyping.
  Sub-activity 1.4. Replacement of the International Standard Bovine Tuberculin (ISBT).
- *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.***
  Sub-activity 1.5. Comparative tests.
- *Art. 94.2.l* ***Where relevant for their area of competence, cooperate among themselves and with the Commission, as appropriate, to develop methods of analysis, testing or diagnosis of high standards.***
  Sub-activity 1.6. Development of complementary molecular techniques for the detection and identification of MTBC from animal tissues.
  Sub-activity 1.7. Evaluation of novel methodologies for ante-mortem diagnosis for bovine tuberculosis.
  Sub-activity 1.8. Occurrence of false positive and negative reactivity to the intradermal test due to the use of fraudulent products.

Sub-activity 1.1. *Database with recommended protocols* (Art. 94.2.a).

Objectives: Create and maintain a database with recommended protocols and instructions for carrying out the official and complementary tests for bovine tuberculosis diagnosis.

Description: Creation and maintainance of a dedicated space in the EU-RL website (EU-RL Databases, BT Protocols Database) where Member States can find a collection of the recommended methods for the diagnosis of bovine tuberculosis (culture, direct detection of MTBC from tissue samples, identification by PCR, DVR-spoligotyping, detection of gamma-interferon, histopathology), protocols for carrying out the techniques and useful information on the critical points and inherent difficulties of the methods.

Expected Output: Creation of a collection of protocols and useful information for the implementation of laboratory methods for the detection of bovine tuberculosis.

Duration: 2018-2020.

Sub-activity 1.2. *Reference material for culture and/or the molecular detection of members of the Mycobacterium tuberculosis complex* (MTBC) *in animal tissues* (Art. 94.2.b).

Objectives: Create a reference material that can be used for the quality control of culture and/or molecular methods for the detection of members of the MTBC in animal tissues.

Description: The EU-RL will collect healthy and naturally infected tissues with members of the *Mycobacterium tuberculosis* complex that will be adequately homogenized and will be used for the creation of a reference material that will be divided in aliquots and properly stored in the installations of the laboratory. A small scale feasibility study will take place in 2018. Data collected from this study will be used for the production of the reference material in a larger scale. Once the material is produced the EU-RL will conduct studies in order to define the main properties of the material (homogeneity, long term and short term stability and characterization). The reference material will be included and will be available to all NRLs through the EU-RL website (EU-RL Databases, BT Reference Material Database).

Expected Output: Creation of a reference material for the quality control of culture and molecular techniques for the detection of bovine tuberculosis in animal tissues.

Duration: 2018-2020.

Sub-activity 1.3. *Reference material for DVR-Spoligotyping* (Art. 94.2.b).

Objectives: Preparation of in house spoligotyping membrane and create a reference material that can be used for the quality control of DVR-Spoligotyping.

Description: The EU-RL will select one strain of each of the main species of the *Mycobacterium tuberculosis* complex (*M. tuberculosis, M. bovis, M. caprae*). The strains will be cultured and the genomic material will be isolated and purified. The DR region of these strains will be defined by Next Generation Sequencing (NGS) and by DVR-Spoligotyping. An appropriate quantity of genomic DNA from each strain will be aliquoted in individual tubes. Assays for the determination of the stability of the material will be carried out. The reference material will be included and will be available to all NRLs through the EU-RL website (EU-RL Databases, BT Reference Material Database). Moreover, upon request, the EU-RL will prepare in house, check for quality and supply spoligotyping membranes to NRLs.

Expected Output: Creation of a reference material for the quality control of DVR-Spoligotyping and provision upon request of in house spoligotyping membranes to NRLs.

Duration: 2018-2020.

Sub-activity 1.4. *Replacement of the International Standard Bovine Tuberculin (ISBT)* (Art. 94.2.b).

Objectives: To participate in the collaborative study organized by the OIE in order to replace the International Standard Bovine Tuberculin (ISBT).

Description: Since 1986 there is an International Standard Bovine Tuberculin (ISBT) that nowadays is stored at -20ºC in the Medicines and Healthcare products Regulatory Agency-National Institute for Biological Standards and Control (MHRA-NIBSC). The ISBT is included as reference reagent in the biological potency tests of PPDs performed in guinea pigs and cattle. Since the stock of this reagent is declining, the OIE has created and *ad hoc* group to set up a timetable and the protocols in order to replace the actual ISBT. In summary, the scheduled programme will include: a) Definition of selection criteria for bulk material; b) Request to manufacturers of the bulk material; c) Selection of ISBT candidates; d) Preliminary fill of ampoules (NIBSC); e) Review of protocols by *ad hoc* OIE group and statistician; f) Evaluation of preliminary fill material (OIE-RL); g) Main fill of 5,000 ampoules (NIBSC); h) International Collaborative Study to test two candidates; and i) Data analysis, report and repository for new ISBT in NIBSC. The EU-RL will participate actively in the *ad hoc* meetings organized by the OIE for reviewing the protocols, in the International Collaborative Study (ICS) and in the evaluation of the results. In the ICS, the EU-RL will test the new ISBT (ISBT-2) in guinea pigs with the live and heat-inactivated protocols and in natural reactors in cattle.

Expected Output: Participation in the ICS (guinea pigs and cattle) to select and store a ISBT-2 to be distributed by NISBC, under request, to all laboratories and manufacturers worldwide for biological potency testing.

Duration: 2018.

Sub-activity 1.5*. Comparative tests* (Art. 94.2.c).

Objectives: Organize two comparative tests (Molecular typing and Histopathology).

Description: The EU-RL has the responsibility of organising periodical comparative tests of diagnostic procedures to ensure high quality and harmonization of laboratory testing of bovine tuberculosis across the European Union. The EU-RL ring trials are focused in three main topics: 1) Bacteriological culture and direct detection; 2) Identification and molecular typing; and 3) Immunological diagnosis. The EU-RL will organize two ring trials in 2018 regarding Molecular Typing (DVR-Spoligotyping and VNTR) and Histopathology. The call to participate, submission of results and reporting will be carried out through the EU-RL website (Ring Trial Application).

Expected Output: To ensure high quality and harmonization of laboratory protocols of bovine tuberculosis in Member States.

Duration: 2018.

Sub-activity 1.6*. Development of complementary molecular techniques for the detection and identification of MTBC from animal tissues* (Art. 94.2.l).

Objectives: Develop analytical tools for the complementation of the molecular methods implemented for the direct detection of MTBC in animal tissues.

Description: In the last years the EU-RL has developed a IS*6110*-Real Time PCR for the direct detection of MTBC in animal tissues. This PCR is currently being applied on a large number of clinical samples in order to evaluate its diagnostic characteristics. Even though the results up to date are very encouraging, the recently described absence of the IS*6110* element in a few MTBC strains and the description of IS*6110*-like elements in other bacterial species challenge the diagnostic performance of this method. The EU-RL will develop, optimize and validate a Real Time PCR protocol for the detection of MTBC based on alternative targets (ex. MPB70, IS*1081*) that can be applied in parallel or in series with the current method in order to increase the performance of the molecular detection of MTBC in animal tissues. Moreover, the EU-RL will develop, optimize and validate molecular protocols for the detection of *Mycobacterium s*pp. and *Mycobacterium avium* complex that will complement the current real time PCR and will create a diagnostic algorithm that will allow a faster and more cost-efficient detection of mycobacteria in clinical samples.

Expected Output: Increase of the diagnostic performance of the current molecular protocol for the detection of MTBC in animal tissues and extension of the identification range of the molecular protocols implemented in the diagnosis of bovine tuberculosis.

Duration: 2018-2020.

Sub-activity 1.7*. Evaluation of novel methodologies for ante-mortem diagnosis of bovine tuberculosis* (Art. 94.2.l).

Objectives: Evaluation of the performance of the recently described methodology phage-RPA (Bacteriophage-based method combined with Recombinase Polymerase Amplification), and the PCR developed in sub-activity 1.6., mainly on blood samples from cattle under different epidemiological situations.

Description: The University of Nottingham has developed a bacteriophage-based method combined with PCR (phage PCR) adapted to the detection of *M. bovis* in blood, using a new isothermal DNA amplification protocol by means of Recombinase Polymerase Amplification (Swift *et al*., 2016. Virulence, 7: 779-88). According to the study, the test has a limit of detection of approximately 10 cells per ml of blood for artificially inoculated blood samples and can detect mycobacteria in blood both from animals with and without visible lesions of tuberculosis. When blood samples from a Single Comparative Cervical Intradermal Tuberculin (SCCIT)- negative beef herd were tested, MTBC cells were not detected from any of the blood samples. However, when blood samples from SCCIT-positive animals were tested, viable MTBC bacteria were detected in 66% of samples and 32% out of these animals had visible lesions. Moreover, the authors reported that the frequency with which viable mycobacteria were detected in the peripheral blood of SCCIT-positive animals changes the paradigm of this disease. Since these results were obtained using a very limited and specific cohort of samples, further studies using a more complete bank of samples from herds under different epidemiological situations would be interesting to study the potential of this test for the ante-mortem diagnosis of bovine tuberculosis.

Expected Output: Use a significant number of mainly blood samples from tuberculosis-free and infected animals showing different severity of lesions and from herds with different prevalence to evaluate the performance of the phage-RPA and new PCRs. The sensitivity (in infected animals) and specificity (in non-infected animals) results provided in the study will complete the data reported in preliminary studies about the potential of these methodologies for diagnosis of *M. bovis* infections.

Duration: 2018-2019.

Sub-activity 1.8*. Occurrence of non-specific reactivity to the intradermal tuberculin test due to the use of fraudulent products* (Art. 94.2.l).

Objectives: Evaluate the use of different fraudulent products that can affect the outcome of the intradermal tuberculin test when applied on the animals/sites of PPD injection.

Description: Several products/substances can be used fraudulently to modify the outcome of the intradermal tuberculin test regardless of the true infection status of the animals. Fraudulent vaccination against paratuberculosis/tuberculosis or the use of caustic or irritating agents have been suggested as a cause of false positive reactions in the intradermal tuberculin tests. On the other hand, the use or corticoids or a presensitization with PPD tuberculins have been suggested as a cause of false negative results. The real effect of these fraudulent activities on the results of the test have not been studied in depth. Moreover, these activities are difficult to confirm in order for the authorities to establish the corresponding penalty provisions. Following one of the priorities for the EU-RL work programme regarding the development of methods to detect fraudulent practices, the EU-RL will compile data about the real impact of corticoids used fraudulently on the results of the intradermal tuberculin test.

Expected Output: Results from these studies will be valuable to determine the real effect of the most commonly used products or substances suggested as a cause of fraudulent negative/positive reactions to the intradermal tuberculin tests, particularly corticoids used topically.

Duration: 2018-2019.

Sub-activity 1.9*. Evaluation of the accuracy of different PPD injection syringes used across Europe* (Art. 94.2.l).

Objectives: Evaluation of the accuracy of different syringes used for PPD injection in Europe.

Description: The performance of the intradermal tuberculin test can be affected by factors related to the animals and to the technique. Previous studies have demonstrated that the intradermal tuberculin test is very sensitive to factors related to the protocol that may reduce the performance of the assay in a significant way. Among these factors, the intradermal injection of a proper volume of PPD (0.1 ml) is essential. Different syringes (Dermojet, McLintock, Synthena, Hauptner, Muto) are used in European countries for the injection of PPD in the intradermal tests but there is scarce information about their accuracy in injecting the correct dose of PPDs, their capability to inoculate intradermally the PPDs, and their maintenance requirements to ensure their correct functioning. Previous studies using Dermojet and McLintock syringes have been performed but no similar studies/information are available for other systems that are currently used in Europe. Compilation of data on this matter and research activities to assess the accuracy of the syringes used to perform the intradermal tuberculin tests are essential in order to guarantee the high performance of the skin test and the reliability of the results.

Expected Output: Information about the different injection syringes used in Europe will be updated and the activities performed in the different countries to ensure maintenance and accuracy of injection syringes will be also compiled. Collection of this data will be useful to know the maintenance activities of syringes that the different countries perform to ensure a correct PPD injection. Moreover, if not available, studies to determine the accuracy of the two syringes that are most used in Europe will be carried out. Results from these studies will be valuable to check the accuracy and correct maintenance of the different injection syringes as a cause of a underperformance of the intradermal tuberculin test in cattle.

Duration: 2018.

Sub-activity 1.10. *Biological Potency of PPDs* (Art. 94.2.l).

Objectives: To define a harmonized protocol based on inactivated *M. bovis* strains (OIE protocol) for guinea pig potency testing (GPPT) to be implemented in the NRLs.

Description: One of the main activities of the EU-RL for Bovine Tuberculosis is to test the biological potency of the Purified Protein Derivatives (PPD or tuberculin) in guinea pigs since they are the reagents for the official *in vivo* (skin test) and *in vitro* (IFN-γ) diagnostic assays based on cell-mediated immune response for the diagnosis of bovine tuberculosis. The EU-RL is currently working on the definition of a standardized protocol for potency testing in order to fulfil the requirements defined by the European Commission, European Pharmacopoeia, OIE and Member States.

Expected Output: Standard protocol for biological potency testing in guinea pigs with inactivated *M. bovis* AN5 strain to be set up in the NRLs.

Duration: 2018-2019.

2 TO PROVIDE SCIENTIFIC AND TECHNICAL ASSISTANCE TO NRLs

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

- *Art. 94.2.d* ***Coordinating practical arrangements necessary to apply new methods of laboratory analysis, testing or diagnosis, and informing national reference laboratories of advances in this field.***

  Sub-activity 2.1. EU-RL website.
- *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.***

  Sub-activity 2.2. Training courses.
- *Art. 94.2.g* ***Providing information on relevant national, Union and international research activities to national reference laboratories.***

  Sub-activity 2.3. Molecular Database-mycoDB.eu.

Sub-activity 2.1. *EU-RL website* (Art. 94.2.d).

Objectives: To inform the NRLs and the European Commission of the advances in bovine tuberculosis through the EU-RL website.

Description: The EU-RL for Bovine Tuberculosis website has several sections to share information with Member States and the European Commission: a) Bovine tuberculosis section with updated information regarding etiology, diagnosis, epidemiology and eradication; b) EU-RL activities section with information regarding the Work Programme, Workshops, Ring Trials, Training mobility, Visits, Meetings and Missions; c) EU-RL Databases section with information regarding protocols, publications and reference materials; and d) Documents section including EU-RL and Bovine Tuberculosis legislation, Manuals, Working Documents, Reports, Scientific Opinions, etc.).

Expected Output: To maintain and update the EU-RL website in order to provide updated information of all the relevant aspects regarding bovine tuberculosis (publications, protocols, ring trials, reference materials, etc.).

Duration: 2018.

Sub-activity 2.2. *Training courses* (Art. 94.2.e).

Objectives: Short visits (2-4 days) for three National Reference Laboratories per year to allow the establishment of laboratory protocols and techniques in their laboratory of origin. To facilitate the implementation of the protocols in the NRLs, training material will be produced and will be available through the EU-RL website.

Description: As defined in article 94 of the Commission Regulation (EC) No 2017/625 the EU-RL must conduct training coursed for staff from NRL and, if needed, from other official laboratories, as well as of experts from third countries. The training mobility is focused in laboratory protocols (bacteriological culture, direct extraction, identification by PCR, molecular characterization, histopathology, and detection of IFN-γ) as well as accreditation process and the workflow in a BSL-3. The trainee will present the activities of his/her NRL to the EU-RL and will submit a brief report after the visit. During

2018, a DVR-Spoligotyping video will be produced with the aim to assist laboratories in the set up of this protocol in their laboratories. The video will be available in the EU-RL website (BT Learning Material).

Expected Output: a) Training of three NRLs staff in mycobacteria protocols (culture, direct extraction, PCR, DVR-spoligotyping, MIRU-VNTR, histopathology, IFN-γ test) and accreditation system; b) Learning Material (DVR-Spoligotyping video).

Duration: 2018.

Sub-activity 2.3. *Molecular Database: mycoDB.eu* (Art. 94.2.q).

Objectives: To maintain and update the specific European Database (mycoDB.eu) to generate epidemiological data (DVR-Spoligotyping profiles) between European countries.

Description: DVR-spoligotyping is still considered as the routine molecular characterization protocol for members of the MTBC. Two main databases are available: the SITVIT Database (Public Health, Demay *et al.* 2012) and the Mbovis.org (Smith *et al.* 2012). In 2015, the Mbovis.org database was migrated to the VISAVET server. During 2016-2017, a specific European database (mycoDB.eu) has been designed. This database includes characterization data of *M. bovis/M. caprae* isolates identified in each Member State by DVR-Spoligotyping and therefore facilitates future epidemiological studies between Member States.

Expected Output: Maintenance of a European molecular database (mycoDB.eu) to share the epidemiological information among Member States for epidemiological studies.

Duration: 2018-2020.

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

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

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

  Subactivity 3.1. Missions.
- *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).***

  Subactivity 3.2. Collaboration with International Agencies.
  Subactivity 3.3. International EU-RL on-line webinar.
- *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.***

  Subactivity 3.4. Isolation, identification and typing of mycobacteria.

Sub-activity 3.1. *Missions* (Art. 64.2.f).

Objectives: Provide scientific and technical assistance to the Commission (and NRLs) in bovine tuberculosis.

Description: As defined in the article 94 (Commission Regulation 2017/625) the EU-RL should provide scientific and technical assistance to the Commission. The EU-RL system to inform the European Commission is based on: a) Telephone or e-mail communication; b) Information downloaded in the website (BT Databases, Ring Trials, etc.); and c) Visit to the European Commission/NRL if necessary.

Expected Output: To provide reliable and updated information to the European Commission (and Member States).

Duration: 2018.

Sub-activity 3.2. *Collaboration with International Agencies* (Art. 94.2.h).

Objectives: Collaborate with laboratories in third countries and International Agencies such as EFSA, EMA, ECDC and OIE.

Description: The EU-RL will inform third countries (ex. REMESA Laboratories) regarding the organization of comparative tests (sub-activity 1.5.). Moreover, the EU-RL will be remain at the disposal of the main Organizations (EFSA, EMA, ECDC, OIE, European Pharmacopoeia, etc.) in order to provide scientific and technical information. In this context, the EU-RL collaborates, through sub-activity 1.4. (Replacement of the International Standard Bovine Tuberculin, ISBT), with the OIE. Moreover, a visit to the ECDC will be organized (sub-activity 3.1. Missions) in order to strength the collaboration between the two organizations and explore the possibility of a collaboration.

Expected Output: An active collaboration with Third Countries Laboratories as well as International Organizations to share scientific and technical information.

Duration: 2018

Sub-activity 3.3*. International EU-RL on-line webinar* (Art. 94.2.i).

Objectives: To organize an International EU-RL on-line webinar for the 10th EU-RL anniversary.

Description: The EU-RL for Bovine Tuberculosis was assigned in 2008 (Commission Regulation 737/2008). A seminar will be organized with relevant lectures on bovine tuberculosis and will be made available online (streaming). Animal and Public Health experts working on tuberculosis (3 speakers) will be invited to the EU-RL premises. The webinar will be open and invitations will be sent to International Organizations as well as Member States and NRLs.

Expected Output: To organize an International EU-RL seminar to give visibility to the EU-RL activities worldwide as well as disseminate relevant information regarding bovine tuberculosis diagnosis.

Duration: 2018.

Sub-activity 3.4*. Isolation, identification and typing mycobacteria* (Art. 94.2.h).

Objectives: To assist the NRLs in the diagnosis of outbreaks in Member States by carrying out isolation, identification by PCR and molecular characterization (DVR-Spoligoyting, VNTR analysis).

Description: Not all the NRLs of the Member States have all the protocols for bovine tuberculosis set up in their laboratories. This fact is more obvious in Officially Tuberculosis Free Member States. In the other hand, the EU-RL has all the methodology implemented and accredited (ISO17025). In this sense, the EU-RL will collaborate with the NRLs that need to apply the whole set of protocols in the eventuality of an outbreak.

Expected Output: Assist NRL regarding isolation, identification and molecular characterization of mycobacteria.

Duration: 2018.

4 REAGENTS AND REFERENCE COLLECTIONS

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

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

  See sub-activities 1.2, 1.3. (BT Reference Material Database) and 1.4. (Replacement of ISBT).

- *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;***

    Sub-activity 4.1. Creation of a reference collection of MTBC strains characterized by Whole Genome Sequencing.
  - ***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.***

    See sub-activities 1.1. (Database with protocols), 1.2., 1.3 (BT Reference Material Database), 2.1. (EU-RL website).

Sub-activity 4.1. ***Creation of a reference collection of MTBC strains characterized by Whole Genome Sequencing*** **(Art. 94.2.k.i).**

Objectives: Initiate the creation of a collection of strains of MTBC characterized by WGS.

Description: Among the tasks of the EU-RL is the application of molecular typing methods for the characterization of the isolates and the conduction of epidemiological studies. As a transition from the traditional molecular typing methods (DVR-Spoligotyping and VNTR) towards whole genome sequencing (WGS) techniques is expected in the coming years the EU-RL plans to initiate the creation of a collection of fully sequenced strains. Strains will be sequenced by WGS techniques. The assembled genomes of these strains will be used to create a database that will be administrated by EU-RL. New entries will be added with time. This collection of strains and the corresponding database with the assembled genomes will be a valuable tool for conducting epidemiological studies based on WGS and for monitoring the performance of NGS techniques.

Expected Output: Initiation of a collection of fully sequenced strains of MTBC and of a database containing the assembled genomes.

Duration: 2018-2020.

5 REQUIREMENTS RELATED TO OTHER LEGISLATION

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

Sub-activity 5.1 *(name of Sub-activity)*

Objectives: Description: Expected Output: Duration:

REMARKS

(if necessary)