MEETING REPORT

First annual meeting of the European Reference Laboratory Network for Tuberculosis

Stockholm, 25–28 January 2010

Executive summary

Effective tuberculosis (TB) control starts with laboratory diagnosis. Recognising the importance of this pillar of TB control, the European Centre for Disease Prevention and Control (ECDC) established the European Reference Laboratory Network for Tuberculosis (ERLN-TB). From 25 to 28 January 2010, delegates from nominated TB reference laboratories representing each European Union (EU) and European Economic Area (EEA) Member State, along with others from candidate countries, met in Stockholm, Sweden. At the meeting the official launch of a start-up, pan-European network of reference laboratories was announced, where work plans for methods harmonisation, external quality assurance (EQA) and other coordination issues related to sharing materials and providing expert scientific advice were discussed. In addition, a one day training workshop on biosafety and quality control issues was provided to all of the participants.

Key outcomes of the meeting included an agreed upon outline and writing plan for a handbook on diagnostic methods and practices for the TB reference laboratory, implementation plans for the year one EQA, and other relevant collaborative work. The consensus follow-up for the meeting included the completion of the following steps: a survey of methods currently used in TB reference laboratories; an inventory of available reference strains and materials; the performance and analysis of the planned EQA rounds; and the selection of 2010 candidates for special training as 'TB laboratory support experts'. The training of these experts will be a key activity towards ensuring that expertise in this specialised area will be available to build capacity in the Member States and beyond EU borders, strengthening TB laboratory diagnosis and control programmes.

Stockholm, June 2010

1 Background

The first annual meeting of the European Reference Laboratory Network for tuberculosis (ERLN TB) was attended by 36 national reference laboratory representatives from 29 EU and other EEA states and candidate countries. A situation analysis of the EU-wide TB reference laboratory services[1] identified the need and added-value that an EU network of reference laboratories would provide in strengthening TB diagnostic methods in the EU. Based on this analysis, as well as following the strategic areas of work in the Framework Action Plan to Fight TB in the EU, ECDC has created and launched the ERLN-TB. (Click here to view the action plan.)

Meeting objectives

- **Information exchange and networking,** in order to gain understanding of the context of the planned work in relation to the ECDC TB programme as well as other key TB initiatives in the EU and globally.
- **Work planning,** to have a clear overview of the framework of activities of the ERLN-TB and planning for 2009-2011
- **Technical implementation 2010**: A capacity-building workshop on biosafety and quality, method harmonisation (i.e., producing an outline of the handbook on TB methods and practices and arranging a writing group), EQA activity launch, and the agreed selection procedure for TB laboratory support experts

[1] Drobniewski FA, Nikolayevskyy V, Hoffner S, Pogoryelova O, Manissero D, Ozin AJ. The added value of a European Union tuberculosis reference laboratory network – analysis of the national reference laboratory activities. Euro Surveill. 2008 Mar 18;13(12). pii: 8076

2 Main discussions

2.1 Welcome and introductory remarks

Partners of the ELRN-TB were welcomed to the ECDC premises. They were presented with an overview of the ECDC mandate and its coordinating role within the EU, highlighting that the Centre works closely with the EU and other EEA member states and relies on the high-quality services provided by national microbiology laboratories. Boosting the progress towards TB elimination in the EU was described in epidemiological and strategic terms and the importance of an EU-wide network of TB reference laboratories was highlighted. In this context, the challenge to coordinate an effective TB reference laboratory network in Europe was presented.

The project leader of the ECDC-funded Consortium for ERLN-TB Network Support (CNS), Francis Drobniewski, provided an overview of the management team, their collaboration with ECDC, role within the ERLN-TB network, and technical work plans for the coming year. It was stressed that good communication on the work plan in progress, overall transparency, and open dialogue for future planning and implementation can be expected from the CNS. In order to achieve the goal of a strong European reference laboratory network, the CNS relies on the input, involvement and commitment to the tasks and time frames from all partners.

Presentations were held by Dick van Soolingen, a representative from the ECDC-funded 'Management of the molecular typing activities of MDR-TB strains at EU level' project and Daniela Cirillo, the European Commission's Seventh Framework Programme for Research project TB PAN-NET representative, highlighting the need to start building synergy with existing projects and initiatives within the TB field. Most of the European reference laboratories are active in several similar EU-projects and it was realised that ERLN-TB could serve as a key forum for the exchange of ideas, dissemination of information, and general coordination and planning of these individual EU-projects.

Regarding broadening synergy-building in a global context, Christopher Gilpin of the Global Laboratory Initiative provided insight into the added value of the ERLN-TB. Complementing the work of the WHO Global TB Supranational Reference Laboratory Network (SRLN), the ERLN-TB will become an important partner, providing support in promoting and implementing quality assured diagnostic methods, support in the development and testing of new diagnostic tools, and for identification of training opportunities and overall capacity building of TB laboratory experts.

2.2 Ensuring methods harmonisation

Plans to develop a handbook of scientific methods and practices in TB diagnostics as an evidence-based resource for the ERLN-TB were discussed. The handbook development is linked to the activities of the ERLN-TB quality control schemes and related training and capacity building initiatives. Drafting the handbook was accomplished by splitting up the ELRN-TB partners into separate writing groups divided per chapter heading. They were tasked with selecting a representative number of methods known to give reliable results and drawn from published material from the network and international sources that had undergone expert review. A follow-up plenary discussion was used to reach agreement on the overall scope and content. As the ERLN-TB has a wide geographical coverage, it was noted that the handbook introduction should highlight any differences between countries. For completion of the handbook, a writing committee was formed and a first draft of the handbook is expected to be ready by summer 2010. This is the first time that the leading experts in Europe are exchanging ideas and working jointly on compiling a document on methods in TB diagnostics. All partners will share authorship of this work, giving them the opportunity to contribute to the work and to maintain the handbook as a 'living' document as work continues in the field, and the evidence base grows for specific methods.

2.3 Development of an EU strain collection

An inventory of existing strain-collections within the ERLN-TB network was carried out by revisiting a previous situational analysis[2], and it was confirmed that the network already has a large number of important isolates. The ERLN-TB engaged in a discussion of the added value of creating a physical bio-resource of such isolates as well as relevant diagnostic material for TB laboratories. The advantages and disadvantages of a single storage site versus a dispersed approach to a collection were also discussed. Furthermore, the use of such materials for EQA and currently existing practices were explored via collaborations with the WHO SRLN.

[2] Drobniewski FA, Nikolayevskyy V, Hoffner S, Pogoryelova O, Manissero D, Ozin AJ. The added value of a European Union tuberculosis reference laboratory network – analysis of the national reference laboratory activities. Euro Surveill. 2008 Mar 18;13(12). pii: 8076

It was agreed that a specific collection, housing between 40 and 50 comprehensively characterised strains (including *Mycobacterium tuberculosis* complex strains and non-tuberculous mycobacteria strains) should be created. A 'virtual' strain collection will be developed in 2010—i.e., a list of available isolates, drawn up by the Health Protection Agency team and endorsed by the Network partners. On the basis of this information, the development of a high quality physical strain collection will be further discussed.

2.4 Providing scientific advice and other laboratory support

The ERLN TB experts will assist ECDC by providing scientific advice. As a first step to map competencies and expertise, a book with the biographies of all participants and their laboratories has been developed and shared with ECDC and the network partners. The Centre will work together with the ERLN-TB to discuss procedures for dealing with scientific questions or other related risk-assessment activities.

Furthermore, there could be situations where MS may need laboratory support from other countries or laboratories. Already today, some EU national reference laboratories provide reference services for other EU states (e.g., Germany for Cyprus, UK for Malta) and this could be a model for engaging in such bilateral agreements when needed.

2.5 Towards strengthening the quality of diagnostic methods

The planned activities for strengthening and promoting quality assurance systems in TB diagnostic methods were presented and discussed with the ERLN-TB partners. In the first year, work will focus on the establishement of a performance base-line of the network partners in smear-microscopy, culture of bacteria, identification and first-line drug suceptibility testing (i.e., rifampicin, isoniazid, ethambutol, pyrazinamide and streptomycin). The preparation of the panels, distribution to the partners, and follow-up analysis and reporting of results will be under the leadership of Sabine Rüsch-Gerdes in collaboration with INSTAND e.V, a WHO collaborating centre for quality assurance and standardisation in laboratory medicine. It was agreed that laboratories will only be expected to participate in the profiency testing of the techniques they routinely use. For safety reasons, no multidrug/extensively drug-resistant TB (MDR/XDR TB) strains will be included in the testing panels, nor in the development phase of the EQA activities of the ERLN-TB. For the future EQA of second-line drug-susceptibility testing, there are strains resistant to single drug classes available in the network that can be used, thereby avoiding sending MDR/XDR strains. Confidentiality of each of the network partners' results, as with all normal EQA testing protocols, will be kept. It was also clarified that these EQA activities of the ERLN-TB will not replace any current EQA rounds from other sources, such as the WHO SRLN, but will rather complement them.

2.6 Building laboratory capacity in the MS

The ERLN TB aims to strengthen the knowledge and expertise in MS laboratories through different types of training initiatives including the following:

- an annual capacity-building meeting for all ERLN-TB partners focusing on broad, key laboratory issues (e.g., biosafety, internal quality assurance practices, management and financial issues for laboratory heads) that are made relevant to TB laboratories' individual circumstances;
- the establishment of a new cadre of TB laboratory support experts through short training workshop meetings; and
- short laboratory exchanges of personnel and twinning type activities, to support implementation of the work in harmonisation methods and primarily quality assurance areas.

During the discussions, there was detailed elaboration of, and support for, the need and added value of the development of TB laboratory support experts. The agreed vision was that such experts (up to 10 persons per two year workshop training cycle) would be prepared to undertake five linked capacity-building workshops covering in-depth topics such as molecular epidemiology, latent TB diagnosis and laboratory management issues. In addition, the trainees would commit to a period of laboratory expert support and further training by contributing to country visits and other short laboratory exchanges with the aim of spreading knowledge and facilitating laboratory performance throughout the EU and other EEA countries. The concept follows the peadagogics of 'train-the-trainers', and the first round of trainees would also be involved in the future capacity building of the next cohort of TB laboratory support experts. It was also emphasised that the TB laboratory support experts will not only be an invaluable resource for the EU, but should also be an important resource to international activities outside EU-boarders. Key issues discussed included the process of application and requirements, the agreement of the hosting institutes of the applicants, assuring them the time to participate in the training and follow-up activities, and the expectations on the trainees and the trainers for future country missions. In addition, the possibility of opening this support expert role to members outside the EU would also be investigated in future years.

Dates and timing for the first call for applications were agreed upon and training workshops will begin in May 2010.

2.7 Workshop topics: Biosafety and internal quality control practices

The ERLN TB partners participated in an interactive workshop (consisting of expert presentations, scenario discussions, and an expert panel question/answer session) on biosafety and the importance of internal quality control (IQC). Many thanks to external experts Åsa Bjornal (Institutional Biosafety Officer) and Tuija Koivula (Biosafety Officer), both from the Swedish Institute for Infectious Disease Control for their contributions to the sessions. There was widespread agreement on the importance of biosafety, biohazards and biorisk principles, and a discussion on the way these principles should be implemented. Relevant European legislations, such as Directive 2000/54/EU, were drawn upon. It was found that one quarter of the meeting attendees had a dedicated safety office in their laboratories. Biosafety, as it is related to disability, was discussed and there was agreement that careful planning and risk assessment, good infrastructure building and laboratory design would enable laboratories to safely accommodate individuals with a wide range of disabilities. Key messages from the IQC session included an overview of IQC, practical tips to implement such practices into the daily laboratory work, and the cultivation and promotion of a general class of laboratory scientist who is committed to achieving high quality practices and not simply required to do so by legislations and authorising bodies.

3 Conclusions

The ERLN-TB partners left the meeting with a good overview of the work of ECDC, the rationale behind the need to establish a European-wide network of TB reference laboratories, and the goal of strengthening quality in TB diagnostic services and building capacity to ensure continued excellence in the field.

The scientific input and overall organisation of this first meeting by the project management team of the Consortium for ERLN-TB Network Support was highly appreciated by all and there was much enthusiasm and commitment expressed by all ERLN-TB partners for future collaborative work in the areas outlined.

Concrete next steps were summarised as follows:

- the completion of a draft handbook of methods;
- the further strategic and physical establishment of an EU collection of selected TB isolates;
- the launch of the first call for applicants for capacity building workshops for TB laboratory support experts; and
- preparation for the second annual meeting to be held in London from 31 January to 3 February, 2011.

Proposed future developments and capacity-building topics to consider include:

- introducing nucleic amplification tests and molecular testing to the next planned EQA rounds;
- the addition of further chapters to the methods handbook (e.g., to address dealing with non-tuberculosis mycobacteria, (NTM));
- Interferon Gamma Release Assay testing, biomarkers, molecular assays, drug susceptibility testing (DSTs); and
- addressing organisational issues/laboratory management, including budgeting, and the management of accidents in laboratories, managing a network/national networks, the clinical relevance of NTM, and dealing with laboratory-contamination.

In summary, the launch of the ERLN-TB and the start-up of activities set the basis for strengthening and optimising laboratory functions in TB control within the EU, in its diagnostic and surveillance support roles.

In particular, the success of the network in supporting the progress towards TB elimination will rest on the achievement of the initial objectives. These are aimed at establishing a functioning EQA system within the EU, populating the pool of TB laboratory experts within the region by structured capacity building workshops, and standardising methodologies around the best available evidence.

By ensuring success in these three fundamental components of the network, a solid basis for accelerating and enhancing TB control will be set. The impact of optimising EU laboratory services will inevitably be of benefit to neighbouring and high burden countries in view of the supranational reference role played by several members of the network.

Acknowledgements

This report was coordinated by the ECDC Tuberculosis programme experts in conjunction with the project management team partners of the Consortium for Network Support on behalf of, and with critical input from, the experts of the European Reference Laboratory Network for Tuberculosis (see Annex 2 for participants list).

Consortium for Network Support:

Sarah Mitchell (Project Manager), Vladyslav Nikolayevskyy (Project Scientist), Francis Drobniewski (Project Leader), Yen Holicka (Financial Manager); and the Health Protection Agency, UK.

Annex 1: Meeting programme

Day 1 January 25 2010

12:30–13:00	Registration at ECDC headquarters
13:00–14:15	**Welcome to Tomteboda—Home to ECDC** *Piotr Kramarz–ECDC Deputy Head of Scientific Advice Unit*
	Boosting the progress towards TB elimination *Davide Manissero–ECDC programme coordinator for TB*
	"No laboratories of its own"—ECDC's challenge to coordinate a TB laboratory network *Amanda Ozin–ECDC microbiology coordinator*
	In the engine room of the ERLN-TB – the role of the Consortium for Network Support (CNS) and expectations from the ERLN-TB network *Francis Drobniewski–CNS Project Leader, Health Protection Agency, UK*
14:15–15:00	**Building synergy with key EU Tuberculosis projects: MDR-TB molecular surveillance project** *Csaba Ködmön–ECDC, Surveillance Unit, Dick van Soolingen–RIVM, Netherlands*
	Building synergy with key EU Tuberculosis projects: TB-PANNET, Framework 7 Programme DG RTD *Daniela Cirillo–CNS Project Management Team, San Raffaele Scientific Institute, Italy*
15:00–15:30	*break*
15:30–16:30	**ECDC "Information Fair" and inside look at ECDC Emergency Operations, "Everything that you did not find out about ECDC and were afraid to ask"** *Isabelle Hubert–ECDC, Health Communications Unit, Paula Vasconcelos–ECDC, Preparedness and Response Unit*
16:30–17:30	**The global perspective and how the ERLN-TB can bring an added value** *Christopher Gilpin–Global Laboratory Initiative*
17:30	**Closing remarks** *Davide Manissero–ECDC, Programme Coordinator for Tuberculosis, Piotr Kramarz–ECDC Deputy Head of Scientific Advice Unit*

Day 2 January 26 2010

08:30–09:00	**Registration** *Sarah Mitchell–CNS Project Manager, Health Protection Agency, UK*
09:00–09:45	**Establishment and the workings of the ERLN-TB Network–Work Package 1** *Francis Drobniewski–CNS Project Leader, Health Protection Agency, UK*
09:45–10:30	**External quality assurance–Work Package 2** *Sabine Rüsch-Gerdes–CNS Project Management Team, Borstel, Germany*
10:30–11:00	*break*
11:00–12:00	**Capacity building–Work Package 3** *Daniela Cirillo–CNS Project Management Team, San Raffaele Scientific Institute, Italy, Francis Drobniewski–CNS Project Leader, Health Protection Agency, UK*
12:00–12:30	**Strengthening TB diagnostics - a "harmonised handbook"** *Francis Drobniewski–CNS Project Leader, Health Protection Agency, UK*
12:30–13:30	*break*
13:30–15:00	**"Breakout!–my ideas count!"–Brainstorming for the handbook** *Project Management Team with individual handbook groups*
15:00–15:30	*break*
15:30–17:00	**Harmonising the handbook–regroup for group discussion** *Francis Drobniewski–CNS Project Leader, Health Protection Agency, UK, Vlad*

	Nikolayevskyy–CNS Project Scientist, Health Protection Agency, UK, Sarah Mitchell–CNS Project Manager, Health Protection Agency, UK
17:00–18:30	**Handbook homework for volunteers**

Day 3 January 27 2010

08:30–09:00	**Registration** *Sarah Mitchell–CNS Project Manager, Health Protection Agency, UK*
09:00–09:30	**"What we need from you"–An overview of finance** *Yen Holicka–CNS Project Administrator, Health Protection Agency, UK*
09:30–10:30	**Year 1 WP1 deliverables–a needs analysis** *Francis Drobniewski–CNS Project Leader, Health Protection Agency, UK*
10:30–11:00	*break*
11:00–12:30	**"What next?"–Planning for years 2, 3 and 4 and requests for 2011 Annual Meeting–an open floor discussion** *Francis Drobniewski–CNS Project Leader, Health Protection Agency, UK, Vlad Nikolayevskyy–CNS Project Scientist, Health Protection Agency, UK, Sarah Mitchell–CNS Project Manager, Health Protection Agency, UK*
12:30–13:30	*break*
13:30–15:00	**"Putting actions into words": Writing of handbook for volunteers.** *CNS Implementation team: Sabine Rüsch-Gerdes–CNS Project Management Team, Borstel, Germany, Daniela Cirillo–CNS Project Management Team, San Raffaele Scientific Institute, Italy* **Work group: Discussing core competencies and selection criteria of TB Laboratory Support Experts ("super TB-experts") (WP 3)** *Francis Drobniewski–CNS Project Leader, Health Protection Agency (UK)*
15:00–15:30	*break*
15::30–16:15	**The inner workings of the "engine room" - Meeting of the CNS. (Non-CNS = handbook homework, free time)** *Francis Drobniewski–CNS Project Leader, Health Protection Agency (UK)*

Day 4 January 28 2010

07:30–08:00	**Registration** *Sarah Mitchell–CNS Project Manager, Health Protection Agency (UK)*
08:00–09:00	**Introduction to biosafety** *Asa Bjornal–Institutional Biosafety Officer, Swedish Institute for Infectious Disease Control (SMI), Tuija Koivula–Biosafety specialist, Swedish Institute for Infectious Disease Control (SMI)*
09:00–10:30	**Everything you needed to know about biosafety and not afraid to ask! - "Expert panel" Q & A** *Asa Bjornal–Institutional Biosafety Officer, Swedish Institute for Infectious Disease Control and Tuija Koivula–Biosafety specialist, Swedish Institute for Infectious Disease Control (SMI) plus Expert panel: Sabine Rüsch-Gerdes–CNS Project Management Team, Borstel, Germany, Vibeke Østergaard Thomsen–CNS Project Management Team, Statens Serum Institut, Denmark, Vera Katalinic Jankovic–Croatian National Institute of Public Health, Croatia, Dick van Soolingen–RIVM, Netherlands, plus CNS Implementation Team*

10:30–11:00	*break*
11:00–12:45	**The "hows and whys" of internal quality control (IQC)** *Sabine Rüsch-Gerdes–CNS Project Management Team, Borstel, Germany*
12:45–13:15	**Closing remarks and action points from the meeting** *Francis Drobniewski–CNS Project Leader, Health Protection Agency, UK, Davide Manissero–ECDC Programme Coordinator for Tuberculosis, Amanda Ozin–ECDC Microbiology Coordinator*

Annex 2: Meeting participants

Country	Name
Austria	Alexander Indra
Belgium	Maryse Fauville-Dufaux
Bulgaria	Elizabeta Bachiiska
Croatia	Vera Katalinic-Jankovic
Czech Republic	Marta Havelkova
Denmark	Vibeke Østergaard Thomsen
Estonia	Tiina Kummik
Finland	Hanna Soini
France	Vincent Jarlier
	Emmanuelle Cambau
Germany	Sabine Rüsch-Gerdes
	Doris Hillman
Greece	Dimitrios Papaventsis
Hungary	Nóra Szabó
Ireland	Noel Gibbons
Italy	Lanfranco Fattorini
	Daniela Cirilo
Latvia	Girts Skenders
Lithuania	Edita Pimkina
Luxembourg	Paul Reichert
Malta	Karl Galea
Netherlands	Dick van Soolingen
Norway	Turid Mannsåker
Poland	Zofia Zwolska
Portugal	Suzana David
Romania	Daniela Homorodean
Slovak Republic	Juraj Trenkler
Slovenia	Urska Bidovec-Stojkovic
Spain	Maria Soledad Jimenez Pajares
	Sofia Samper
Sweden	Sven Hoffner
Turkey	Gülnur Tarhan
United Kingdom	Francis Drobniewski
	Yen Holicka
	Sarah Mitchell
	Vladyslav Nikolayevskyy
ECDC	Emma Huitric
	Davide Manissero
	Amanda Ozin
	Csaba Ködmön

Guest speakers

Piotr Kramarz – ECDC, Deputy Head of Scientific Advice Unit

Isabelle Hubert – ECDC, Health Communications Unit

Paula Vasconcelos – ECDC, Preparedness and response Unit

Chris Gilpin – Global Laboratory Initiative

Asa Bjornal – Institutional Biosafety Officer, Swedish Institute for Infectious Disease Control

Tuija Koivula – Biosafety Officer, Swedish Institute for Infectious Disease Control