



TECHNICAL REPORT

Core functions of microbiology reference laboratories for communicable diseases

June 2010

ECDC TECHNICAL REPORT

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This report was produced by the ECDC Microbiology Coordination team* with contributions from a writing group† on behalf of Member-State-appointed National Microbiology Focal Points (this includes present, former and alternate NMFP members)‡.

* Daniel Palm, Aftab Jasir, Alexandra Clarici, Amanda Ozin

† Ingeborg Sundsvaen Aaberge, Berrin Esen, Waleria Hryniewicz, Marion Koopmans, John Parry, Magnus Thore, Jaana Vuopio, Guido Werner

‡ Antonios Antoniadis, Fernando Baquero, Christopher Barbara, Sophie Bertrand, Peter Borriello, Laura Brum, Inmaculada Casas Flecha, Antonio Cassone, Iva Christova, Jean-Marc Collard, Manuel Cuenca-Estrella Sinde, Robert Cunney, Snieguolė Dauksiene, Sabine Erne, Maryse Fauville Dufaux, Niels Frimodt-Møller, Pentti Huovinen, Gabriel Ionescu, Vilma Jonaitiene, Cyril Klement, Karl G. Kristinsson, Pavla Křížová, Annika Linde, Eleanor McNamara, Jolanta Miciuleviciene, Gordana Mlinarić-Galinović, Joël Mossong, Robert Muchl, Jaime Nina, Heléne Norder, Eoghan O'Neill, Metka Paragi, Rita Peetso, Despo Pieridou Bagatzouni, Ioan Mircea Popa, Sanja Predavec, Anna Przondo-Mordarska, Alexandru Rafila, Inna Sarv, Christine Saura, Jelena Storoženko, Reinhild Strauss, Alkiviadis Vatopoulos, Ildikó Visontai, Maria Zambon

For full details of affiliations please visit:

http://ecdc.europa.eu/en/activities/microbiology/Pages/MicrobiologicalCooperation_NationalMicrobiologicalFocalPoints.aspx

We recognise the DG SANCO colleagues for their continuous support and coordination on laboratory collaboration strategies for the EU.

Suggested citation: European Centre for Disease Prevention and Control. Core functions of microbiology reference laboratories for communicable diseases. Stockholm: ECDC; 2010.

Stockholm, June 2010

ISBN 978-92-9193-211-5

doi 10.2900/29017

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Glossary and abbreviations

Public health microbiology

The following working definition of microbiology with a public health role was developed through consensus opinion of the National Microbiology Focal Points (NMFPS):

'Public health microbiology' is a cross-cutting area that spans the fields of human, animal, food, water and environmental microbiology, with a focus on human health and disease. It requires laboratory scientists with the ability to work effectively across disciplines, particularly epidemiology and clinical medicine. Public health microbiology laboratories, or laboratories with these functions, play a central role in infectious disease detection, monitoring, outbreak response and providing scientific evidence to prevent and control disease.

In this document, the term 'microbiology reference laboratory' refers to public health microbiology related to communicable human diseases.

Microbiology reference laboratories

'National reference laboratory (NRL)' and 'National reference centre (NRC)' are both commonly used terms. However, usage is often country-specific and different interpretations exist (Annex 1). To avoid confusion and to ensure that the report establishes a common reference point, we use the term 'microbiology reference laboratory' in this context.

Function

The word 'function' is used in this report in two ways: first, to describe the role of microbiology reference laboratories as part of the public health microbiology system; secondly, it is used as a label to group together a list of related activities and essential properties of microbiology reference laboratories.

Accreditation

The use of the word 'accreditation' in this document describes a process which provides public notification that an institution has the required competence and credibility for a specific service or product. This process can be achieved through official national recognition of laboratory quality, or national accreditation bodies that adhere to international standards.

List of abbreviations

AST	Antimicrobial susceptibility testing
ECDC	European Centre for Disease Prevention and Control
EU	European Union
DG SANCO	Directorate General for Health and Consumer Affairs
ISO	International Standardization Organization
NMFP	National Microbiology Focal Point
NRL	National reference laboratory
NRC	National reference centre
PH	Public health
PHM	Public health microbiology
QA	Quality assurance
SOP	Standard operating procedure
UK	United Kingdom
WHO	World Health Organization
IHR	International Health Regulation
IT	Information Technology

Executive summary

Introduction

Public health microbiology laboratories play a central role in detection, monitoring, outbreak response and the provision of scientific evidence to prevent and control infectious diseases.

This report identifies the core functions and activities of microbiology reference laboratories as part of public health microbiology. It is intended to support Member States in implementing these functions in the context of their national public health systems. Moreover, this information can provide a foundation for strengthening international cooperation between microbiology reference laboratories, thus contributing to both the mandate of the European Centre for Disease Prevention and Control [1] and fulfilling obligations placed on Member States by the International Health Regulations (IHR) [2].

Material and methods

In 2007 ECDC initiated a process of officially nominating a group of experts by asking each Member State's health authority to designate a National Microbiology Focal Point (NMFP).

In a series of meetings held between 2007 and 2010, the NMFPs worked on clarifying what the core activities of microbiology reference laboratories should be. Additionally, in 2008 the group conducted an in-depth survey of public health microbiology organisations and their functions in the Member States, in order to compare existing practices and approaches in the different Member States.

Results

The current systems of reference laboratories in the European Union vary considerably between countries (Annex 1). There is reference laboratory capacity for all of diseases listed in Decision No 2119/98/EC, including amendments 4–7. However, countries use different definitions of the term 'reference laboratory' and use different selection and evaluation procedures (see Figure 1 in Annex 2).

Based on the survey results and discussions in working groups, the NMFPs reached a consensus on key activities of microbiology reference laboratories as part of public health microbiology.

These activities were subsequently grouped under five headings, referred to herein as 'core functions'.

- Function 1: Reference diagnostics
- Function 2: Reference material resource
- Function 3: Scientific advice
- Function 4: Collaboration and research
- Function 5: Monitoring, alert and response

The NMFPs agreed on the general terms and conditions that constitute the basic requirements for performing the above core functions and thus make it possible for a laboratory to operate as a microbiology reference laboratory in the public health field:

- A mandate to serve reference functions in the public health microbiology sector, in accordance with the country's system and the relevant authorising body/bodies.
- Recognition as an expert institution and strong key partner connections with laboratories and stakeholders within Member States and internationally.
- Sufficient knowledge and application, where appropriate, of international standards and practices.
- Suitable equipment, basic materials, adequate resources, appropriate products and sufficient time to be able to perform functions and activities assigned to the laboratory.
- An appropriate infrastructure (i.e. building and administrative infrastructure) to support activities. With regard to the infrastructure of the building, this goes beyond equipment and materials and includes specialised laboratory containment facilities and biorisk management systems for working with certain pathogens.
- Suitably qualified staff with adequate training and experience, such as to ensure a sufficient level of competence to carry out the assigned tasks.
- Compliance with laws concerning data protection, transportation and material transfer agreements.
- Sufficient funding that supports and guarantees continuous and qualified work.

Discussion

ECDC's founding regulation states that ECDC – by encouraging cooperation between expert and reference laboratories – shall foster development of sufficient capacity within the Community for the diagnosis, detection, identification and characterisation of infectious agents which may threaten public health [1]. Since quality and comparability of results from laboratories depends on the existence of reference laboratories, a harmonised description of the core functions and activities will contribute to an improved situation across Europe.

This report provides a functional definition of microbiology reference laboratories based both on discussions with representatives from all EU/EEA countries and a survey on public health microbiology organisation and functions of the Member States.

The definition put forward in this report is based on common activities of reference laboratories and consists of five overarching core functions. The listed core activities and functions are intended to be applicable as a framework for action in any microbiology reference laboratory within the EU, regardless of pathogen, current public health laboratory structure or advancement level. Countries can use this technical report for discussion and implementation, adapting concepts according to their needs.

Conclusion

The organisation, selection and evaluation processes for microbiology reference laboratories in Europe are very heterogeneous. Common and harmonised standards are an important precondition when aiming for high-quality work at European microbiology reference laboratories. A coordinated approach is essential to make progress and requires both technical and political commitment for full implementation.

This report can serve as the basis of discussion on legislation in Member States directed at the strengthening, planning, or implementing of reference laboratory systems. In addition, it should be regarded as an essential document for any discussions on an EU reference laboratory system.

ECDC will continue to work within its mandate with the Member States to evaluate the impact of this collaborative technical report and plan for continued strategic development to reinforce laboratory capacity in the EU.

In close partnership with the European Commission and WHO, ECDC is currently exploring areas of work within its mandate that fall within the remit of this technical report on core functions of microbiology reference laboratories. This will be helpful for strengthening laboratory capacity in the EU and globally.

Introduction

Scope and purpose

All EU citizens have the right to high-quality clinical and public health microbiology services in the European Union and it is up to the Member States together with the Commission to develop strategies and actions to implement activities to strengthen microbiology in the EU. [8]

Microbiology reference laboratories are critical for developing high-quality clinical and public health microbiology services in Europe. They are defined, organised, and operate differently from country to country. These differences have implications for sharing services, materials and data as well as international public health activities in monitoring, alert, response, advice and collaboration regarding the control and prevention of communicable diseases. This report aims at identifying the core functions and activities of microbiology reference laboratories as part of improving the public health microbiology provision in the EU and is intended to support Member States when implementing these functions in the context of their national public health systems. Moreover, this information can provide a foundation for strengthening international cooperation between microbiology reference laboratories, thus contributing to both the mandate of the European Centre for Disease Prevention and Control and fulfilling obligations placed on the Member States by the International Health Regulations (IHR) [2].

This report was developed by the National Microbiology Focal Points (NMFP), a body of microbiologists designated by the Member States [3]. In the context and scope of this report, the NMFP forum does not provide specific comments on best practices in microbiology reference laboratory organisation nor make any assumptions about the quality of individual laboratory performance.

The background to this report

All Member States have taken steps at the national level — in some cases through third countries — to provide and maintain the laboratory capacity to confirm a defined list of pathogens (and the diseases caused by these pathogens) and provide timely reporting of disease data [4]. To fulfil this obligation and to make data comparable, support from reference laboratories is of utmost importance. In the EU context, this implies that each country, under certain conditions, needs access to its own reference laboratory facilities (or those of another Member State) to verify the existence of pathogens and provide further characterisation of these pathogens.

The revised International Health Regulations stipulate that each country should have the capacity to provide support at regional and community levels for the laboratory analysis of samples, either domestically or through cooperating centres [2]. Therefore, high-quality reference laboratory services, and access to them, is not only an issue for EU Member States, it is a global responsibility which translates into an obligation to strengthen cooperation and coordination.

ECDC's mission is to identify, assess and communicate current and emerging threats to human health from communicable diseases [1]. All these activities are based on high-quality clinical and public health microbiological activities undertaken in the EU Member States. Accordingly, there is an obligation for ECDC and the Member States to cooperate in the field of microbiology to assess and ultimately improve Europe's laboratory capabilities and capacities. As a starting point for this joint work, a strategy and framework of actions have been prepared and endorsed by the Member States [8].

How this report contributes to other work in this field

The identification of core functions of microbiology reference laboratories is a crucial topic for many countries, particularly those that are establishing or further developing their public health microbiology laboratory systems. There are studies underway at the EU level (NMFP meeting, October 2009) to determine the feasibility of establishing a system of European reference laboratories for human pathogens as part of the public health programme of DG SANCO. Such a system would also meet the demands of the International Health Regulations.

What this document is

This document is a technical report. It is intended to provide a common understanding of the core functions and activities of microbiology reference laboratories. These core functions are intended to be applicable regardless of

the pathogen, the disease area or the country. In addition, these core functions can be directly applied to any development of reference activities at the regional, national, or supranational levels.

What this document is not

This document is neither a guideline nor does it provide guidance. It does not include a comprehensive list of requirements for laboratories that are necessary for performing reference functions. Such requirements and criteria are available through the International Organization for Standards (ISO) [9]. This document is also not intended as a means of assessing laboratories for the purpose of accreditation.

Intended use and users

The list of core functions and activities of microbiology reference laboratories published in this report is intended as a background document for institutions and policy makers in the field of public health in the EU Member States. It is also relevant to a much broader international audience, including public health specialists and technical experts operating or working in reference laboratory institutions.

This publication can be used as technical support in countries which are:

- planning and implementing new microbiology reference laboratory systems; or
- consider reviewing and updating already existing systems.

In addition, this report can also be used as a basis for broader strategic planning and the implementation of supranational reference laboratory structures and cooperation.

Material and methods

To facilitate collaboration with the Member States on issues of microbiology, ECDC asked each Member State's health authority to designate a National Microbiology Focal Point (NMFP). These experts were selected on the basis of their expert knowledge of microbiology systems, their familiarity with the structures in their home countries, and their ability to act as liaisons and technical partners between ECDC and the Member States on all issues related to microbiology and laboratories [3].

Between 2007 and 2010, the NMFPs held six meetings. In 2008, ECDC conducted an in-depth survey among the NMFPs on the public health microbiology organisation and functions of the Member States, with a strong focus on the core activities of reference laboratories.

The overall response rate of the public health microbiology survey was 90% (27/30 EU and EEA countries). A few countries could not respond because of administrative difficulties. For this report, these countries were asked to reply to several open questions on reference laboratory systems and structure. The main limitation of the study in terms of data interpretation is missing country data and a number of questions that received a low response rate.

Based on the results of this survey and subsequent discussions in the working group, a consensus agreement on the core activities and functions of microbiology reference laboratories in the context of public health microbiology was reached.

The ECDC Microbiology Coordination Team consolidated this work into this technical report, drawing on input from an NMFP writing group on behalf of the entire NMFP forum. The final version of this report was reviewed and endorsed by the NMFP forum, representing all EU/EEA Member States and the two candidate countries Turkey and Croatia.

Results

Core functions and activities of microbiology reference laboratories

The current systems of reference laboratories in the European Union vary considerably between countries (Annex 1). There are reference laboratories covering all diseases within the mandate of ECDC, but countries define the term 'reference laboratory' differently. Similar differences exist for selection and evaluation procedures (Annex 2).

After a thorough process of deliberation, a European definition of 'microbiology reference laboratory' (describing core functions and activities) was reached by consensus between officially nominated representatives from all EU/EEA countries. Also outlined were the general conditions and requirements for microbiology reference laboratories that were considered essential for performing these core functions. These were selected as they represent the most fundamental elements of a laboratory that provides reference functions.

The core functions of reference laboratories are shown in Table 1, in no particular order of preference or importance. For each core function, a short description and a practical example is given.

Table 1. Core functions and activities of microbiology reference laboratories

Function 1: Reference diagnostics

The reference laboratory has state-of-the-art validated laboratory methods in operation and the ability to deliver accurate confirmation of diagnostic results within its field of expertise. This may include the analysis of samples in a variety of areas, such as the verification of results (e.g. detection or confirmation) reported by external laboratories, the detection of specific microbial markers and the investigation of atypical samples.

Activities

- 1a. Have up-to-date reference methods in operation for specific pathogen/disease characterisation.
- 2b. For selected pathogens: offer diagnostic confirmation services (i.e. validate diagnostic test results, provide advice and support).
- 3c. Investigate atypical samples.

Example

An outbreak of pharyngitis is detected in a day-care facility. At the same time, a teacher dies of streptococcal toxic shock syndrome. Group A streptococci were isolated from blood culture of the teacher before death. The reference laboratory is involved in the outbreak investigation through characterisation of the group A streptococcal isolates collected from throat culture of the children and teachers. This is done by specialised reference diagnostic methods including sequencing of the M protein gene which is an effective marker of the relatedness between isolates, providing objective evidence for epidemiological investigations. This type of analysis requires appropriate equipment and specialised skills and knowledge.

Function 2: Reference material resources

If necessary, the reference laboratory develops and maintains — in accordance with international standards and procedures — a collection of relevant reference material that is to be shared with laboratories and organisations that request such materials. These materials can include reference laboratory strains and cultures, clinical isolates, sera, genetic materials, etc. These resources are important for the varied purposes of quality assurance systems, method evaluation and validation.

Activities

- 2a. Develop, maintain and/or have access to relevant source reference materials.
- 2b. Provide and/or facilitate access to reference material for relevant laboratories and organisations.

Example

A microbiology reference laboratory at the national level for influenza diagnoses a patient with pandemic influenza A(H1N1). Virus is cultivated and nucleic acid extracted and stored. Positive controls, to be used in diagnostic PCR testing, are developed from this material and distributed to regional laboratories upon request.

Function 3: Scientific advice

The reference laboratory is a resource and coordination point for expertise within its specific area and shares information and advice with relevant stakeholders. This can include technical advice on methods and procedures, scientific support and advice on the interpretation and relevance of laboratory findings on pathogens to relevant public health authorities (policy makers and public health professionals).

Activities

- 3a. Provide scientific advice and recommendations to public health authorities.
- 3b. Provide technical support for policy development, e.g. vaccine issues, outbreak response management and preparedness planning.
- 3c. Provide advice and support to laboratories (i.e. including activities such as conducting workshops and other training activities based on needs but also for the implementation of new methods and policies).

Example

Vaccines against bacterial diseases like meningococcal or pneumococcal invasive infections are type-specific. Advice and information from the reference laboratory about circulating strains is shared with public health professionals, epidemiologists, vaccine producers, regulatory authorities and regional laboratories. This can lead to changes in vaccine policies and helps to monitor vaccine coverage in the population.

Function 4: Collaboration and research

The reference laboratory is at the forefront of technological and scientific development in its field of expertise, particularly in areas relevant to public health action. Contacts with regional and international laboratory networks as well as related initiatives should be established and maintained. Examples of collaboration are involvement in EU and other international disease-specific networks, network activities of regional laboratories, or global initiatives via WHO or the US CDC.

Activities

- 4a. Participation in regional/international public health microbiology laboratory networks.
- 4b. Participation in other regionally or internationally relevant projects and initiatives, including research and development activities to underpin the quality, scope and development of core reference laboratory activities; participation in, and contribution to, international surveillance.

Example

A reference laboratory for *Cryptosporidium* participates in an EU-funded project that develops and evaluates detection and typing methods. The project results in a validated method for PCR detection of the parasite and the method is eventually disseminated to regional laboratories.

Function 5: Monitoring, alert and response

The reference laboratory performs or contributes to surveillance activities, or has established channels of communication with the national surveillance body to regularly report incidence data and provide an 'alert function' for unusual occurrences. These can include failure of a diagnostic test, detection of changes in incidence, virulence, drug resistance, emergence of a possibly infectious disease of unknown aetiology, etc. In the case of an outbreak, the reference laboratory supports outbreak investigations, e.g. by offering diagnostic services, advice and technical expertise, and, upon request, provides surge capacity for diagnostics.

Activities

- 5a. Provide data to national surveillance institutes or, if part of a national surveillance institute, to other appropriate bodies.
- 5b. Provide surge capacity as part of a national preparedness plans.
- 5c. Provide advice and technical support in outbreak investigations.
- 5d. Provide early warnings in case of unusual occurrences.

Example

The reference laboratory is involved in an outbreak investigation and reports laboratory data to the national surveillance body and regional healthcare professionals. An outbreak of *Salmonella typhimurium* is detected and communicated to relevant stakeholders, upon which the reference laboratory initiates enhanced testing and epidemiological typing of the bacteria.

Identification of general conditions to perform the microbiology reference laboratory functions

The core functions and activities of a microbiology reference laboratory should adhere to international standards [9]. Taking ISO standards into account, the NMFPs exchanged opinions on the overarching criteria and conditions that should be met for the optimal fulfilment of all core functions outlined in this technical report. The following criteria and conditions were identified:

- The mandate to provide reference functions in the public health microbiology sector, in accordance with the country's systems and authorising body/bodies.
- Recognition as an expert institution and strong ties to laboratories and stakeholders within the Member State and internationally. Research activities should be taken into account.
- Sufficient expertise and knowledge, applied appropriately and according to international standards and practices.
- Suitable equipment, basic materials, adequate resources, appropriate products and sufficient time to be able to perform functions and activities assigned to the laboratory.
- An appropriate infrastructure (i.e. building and administrative infrastructure) to support activities. With regard to the infrastructure of the building, this goes beyond equipment and materials and includes specialised laboratory containment facilities and biorisk management systems for working with certain pathogens.
- Suitably qualified staff with adequate training and experience, such as to ensure a sufficient level of competence to carry out the assigned tasks.
- Compliance with laws concerning data protection, transportation and material transfer agreements.
- Sufficient funding that supports and guarantees continuous and qualified work.

Discussion

Microbiology reference laboratories support the public health response to communicable disease threats. In order to achieve effective and timely responses, the EU depends on a strong reference capacity and high-quality diagnostic results. From a European perspective, the role of liaison to public health microbiology activities in the individual countries naturally falls to the reference laboratories. However, these microbiology reference laboratories are defined, organised, maintained and operated differently in the various European countries (see Annex 1 and 2). These differences have implications for sharing services, materials and data, as well as international public health activities.

The functional definition of microbiology reference laboratories presented in this report is based on a consensus agreement among officially nominated representatives from all EU/EEA countries and candidate countries Turkey and Croatia. This initiative is an important first step toward the goals outlined in ECDC's founding regulation which states that the Centre – by encouraging cooperation between expert and reference laboratories – shall foster

development of sufficient capacity within the Community for the diagnosis, detection, identification and characterisation of infectious agents which may threaten public health [1].

Laboratory standards for general activities of microbiology laboratories are available through the International Organization for Standards (ISO) [9], and there are also standards covering highly specific areas like antimicrobial susceptibility testing (AST). However, there is no single set of internationally accepted comprehensive standards which specifically covers microbiology reference laboratories. Since the quality and comparability of results between different laboratories depends on the existence of reference laboratories – which also provide a pivotal role in laboratory networks – a harmonised description of laboratory core functions and activities is essential.

The general criteria and conditions listed in this document are the results of discussions with the NMFP forum and reflect the representatives' agreement on the foundations of public health reference laboratories. This document is neither a guidance document nor a guideline, and it is not intended to be used in a regulatory manner. Furthermore, it is not intended as a means of assessing laboratories for the purpose of accreditation. However, this document may initiate a debate on the need for the regulation and accreditation of public health microbiology laboratories in general, and microbiology reference laboratories in particular.

Reference laboratories perform many important roles and responsibilities associated with accurate diagnosis, effective treatment and prevention of spread of infectious diseases (see Table 1: Examples). For example, outbreak investigations depend on the confirmation of cases by methods that are not commonly available in a routine laboratory setting. Timely and accurate response to outbreaks is essential for controlling such events. Also, information about circulating strains and exact types/serotypes is crucial for developing vaccines. This cannot be achieved without state-of-the-art methodologies and equipment. It is therefore vital to initiate research on these activities. Laboratories without research programmes of their own need to be connected to research institutions so they can update their knowledge and practices. The scientific community, policy makers and pharmaceutical companies (in order to adjust vaccine/antibiotics production) also need advice and information from reference laboratories.

The listed core activities and functions are intended to be applicable as a framework for action in any microbiology reference laboratory within the EU, regardless of pathogen, current public health laboratory structure or level of development. Also, due to regional differences in the endemicity of particular infections, some countries may find certain aspects to be more important than others. Depending on the organisation of the current reference laboratory system, not all functions may be performed in a single institution but instead would be divided up among cooperating laboratories. It is crucial that these functions are in place in each country, regardless of the method of implementation used. If not, alternative arrangements should be made by establishing bilateral agreements with third countries. This document can also contribute to building capacity, helping to maintain independence and assuring rapid response in emergency situations.

Equal access to and provision of reference services across the EU is important. This will maximise the contribution of public health microbiology to the health of the population. Good diagnostics, laboratory surveillance, IT, statistics and epidemiological intelligence – efficiently connected at all levels (regionally, nationally, EU-wide and globally) – ensure the most effective and timely evidence-based public health actions, both pre-emptive and reactive.

Conclusions

The organisation, selection and evaluation processes for microbiology reference laboratories in Europe are very heterogeneous. Common and harmonised standards are an important precondition when aiming for high-quality work at European microbiology reference laboratories.

This report provides a practical definition of microbiology reference laboratory functions, developed and agreed by all Member States and participating candidate countries. It is intended to support countries in strengthening capacity: 'By encouraging cooperation between expert and reference laboratories, the Centre shall foster the development of sufficient capacity within the Community for the diagnosis, detection, identification and characterisation of infectious agents which may threaten public health' [1]. Specifically, it will build and facilitate confidence in the international exchange of data, services and materials and provide countries with the right tools to respond rapidly in emergency situations. In addition, it should be regarded as an essential document for any discussions on an EU reference laboratory system.

Judging from the survey results and the views expressed in the NMFP forum, there is an obvious need to develop common and harmonised standards for microbiology reference laboratories. Therefore, a coordinated approach will be essential to make effective progress. Both technical and political commitment will be required for full implementation.

This report can serve as the basis of discussion on legislation in Member States directed at the strengthening, planning, or implementing of reference laboratory systems. ECDC will continue to work with the Member States

within its mandate to evaluate the impact of this collaborative technical report and plan for continued strategic development in order to reinforce laboratory capacity in the EU.

The NMFP forum will be instrumental in further developing strategies for building capacity in public health microbiology in the Member States. In close partnership with the European Commission and WHO, ECDC is currently exploring areas of work within its mandate that fall within the remit of this technical report on core functions of microbiology reference laboratories. This will be helpful for strengthening laboratory capacity in the EU and globally.

References

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- 9 http://www.iso.org/iso/iso_catalogue.htm

Annex 1. Organisation of reference laboratories

All countries reported having reference laboratory capacity, but only half stated that they have a definition of the term 'national reference laboratory'. Only three countries could refer to definitions in official or legal documents. The way countries organise their national reference laboratory functions differs widely, ranging from highly centralised within one or a few institutions (14 out of 30 EU/EEA countries) to variably distributed among different institutions, hospitals, university laboratories, or even private companies. There is no clear correlation between these arrangements and the size or population of a country.

There are international standards [9] applicable to microbiology laboratories, but there is a considerable degree of variation in how they are applied in the different Member States and how they are interpreted and implemented (Figure 1). Existing reference laboratories in the European Union cover diagnostics of all diseases within the mandate of ECDC (Table 1).

Figure 1. Responses from European Public Health Microbiology survey, 2008. Is any type of official recognition of laboratory quality level required for public, private or reference laboratories?

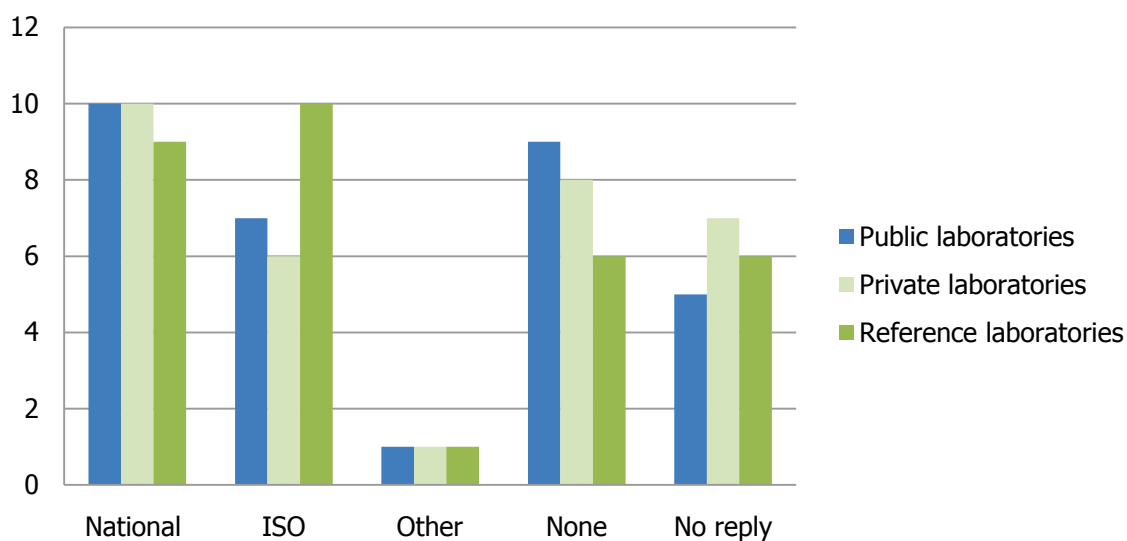


Table 1. Number of laboratories* per pathogen, disease, or specialised area within the European Union that perform reference level functions as reported by NMFPs in 2008

20–25*	15–19*	10–14*
Influenza	Antimicrobial resistance	Chlamydia infection
Meningococcal disease	Campylobacteriosis	Cryptosporidiosis
Salmonellosis	Haemophilus influenza	Echinococcosis
Hepatitis B	Legionellosis	Gonococcal infection
Measles	Mumps	Nosocomial infections
Poliomyelitis	Pneumococcal infection	Plague
Shigellosis	Toxoplasmosis	Viral haemorrhagic fevers
Hepatitis A	Yersinosis	Rabies
Hepatitis C	Pertussis	Giardiasis
HIV infection	Hepatitis D	HPV infection
Tuberculosis	Hepatitis E	Brucellosis
Listeriosis	Diphtheria	Trichinosis
Pathogenic <i>E. coli</i>	Norovirus infection	Spongiform encephalopathies
Rubella	SARS	Tularemia
Staphylococcus/MRSA	Malaria	
	Syphilis	
	Adenovirus infection	
	West Nile Virus infection	
	Botulism	
	Cholera	
	Leptospirosis	
	Anthrax	
	Chikungunya infection	
	CMV infection	
	Hantavirus infection	

Annex 2. Selection and evaluation practices of reference laboratories

Reference laboratories are selected differently. The selection methods can be grouped into three main categories: (A) tender process (two countries); (B) official nomination (nomination by the ministry of health or other legal structure: 17 countries); (C) other processes, which include those laboratories that are not officially nominated but which de facto fulfil an NRL role (eight countries) (Table 2). Fifteen responding countries stated that the NRLs receive specific funding for reference activities. Most NRLs are in the public sector (20 countries), and no countries report NRLs that are solely part of a private/commercial system.

Once nominated, most of the NRLs are appointed for an undefined time period (19 countries). In three of the surveyed countries the status of the NRLs is reviewed at least once every four years. Sixteen countries report that they perform some type of auditing (assessment, evaluation and monitoring procedures) on their NRLs.

Table 2. Responses from European Public Health Microbiology survey, 2008. How are the national reference laboratories selected?

Tender process:	2
Official nomination:	17
Other/de facto:	8
No reply:	3