



## Establishment of requirements and management systems of a national reference laboratory for infectious diseases

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It is essential to establish a laboratory response system for safe, prompt and accurate diagnosis of emerging infectious diseases. There was a crisis of diagnostic capacity during MERS outbreak of 2015, which was caused by lack of reference laboratories as well as on-site laboratories of healthcare systems in Korea. There has not been national reference laboratory (NRL) system for infectious diseases established in Korea, although Korean Center for Disease Control and Prevention has a practical role of NRL. To establish a national level NRL system that can maximize the diagnostic capacity of infectious diseases, collaboration of the private as well as public microbiological laboratories would be required. Here the requirements and management systems of a NRL for infectious diseases were summarized as the results of benchmarking and ad hoc investigation of experts' opinion.

The national reference laboratory is the premier microbiology laboratory that plays a pivotal role in the diagnosis, surveillance and epidemic response for infectious diseases with national level of public health and provides a scientific basis for infection control and prevention (Table 1).

Table 1. Core functions and activities of microbiology reference laboratories

Function	Activities
<b>1. Reference diagnostics</b> 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.	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.
<b>2. Reference material resources</b> 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.	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.
<b>3 Scientific advice</b> The reference laboratory is a resource and coordination point for expertise within its specific area and shares	3a. Provide scientific advice and recommendations to public health authorities.



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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).

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).

#### 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.

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.

#### 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.

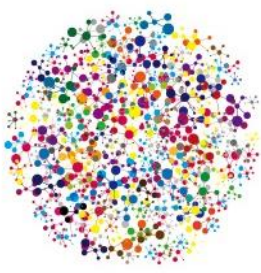
5a. Provide data to national surveillance institutes or, if part of a national surveillance institute, to other appropriate bodies.

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.

The demand for building the efficient and communicable national reference laboratory was high because of the delay in reporting the results of the confirmation test, lack of confirmation testing service, and inconvenience of the consignment system such as sample logistic (Figure 1). The NRL system has been proposed to maximize the country's ability to diagnose infectious diseases, so that a NRL model was proposed to establish in open format to all eligible microbiological laboratories of public and private sectors (Figure 2). While public sector must include Korean CDC, 17 municipal public health laboratories, and 3 quarantine laboratories, private sector may include clinical laboratories representing large regions and nationwide commercial reference laboratories and university-based or independent research institutes such as The Korean Institutes of Tuberculosis. The Korea CDC and provisional NRL Association could be responsible for the administrative functions of organizing and maintaining the public and private sectors, respectively. National reference laboratory will be a major component of laboratory preparedness for emergency and national surveillance network of infectious disease in peace. KCDC serves as a control tower in



the event of a national infectious crisis and strengthen response based on capacity of national reference laboratories.

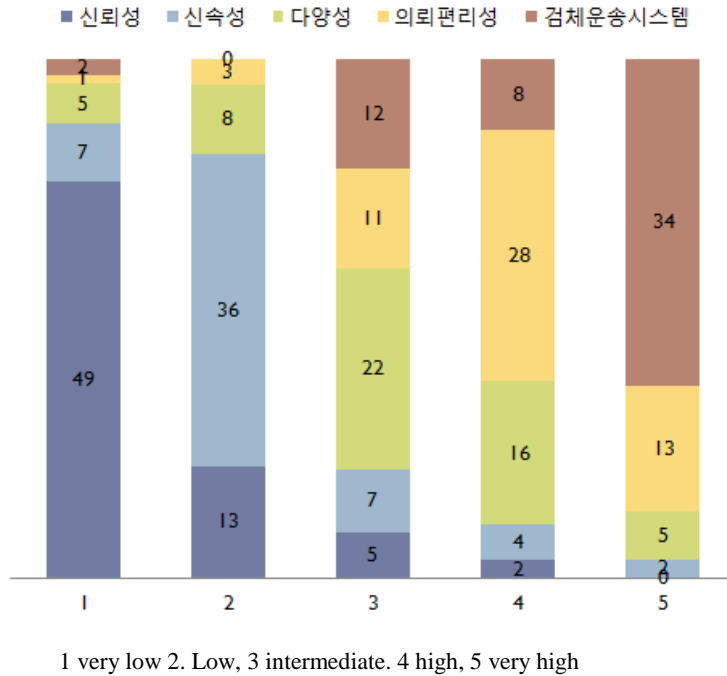


Figure 1. Priority in functions of reference laboratories

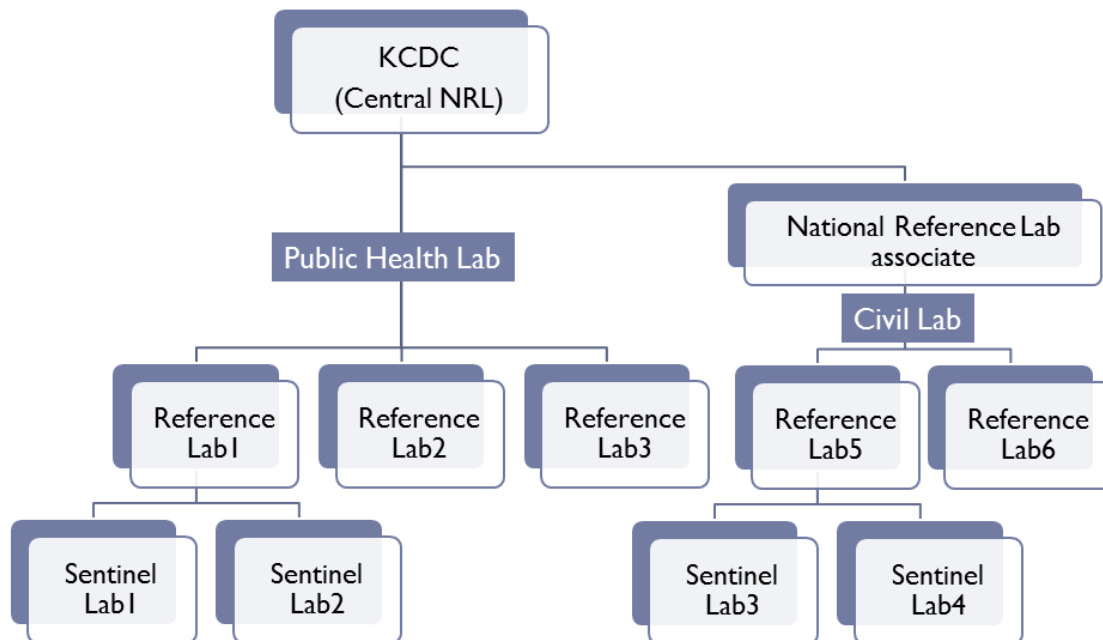
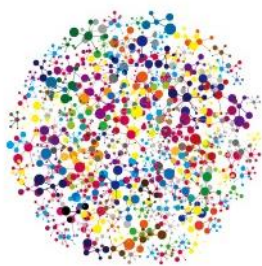


Figure 2. Proposed model of national reference laboratory system for infectious diseases in Korea

A national reference laboratory should be qualified by requirements and quality management



programs corresponding to national reference laboratories. The requirements are in accordance with the country's systems and authorising body/bodies as well as performance standards, qualified staff with adequate training and experience, administrative standards, infrastructure standards, and emergency operation standards. Certification and recertification system is preferred with participation of experts outside the NRL system to guarantee continuous improvement of NRL.

In this way, huge economic and healthcare benefit will be expected by marked improvement of the national diagnostic capability. Therefore, it is necessary to provide national financial support to establish and maintain sustainable development of this system.

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