Preparedness and Rapid Implementation of External Quality Assessment Helped Quickly Increase COVID-19 Testing Capacity in the Republic of Korea

Running Head: Rapid Expansion of COVID-19 Testing Capacity

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List of abbreviations: COVID-19, coronavirus disease 2019; EUA, emergency use authorization; EQA, external quality assessment; KCDC, Korean Centers for Disease Control and Prevention; KSLM, Korean Society of Laboratory Medicine; KEQAS,

Korean Association of External Quality Assessment Service; KFDA, Korean Food and Drug Administration; KLAP, Korean Laboratory Accreditation Program.

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To the Editor:

The current outbreak of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2, continues to spread, and as of March 31, 2020, it has reached 200 countries, with 785,219 cases and 37,797 deaths *(1)*. Since the first case was reported in the Republic of Korea on January 19, 2020, more than 9,500 confirmed cases had been identified by March 31. Since March 2, the number of newly-reported cases appeared to have been declining, and the reported cases have been mostly related to certain provinces. As of March 31, the Republic of Korea (population of 51 million) was testing more than 20,000 patients per day. Clinical pathologists and microbiologists of other countries wonder how our nation rapidly expanded its capacity for COVID-19 testing in such a short period. The key factors in this rapid expansion of testing capacity were the establishment of an emergency use authorization (EUA) system, an external quality assessment (EQA), and the collaboration between the public and private sectors.

After the Korean outbreak of Middle East Respiratory Syndrome (MERS) in 2015, which involved 186 cases including 38 fatalities *(2)*, the Korean Centers for Disease Control and Prevention (KCDC), the Korean Society of Laboratory Medicine (KSLM), and the Korean Association of External Quality Assessment Service (KEQAS) established the rapid response processes for emerging infectious diseases such as an EUA system, similar to that of the U.S. FDA *(3)*. In order to control future outbreaks of emerging infectious diseases, a KCDC-sponsored EQA molecular testing drill for Zika virus and MERS coronavirus was carried out by the KEQAS in 2016 in accordance to the established rapid response process *(4)*. The

KEQAS developed a system to receive the proficiency test results at that time. On January 16, 2020, the KSLM launched a COVID-19 Laboratory Response Task Force (LR-TF) to facilitate clinical laboratories to establish the diagnostic testing of COVID-19 (Fig. 1). On the next day, the KCDC and the KSLM LR-TF had the first meeting on the expansion of COVID-19 testing by non-governmental clinical laboratories. The KCDC and the KSLM LR-TF agreed to cooperate on the training of laboratory personnel, the EQA program, and the evaluation of EUA kits for the diagnosis of COVID-19.

On January 27, the KCDC and the KSLM LR-TF met representatives from domestic molecular reagent manufacturers to explain our objective and the schedule of EUA approval for COVID-19 molecular diagnostics. By the time, three confirmed COVID-19 cases had been reported in Korea. On February 4, the KCDC and the Korean Food and Drug Administration (KFDA) approved the PowerChek 2019-nCoV Real-time PCR kit (Kogene Biotech, Seoul, Korea) for diagnosis of COVID-19 after co-evaluation by the KCDC and the KSLM. For evaluation materials, specimens from the three confirmed individuals were triplicated in blind and then serially diluted into four different concentrations. Plasmid DNAs containing the *E* gene and *RdRp* gene also served as evaluation specimens. The usual respiratory pathogen positive samples including coronavirus 229E, NL63, OC43, HKU1 were used as negative controls as well as respiratory virus negative specimens.

On February 5, the proficiency test panel comprised of six plasmid DNAs with varying concentrations (one *E* gene plasmid only, one *RdRp* gene plasmid only, and four concentrations from serial dilution of combined *E* gene and *RdRp* gene plasmids) and one negative control were shipped on dry ice to the Korean Laboratory Accreditation Program (KLAP)-accredited laboratories willing to participate in COVID-19 testing through molecular

diagnostics. Delivery to all laboratories including Jeju Island was completed within 10 hours. The KEQAS was responsible for transporting the EQA material, collecting the EQA results, and judging the results. Only samples with an 80% or more agreement rate compared to the expected results were evaluated. Approval for COVID-19 molecular testing was given when a laboratory had correctly answered all the evaluable results. By February 6, the KEQAS had certified 46 out of the 47 laboratories that entered the results. Forty-six non-governmental clinical laboratories were able to begin COVID-19 testing using a commercial EUA kit from February 7. Due to high testing demand at the beginning, testing complied with the inclusion criteria. The COVID-19 real-time RT-PCR is indicated for confirmation of suspected COVID-19 patients who present with fever (37.5□ or higher) and/or respiratory symptoms (cough, sore throat, etc.) and history of close contact with a confirmed individual within the previous 14 days. It is also indicated for screening of asymptomatic individuals in close contact with confirmed COVID-19 patients and for differential diagnosis of cases with unknown respiratory syndromes *(5)*. There are no specific exclusion criteria for testing, although testing done outside the criteria are denied of national healthcare system reimbursement for the testing fee. Two more EQAs using the same plasmid DNAs were conducted and 49 additional non-governmental clinical laboratories were enrolled. We have finished the EQA using the inactivated cultured SARS-CoV-2 spiked into pooled respiratory samples.

As of March 31, a total of 95 non-governmental clinical laboratories are conducting more than 20,000 COVID-19 tests per day using five different EUA kits. The five EUA kits' output reached 20,000 kits per week, covering a total of 350,000 clinical samples.

In conclusion, preparedness and rapid implementation of EQA have supported the rapid expansion of COVID-19 testing capacity in the Republic of Korea. Owing to the increasing diagnostic capacity, our nation was able to slow down the COVID-19 epidemic without enforcing city-wide lockdowns or collapse of the national healthcare system. The quality of COVID-19 diagnostic testing was ensured by the KLAP and the EQA programs.

Nonstandard abbreviations: EUA, emergency use authorization; EQA, external quality assessment; KCDC, Korean Centers for Disease Control and Prevention; KSLM, Korean Society of Laboratory Medicine; KEQAS, Korean Association of External Quality Assessment Service; KFDA, Korean Food and Drug Administration; KLAP, Korean Laboratory Accreditation Program.

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All authors contributed to the conception of the correspondence. HS and WKM wrote the correspondence. All authors contributed to the review of the correspondence.

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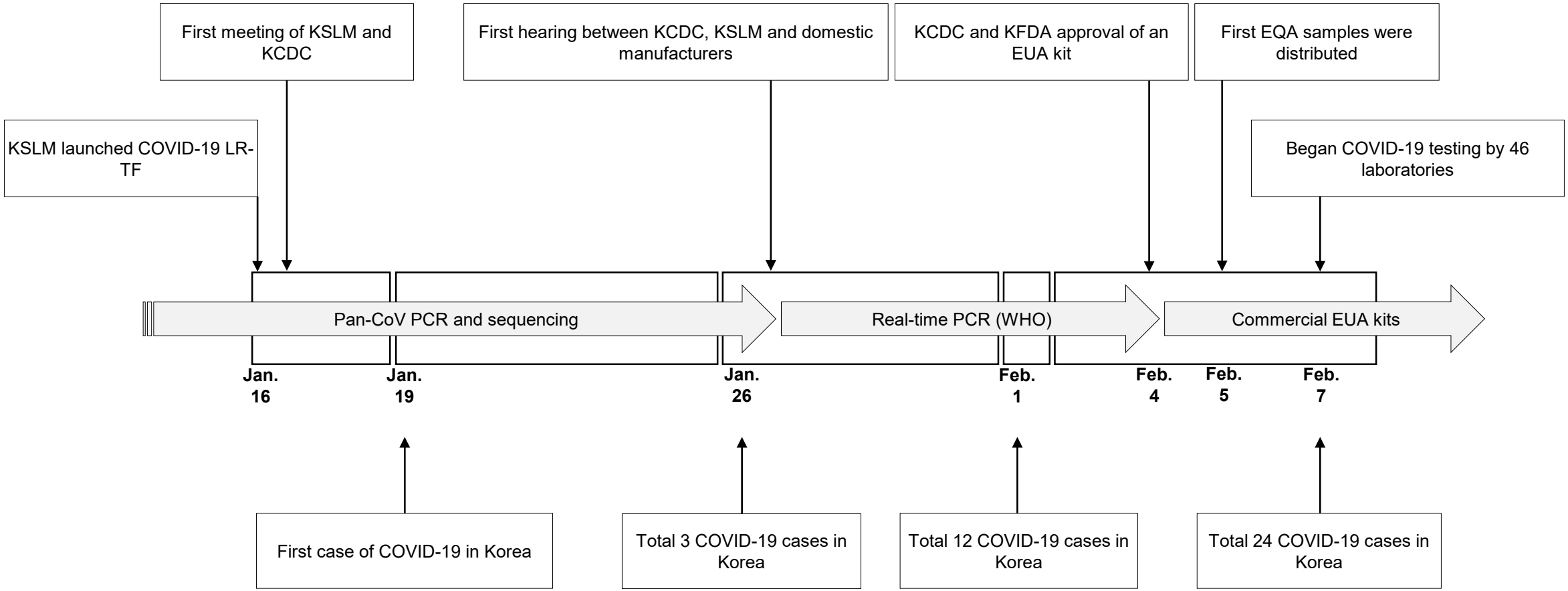
Figure legend

Figure 1. Timeline of COVID-19 testing-related collaborations between the public and the private sectors

Abbreviations: KSLM, Korean Society of Laboratory Medicine; KCDC, Korean Centers for Disease Control and Prevention; KFDA, Korean Food and Drug Administration; EQA, external quality assessment; LR-TF, Laboratory Response Task Force; Pan-CoV, pan-coronavirus; EUA, emergency use authorization.


First meeting of KSLM and KCDC
First hearing between KCDC, KSLM and domestic manufacturers
KCDC and KFDA approval of an EUA kit
First EQA samples were distributed
KSLM launched COVID-19 LR-TF
Began COVID-19 testing by 46 laboratories
Pan-CoV PCR and sequencing
Real-time PCR (WHO)
Commercial EUA kits
Jan. 16
Jan. 19
Jan. 26
Feb. 1
Feb. 4
Feb. 5
Feb. 7
First case of COVID-19 in Korea
Total 3 COVID-19 cases in Korea
Total 12 COVID-19 cases in Korea
Total 24 COVID-19 cases in Korea