ASEAN Dx Preparedness Webinar: Testing Platforms

It has been more than 18 months since COVID-19 pandemic happened. As of July 2021, 903,286 sequences of SARS-CoV-2 had been uploaded by 93 countries[1], noting at least 4 variants of concern (VOC)[2]. At this rate of the evolution of this virus, it is more likely that SARS-CoV-2 will become endemic like flu and dengue etc, rather than be eliminated like SARS-1 and smallpox etc. Humankind will need to learn to live with it.

It has been emphasized by many that the key to sustaining and prevailing a pandemic is in testing, testing, testing. Although testing is not the only or most important weapon in this war, it is the first defense mechanism which we must be prepared for. Testing will continue to be important in the new-normal. Living with SARS-CoV-2 in a new-normal would require multiple levels of collaboration between the general population and policy makers. In view of the various waves of COVID-19 across the globe, a country must safeguard itself from the evolving VOCs. Thus, the speed to innovate and come up with innovative screening methods is vital. To enable this, the policy makers need to also change the testing guidelines appropriately and quickly.

Collaboration involves the population's compliance to follow the updated guidelines for social management measures as well as the trust that any infection and testing data is provided transparently to inform best judgement on individual levels. Collaboration also means a willingness to have the paradigm shift in mindset from diagnostics to screening, to allow for more innovative methodologies, such as direct PCR, antigen test, breath test etc, to stay ahead of the virus.

Characteristics and performance requirements on testing assays differ depending on the use case of diagnostics or screening. Diagnostics requires high level of sensitivity and specificity to better guide clinical management; while screening in a general population requires adequate accuracy to triage a subset of cases for diagnostics, thus reducing turnaround time and burden to the infrastructure. Ultimately, it is paramount to always provide more than enough testing capacity, to enable for effective tracing when there is a spike with an aim to capture, isolate and thus contain the infection as quickly as possible.

As part of screening exercise, routine screening of the certain population, such as schools, hostels, workers' dormitories, can also be better facilitated when we are able to embrace more screening testing methodologies. Ideally, there will be different tests for diagnosis and screening based on different use cases. Having the different types of testing methodologies available is getting ourselves prepared for all possible scenarios.

Purpose of the ASEAN Dx Preparedness Webinar Series is to seed ideas and stimulate conversations amongst laboratories and practitioners to think about innovative solutions and alternatives, so that we can better deal with this COVID-19 pandemic, which is far from over, and to prepare for what may come next. Amongst the various alternative testing methodologies, the first webinar focused on the use of direct PCR as an alternative platform for lab-based diagnostics and its use to manage COVID-19 testing demands.

- There were 645 registrations and 432 attendees. 88% attendees were from ASEAN.

The following experts contributed to the discussion:

1. Dr Kristine Alvarado-Dela Cruz Pediatrics, Infectious Diseases, Head of Microbiology, Research Institute for Tropical Medicine, Philippines

2. Dr Eric Vail - Director, Molecular Pathology, Cedars-Sinai Medical Centre, United States

3. Dr Wong Mun Yew - Chief Executive Officer & Founder, Asia Genomics, Singapore

4. Dr Joseph Yao - Associate Professor, Laboratory Medicine and Pathology, Mayo Clinic, United States

The session was moderated by Dr Benedict Yan, Pathologist and Director, Molecular Diagnostics Centre, National University Health Systems, Singapore.

The webinar was jointly chaired by ASEAN Dx Initiative co-chairs Dr Sidney Yee, Chief Executive Officer, Diagnostics Development Hub, Singapore and Dr Jamie Montoya, Executive Director, Council for Health Research and Development, Philippines (PCHRD).

Challenges were faced with the surge in testing demand

At the start of the pandemic the key purpose of COVID-19 test was to diagnose and quarantine the infected individuals. As the testing demand surged rapidly, ramping up the testing facilities became a major challenge globally. Lack of preparedness in terms of demand in regular laboratory supplies, manpower and equipment as well as test kits was exposed. Similar issues were faced at hospitals, regional testing centers as well as reference laboratories as everyone was caught off guard. The testing demand surge took heavy toll on laboratory consumables and manpower, amongst others.

In this webinar, the panelists highlighted the issues when they had to suddenly increase the testing capacity in response to the sudden outbreak of the pandemic. As an example, even after ramping up over several months, Mayo Clinic could carry out only 80% of the tests per day and could not operate at their maximum capacity due to operational constraints such as space, manpower and consumables. Cedars-Sinai Medical Centre also faced similar space and manpower issues. The magnitude of strain on the laboratory consumables can be gauged by the fact that the whole world ran out of pipette tips in September last year, as commented by Dr Vail.

As compared to the US which has many testing centers, the Philippines faced different set of problems. The Research Institute for Tropical Medicine (RITM), the national reference laboratory responsible for validating all diagnostic tests before clinical use in Philippines, faced several challenges to scale up COVID-19 testing in response to demand surge. At the onset of the outbreak RITM was the only confirmatory testing laboratory in the Philippines. They needed to quickly set up an assay based on published protocols and optimize it in addition to evaluating new commercial diagnostic tests that became available. With the surge in testing demand, RITM had to reorganize departments at the institute level and deploy resources for COVID-19 testing. Concurrently, RITM also coordinated with other National Reference Laboratories (NRLs) to augment the national response. With all these efforts,

several laboratories in the Philippines are now using diagnostic tests for SARS-CoV-2 detection.

In addition to above-mentioned issues, another big question was which test to use? The priority at the stage was to test, identify and isolate COVID-19 patients to control the spread. The world needed a solution that can handle large volume of patient samples with a rapid turnaround time (TAT). For this use case, WHO has recommended nucleic acid amplification tests (NAATs) as they directly detect viral RNA (antigen) even before symptoms appear. In the US there were 235 FDA-authorized molecular tests as of December 2020 covering several types of tests such as Polymerase Chain Reaction (PCR), transcription-mediated amplification (TMA) and loop-mediated isothermal amplification (LAMP). Majority of the adopted tests were RT-PCR, wherein, the preparation protocol makes the overall duration of a test about 8 hours. The use of direct PCR was directly in response to the shortages of nucleic acid extraction reagents, longer TAT. In direct PCR, the clinical sample (nasopharyngeal/ nasal mid-turbinate swab, or deep throat saliva) is added directly to an amplification reaction without being subjected to prior DNA extraction, purification, or quantification. This significantly reduced the TAT, from swab to test result, from 8 hours to 4 hours. Notwithstanding that, direct PCR tests such as RESOLUTE 2.0 has also been reported by Cedars Sinai Lab and Asia Genomics lab to be meeting the required sensitivity and specificity for their respective use cases.

Collaboration is crucial to counter a pandemic

There is need for urgency in a pandemic and so innovation speed is very important. It was heartening to see scientific community, clinical community and regulatory bodies come together to solve the problem in a collaborative yet efficient way. Although the initial stage of the pandemic is under control, SARS-CoV-2 is continuously evolving. Some of the use cases are for checkpoint control to allow economic activities, pre-event testing such as live performances, wedding, event planning and home testing for self-quarantine. These use cases would require easy-of-use, quick TAT, Point of Care (POC) tests. Tests such as Antigen Rapid Test (ART) can be used at or near the POC, without the need for laboratory infrastructure or expensive equipment, but should only be used in repeat testing regime due to its lower sensitivity.

There are also increasing uses of different specimens, such as breath, and saliva, specifically deep throat saliva, for testing instead of nasal cavity swabs. While breathalyser measures the likelihood of infection based on finger-prints of the infection generated inflammatory proteins, deep throat saliva is a non-invasive way to detect the pathogens directly. As a result, as borders reopen and as COVID-19 is evolving from pandemic into endemic position, non-invasive and direct-pathogen detection regime such as deep throat saliva is increasingly being considered by some countries as Rostered Routine Testing (RRT) tools for continuous monitoring and surveillance purposes.

The panel reiterated that the testing needs have evolved from actively testing for quarantine and treatment, to testing and screening to open the economy. Collaboration on the ground

is crucial to develop and onboard more innovative tests and testing regime and stay focused on innovation, in addition to embracing changes to prepare for the next pandemic.

References:

1. https://www.ncbi.nlm.nih.gov/sars-cov-2/
2. https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/