Global workshop on enhancing sequencing to monitor SARS-CoV-2 evolution

Report of a virtual meeting, 19 March 2021

World Health Organization

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Background

As of March 2021, several genetic variants of SARS-CoV-2, the causative agent of COVID-19, had been detected. The Alpha, Beta, Gamma and Delta variants carry mutations that may be associated with different virus properties, such as increased transmissibility, or may have a negative impact on the effectiveness of countermeasures. Such variants may be designated as variants of interest (VOIs) or variants of concern (VOCs), according to WHO working definitions (2). All genetic variants that do not meet these definitions will hereafter be referred to as variants in this report. In response to the recent increase in the detection of variants, the sixth meeting of the International Health Regulations (IHR) Emergency Committee for COVID-19 provided additional temporary recommendations to States Parties, including to increase molecular testing and genetic sequencing, and to share sequences and metadata with WHO and through publicly accessible databases (3).

A high level of global sequencing coverage is required to ensure genomic surveillance to detect variants and monitor virus evolution worldwide. WHO has produced guidance on SARS-CoV-2 sequencing for public health goals *(4)* and an implementation guide on genomic sequencing for maximum impact on public health *(5)*. In line with the COVID-19 Strategic Preparedness and Response Plan *(6)*, WHO is updating its global SARS-CoV-2 sequencing strategy to increase Member States' access to sequencing and encourage timely sharing of geographically representative virus genetic sequences and supporting data. To understand the current status of sequencing for SARS-CoV-2 and inform capacity-building efforts worldwide, a virtual global sequencing workshop attended by a variety of stakeholders was held on 19 March 2021.

Agenda

The agenda consisted of an introductory session on the global risk monitoring and assessment framework for SARS-CoV-2 VOCs and three technical sessions as follows.

- Session 1. Mapping sequencing capacities and addressing gaps globally: where can and should sequencing be conducted?
- Session 2. Sharing of sequences, metadata and bioinformatics for public health action.
- Session 3. Planning next steps: what are we asking of ministries, networks, partners, donors, and industry?

Annex 1 to this report contains the full agenda. The full list of chairs, moderators, speakers and panellists and their affiliations is in Annex 2; and a summary of participants is in Annex 3.

Objective

To agree on a common strategic vision and way forward for a global coordinated plan to increase SARS-CoV-2 genetic sequencing capacity to detect SARS-CoV-2 mutations and variants and monitor the evolution of the virus worldwide.

Introductory session

This session included three speakers who presented information on sequencing and SARS-CoV-2 variants to set the scene from the WHO perspective.

Opening the meeting, Dr Mike Ryan highlighted the importance of sequencing as part of the global response to infectious disease outbreaks. He emphasized that while SARS-CoV-2 has been evolving since its emergence, monitoring is pertinent to our ability to control the virus, particularly in the light of ongoing efforts to roll out vaccines.

Dr Maria Van Kerkhove outlined the objectives and expected outcomes from the workshop, which were primarily to align on a common vision and way forward for a global, coordinated plan to increase SARS-CoV-2 sequencing capacity to detect mutations and monitor variants. By understanding the current status of sequencing worldwide we can better inform efforts to improve these capacities. The secondary objective of this meeting was to encourage information sharing from all stakeholders to enhance geographical diversity and representativeness of sequencing data. The workshop was intended to initiate high-level discussions on global sequencing needs, while considering longer term sustainable actions.

Dr Sylvie Briand gave an overview of WHO's global risk monitoring and assessment framework for SARS-CoV-2 VOCs.

As part of the WHO risk monitoring and assessment framework, the SARS-CoV-2 Virus Evolution Working Group (VEWG), formed in June 2020, tracks variants and investigates their phenotypic impact. The scope of the VEWG is an important component of an overall process to define the impact of each variant, and the implications for vaccine composition, policy and regulatory aspects. Dr Briand reminded the group that as a global community we should build on previous experiences and lessons learned from responses to influenza, Ebola, Zika and other pathogens, to develop a global coordination mechanism for SARS-CoV-2.

Session 1. Mapping sequencing capacities and addressing gaps globally: where can and should sequencing be conducted?

This session looked at existing global sequencing capacities and networks and how they have been adapted and scaled up during the response to SARS-CoV-2. Efforts across the WHO African Region, the Region of the Americas and the European Region were highlighted, but it should be acknowledged that networks and support systems were in place across all regions.. This session included presentations from five speakers on the theme of strengthening existing networks, followed by a panel discussion with all speakers.

1. Spotlight on the Americas

Dr Marilda Siqueira presented the experience in the Region of the Americas during the COVID-19 response. The distribution of laboratories for influenza surveillance and genomic capacity was uneven across the Region. Therefore, referral networks with designated reference laboratories had been critical throughout the response, providing intra-Regional support to strengthen capacity across countries through protocols and training and providing support for sending samples. The continuous surveillance and monitoring of events of interest in Brazil had enabled detection of new variants; and processes had been rapidly standardized to monitor emergence and spread of these variants. There were ongoing needs for technical support to expand sequencing capacity in areas with limited infrastructure, financing and human resources. However, maintaining genomic surveillance networks could be challenging.

2. Spotlight on Africa

Dr Yenew Kebede Tebeja described the current situation and recent developments across the African continent, including the Africa Centres for Disease Control and Prevention Pathogen Genomics Initiative, which mobilizes partners across its network and leveraging existing capacity to support countries. Currently, more than 80% of laboratories with sequencing capacity in Africa are situated in research and academic institutions. Dr Tebeja emphasized the importance of integrating those institutions into public health laboratory networks to support the response. He noted that delays in sequencing and laboratory activities persisted due to challenges with logistics, importation of materials and lengthy processes for material transfer agreements; work was ongoing with policy-makers and regulatory authorities to address these issues as well as to consider the development of both regional and national policies and guidelines. Finally, there was a need to develop the workforce and strengthen bioinformatics, in particular, to facilitate the translation of scientific data to inform public health decision-making.

3. Spotlight on Europe

Dr Erik Alm presented a brief history of the sequencing response to the COVID-19 pandemic across the European Union. In the early stages, efforts had been made to rapidly implement sequencing and share protocols across countries as part of preparedness activities. Following the increased detection of variants, the need for sequencing had greatly increased. Some countries had required immediate support, so the European Centre for Disease Prevention and Control (ECDC) launched an emergency contract with a commercial provider to meet short-term needs. This mechanism enabled sequencing of

approximately 3000 samples per week from around 10 countries. This initiative was not intended to be prescriptive; ECDC was looking to connect with Member States to understand individual country needs to contribute to international efforts to detect and assess variants.

4. Leveraging existing networks for SARS-CoV-2

Dr Wenqing Zhang presented the Global Influenza Surveillance and Response Strategy (GISRS) and described how it had been successfully leveraged for the SARS-CoV-2 response. GISRS had long fostered global confidence through effective collaboration and sharing, with a network that included 158 institutions in 123 Member States carrying out sentinel surveillance for influenza-like illness (ILI) and severe acute respiratory illness (SARI). Characterization of influenza viruses and risk assessment was undertaken mainly in WHO collaborating centres and national influenza centres. The Global Influenza Programme had emphasized the importance of high-quality, timely and representative genetic sequence data (GSD) and associated metadata, addressing why sequencing was needed and to what extent. Dr Zhang concluded by highlighting the importance of global advocacy to encourage a systematic and standardized approach to sequencing to operate at a global level.

5. Country-specific experience in the United Kingdom

Dr Leena Inamdar presented experience from the United Kingdom of Great Britain and Northern Ireland, including the process by which they had successfully scaled up a national response. The United Kingdom had developed an integrated genomics research and service programme capable of delivering surveillance through both diagnostics and sequencing at scale. Dr Inamdar also described the New Variant Assessment Platform (NVAP), consisting of two components: the provision of a comprehensive genomics service to countries that had limited sequencing capability, including sequence generation, analysis and comparison of data to grade mutations; and the development of global partnerships through establishing or supporting international sequencing hubs, working bilaterally with countries based on their needs. Support through the NVAP to strengthen sequencing capacity worldwide was of local and international benefit.

Panel discussion

During the panel discussion, each of the five speakers addressed the current drive to build sequencing capacities globally, and how this could be addressed in a sustainable way, while looking at how much sequencing is enough from across regional perspectives. Capacity in existing systems, such as in academic institutions, could be further leveraged to scale up genomics, providing there were strong links between these institutions and public health authorities, and an understanding of financial sustainability over time.

Recommendations from various organizations ranged from 15 to 500 high-quality representative samples needed per week for sequencing. There was a clear need to develop further guidance around sampling strategies, which should differ according to the objectives of sequencing, while considering the feasibility of implementation. Random sampling had been recommended as a proxy for representative sampling for the purpose of detecting variants, but prioritization of certain samples for sequencing might be needed if resources were limited. In this case, there might be a need to focus on

sequencing cases that were considered high risk, such as those with suspected reinfection or vaccine breakthrough.[1]

Discussions throughout the workshop highlighted the role of existing networks and how countries with established genomics capabilities were leveraging excess capacities to provide international support to countries with resource constraints. This work was crucial given the current unprecedented demand for sequencing, but challenges must be addressed in translating this genomics capacity for public health decision-making, while considering sustainability, consistent standardized systems and appropriate sampling strategies.

Session 2. Sharing of sequences, metadata and bioinformatics for public health action

This session was a moderated panel discussion covering issues pertaining to the sharing of sequences, metadata and bioinformatics for public health action and sought to identify current enabling or limiting factors.

Panel discussion

The primary goal of producing data during a pandemic was to inform the public health response. Making data publicly available provided transparency and facilitated the rollout of evidence-based public health interventions. However, according to GISAID, the average time for sharing GSD was around 40 days from sample collection to upload. Practical issues may delay sharing of sequence data. For example, it takes time to physically transport samples to sequencing facilities. In addition, the impact of sharing data must be demonstrable through public health outcomes.

Many partners that had traditionally not been a part of the public health system had been engaged during the response to SARS-CoV-2. Academic interest may amplify complications and delays in sharing GSD, particularly in places without a national programme, where funding for programmes may be through research budgets and there is a need to demonstrate outputs, typically through publications. Therefore, it may be beneficial to augment these academic efforts through national programmes that support sequencing for the public health response. The global community must maintain a harmonized message to incentivize GSD sharing, including through appropriate acknowledgements of data sources and contributors. In addition, when rapid data sharing is seen to directly influence public health responses

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