

— MEETING REPORT —

1st Global Consultation on SARS-CoV-2 Variants of Concern and the Impact on Public Health Interventions

29 March 2021



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Global Consultation on a Decision Framework for Assessing the Impact of SARS-CoV-2 Variants of Concern on Public Health Interventions, 29 March 2021: Meeting Report

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Abbreviations

EMA	European Medicines Agency
FDA	US Food and Drug Administration
GDG	WHO Guideline Development Group
IVB	WHO Immunization, Vaccines, and Biologicals Department
SAGE	WHO Strategic Advisory Group of Experts on Immunization
SCI	WHO Science Division
STAG-IH	WHO Strategic and Technical Advisory Group for Infectious Hazards
TIPRA	WHO Tool for Influenza Pandemic Risk Assessment
VEWG	SARS-CoV-2 Virus Evolution Working Group
VOC	Variant of concern
VOI	Variant of interest
WHE	WHO Health Emergencies Programme

Introduction

As the COVID-19 pandemic has progressed, variants of the virus have emerged, and more are expected as the virus continues to evolve, but not every variant will be of interest or of concern. Noting the urgent needs for shared access to information, coordination and prioritization of research to assess their potential impact, consistent communications, and joint action, WHO has developed an integrated approach to monitoring and assessing SARS-CoV-2 variants of concern (VOCs) and their impact on public health interventions, including public health and social measures, vaccines, diagnostics, and therapeutics.

There is an urgent need for the international community to come together to synthesize the available evidence of the impact of VOCs on public health interventions and to discuss the way forward for deciding how to adapt the public health interventions, if necessary. This will ensure a coordinated and harmonized approach to interpreting results, issuing recommendations, and communicating to the public.

On 29 March 2021, WHO convened the consultation to advance this integrated approach with all stakeholders, including Member States, regulators, technical expert groups, industry, and other partners. The consultation was open to all stakeholders and was advertised through the WHO website. This consultation provided WHO the opportunity to propose the integrated approach to monitoring and assessing VOCs and outline a decision-making process for the prevention and control of COVID-19, with a specific focus on the impact on COVID-19 vaccines.

The consultation was guided by the following key questions:

- What information is needed to guide COVID-19 prevention and control decision-making by all stakeholders, what are the standards, and how and when will information be collected and shared?
- What are the triggers for decision-making?

The objectives of the consultation were:

1. Review and summarize the existing evidence of the impact of VOCs on public health interventions
2. Engage global stakeholders to outline information needs and decision-making processes for assessing the impact of VOCs on public health interventions
3. Using COVID-19 vaccines as an example, review how a decision-making process could look with respect to analyzing the impact of VOCs and issuing policy recommendations

The four-hour virtual consultation was attended by 1,095 participants from 120 countries, territories, and areas. The following sections represent the information presented as of 29 March 2021.

Opening session

Dr Mike Ryan (WHO/WHE) opened the global consultation and signaled the need to focus global attention on relevant SARS-CoV-2 variants and for the global community to come together to strengthen and coordinate existing systems to monitor the variants and their impact on public health interventions. This must be done in such a way that all interventions are leveraged and can be adapted in response to the evolution of the virus. Dr Ryan iterated the global collaboration needed to develop a risk monitoring and assessment framework for SARS-CoV-2 variants that harness the strength of existing networks and partnership to drive forward collective public health action.

Dr Sylvie Briand (WHO/WHE) provided a brief overview of WHO's initial approach to monitoring and assessing SARS-CoV-2 variants and their impact on public health interventions. With the emergence of the variants, there is an urgent need to fill knowledge gaps and make rapid, evidence-based decisions. WHO has convened an internal coordination mechanism to design the global risk monitoring and assessment framework that will address monitoring and surveillance of variants, evidence needs and assessment methodologies and approaches, and integrated decision-making and public health action.

Session 1:

Focus on SARS-CoV-2 Variants

1.1 Epidemiology Update on SARS-CoV-2 Variants of Concern

Dr Boris Pavlin (WHO/WHE) provided the epidemiological update on current SARS-CoV-2 VOCs and presented the overall processes WHO has established for the monitoring and reporting of VOCs.

WHO has an established mechanism for the detection; assessment; and global tracking, investigation, and communication of SARS-CoV-2 variants. Working definitions of variants of interest (VOIs) and VOCs (see Tables 1 and 2) and associated actions are provided to support WHO Member States and their national public health institutes and reference laboratories with general and non-exhaustive guidance on the prioritization of variants of greatest public health relevance in the context of wider COVID-19 transmission and established response mechanisms. The definitions will be reviewed regularly and updated as necessary. The threshold for determination of a VOI is relatively low to maintain sensitive surveillance for potentially important variants. The threshold for determination of a VOC is high to focus attention and resources on the variants with highest public health implications. The focus is on global risk; however, national authorities may designate variants of local interest or concern.

As of 29 March 2021, WHO had designated three VOCs globally: B.1.1.7, with 125 countries reporting cases as of 23 March 2021; B.1.351, with 75 countries reporting cases as of 23 March 2021; and P.1, with 41 countries reporting cases as of 23 March 2021.¹ Increased transmissibility is a common factor to date, and there has been a steady replacement by B.1.1.7 in reporting countries. There has been some, but varied, evidence of impacts on severity or countermeasures, and there is variability in methodological approaches and challenges with interpretations. Additional studies are needed to fully understand the impacts. WHO continues to advise a holistic response be taken against all SARS-CoV-2 transmission, and the application and adjustment of public health and social measures should be driven by detailed data analyses of epidemiology at the most local level possible.

¹ Please note that as of 11 May 2021, WHO determined that viruses within the lineage B.1.617 are characterized as a VOC based on early evidence of phenotypic impacts compared to other circulating virus variants. Please refer to: <https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---11-may-2021>.

Table 1: Variants of Interest – Working definition and actions:

Definition	Actions for potential VOIs
<p>A SARS-CoV-2 isolate that is phenotypically changed compared to a reference isolate or that has a genome with mutations that lead to amino acid changes associated with established or suspected phenotypic implications; AND has been identified to cause community transmission/multiple COVID-19 case clusters, or has been detected in multiple countries;</p> <p>OR</p> <p>is otherwise assessed to be a VOI by WHO in consultation with the WHO SARS-CoV-2 Virus Evolution Working Group (VEWG).</p>	<p>Member States:</p> <ul style="list-style-type: none"> ● Inform WHO of VOI-associated cases (person, place, time, clinical and other relevant characteristics) through established WHO Country Office and Regional Office channels/networks ● Submit full genome sequences and metadata to public database ● Perform field investigations to improve understanding of the potential impacts of the VOI (epidemiology, severity, effectiveness of countermeasures, or other relevant characteristics) <hr/> <p>WHO:</p> <ul style="list-style-type: none"> ● Assessment by WHO SARS-CoV-2 VEWG. If meets criteria, designation as VOI ● If determined necessary, coordinate lab investigations with Member States and partners ● Monitor global spread of VOI

Table 2: Variants of concern – Working definition and actions:

Definition	Actions for potential VOCs
<p>A VOI (as defined in Table 1) that, through a comparative assessment, has been demonstrated to be associated with:</p> <ul style="list-style-type: none"> ● Increase in transmissibility or change in the epidemiology; ● Increase in virulence or change in disease presentation; OR ● Decrease in effectiveness of available diagnostics, vaccines, therapeutics, or public health and social measures. 	<p>Member States, if a VOC is identified:</p> <ul style="list-style-type: none"> ● Report initial cases/clusters to WHO through IHR mechanism. ● Submit complete genome sequences and associated metadata to a publicly available database. ● Where capacity exists and in coordination with the international community, perform field investigations to improve understand of the potential impacts of the VOC on COVID-19 epidemiology, severity, effectiveness of countermeasures, or other relevant characteristics. ● Perform laboratory assessments on the impact of the VOC on diagnostic methods, immune responses, antibody neutralization or other relevant characteristics, when such lab capacity is available. <hr/> <p>WHO, for a potential VOC:</p> <ul style="list-style-type: none"> ● Assessment against global risk, and if meets criteria, designation as VOC. ● Assessment by VEWG and, if determined necessary, coordinate lab investigations with Member States and Partners. ● Conduct rapid risk assessment as warranted. ● Communicate new designations and findings to Member States and public ● Evaluate WHO guidance and update, if necessary.

1.2 Status of assessment of mutations, VOI and VOC in terms of understanding transmissibility, severity and potential impact on countermeasures

Drs Frank Konings (WHO/WHE) and **Volker Thiel (University of Bern)** provided overviews of global efforts to monitor and characterize SARS-CoV-2 mutations.

At the start of the COVID-19 pandemic, WHO organized the COVID-19 reference laboratory network, which consists of 26 laboratories across the world. Building from this network, WHO also established the VEWG, which consists of 16 experts from 13 institutions representing expertise in sequencing, bioinformatics, and in vitro and in vivo studies. The VEWG specifically focuses on:

1. Identification and prioritization of relevant mutations;
2. Monitor potential impact on viral characteristics (e.g., in virulence, transmission) and countermeasures (e.g., diagnostics, vaccines, therapeutics);
3. Research the impact of specific mutations – including technical discussions and coordination among peers; laboratory in vitro and in vivo studies;
4. Contribute to the evaluation of possible mitigation strategies to reduce the negative impact of mutations; and
5. Provide scientific advice regarding classification of variants as VOI or VOC.

The VEWG is the forum for describing the genetic make-up of variants, including virus evolution, assigning virus lineages/clades, and identification of mutations. The steps for investigating and characterizing mutations among the VEWG include identification and prioritization of mutations, cloning of mutations, in vitro evaluation, and in vivo evaluation.

A coordinated and standardized approach to laboratory investigations is essential for WHO and external partners so that comparable results can be generated and triggers for action can be established. Increasing sequencing capacities in a strategic way is important for informing the work of the VEWG and others to better understand the evolution of SARS-CoV-2. There are a series of experiments required to investigate the impact of mutations on virus properties and countermeasures. They feed into broader risk assessments that include epidemiological and clinical findings. These experiments take time, coordination, and sharing. As the impact of mutations is better understood, the approach to SARS-CoV-2 variants may become more predictive.

1.3 How WHO assesses knowledge and knowledge gaps and develops advice and guidance

Drs Janet Diaz (WHO/WHE) and **April Baller (WHO/WHE)** provided an overview of WHO's processes for assessing knowledge and knowledge gaps and developing advice and guidance with respect to clinical management and infection prevention and control and the impact of VOCs.

WHO works with various external experts and groups, including the Strategic and Technical Advisory Group for Infectious Hazards (STAG-IH), Guideline Development Groups (GDGs), including those for clinical management and IPC, and other technical advisory bodies, to critically review, synthesize, and appraise available evidence and formulate recommendations. This ongoing process leads to the dynamic publication and update of living guidance and information products.

Regarding the impact of VOCs on clinical management, as of 29 March 2021, there had been no changes in WHO's recommendations for supportive care interventions (e.g., screening, triage, testing, and oxygen), repurposed antivirals, immunomodulators (e.g., anti-inflammatories, steroids), and anticoagulation. For monoclonal antibodies, WHO does not currently have recommendations for the use of these therapeutics, but the next steps include: 1. await randomized control trials full study results, 2. complete grading of evidence, 3. concurrently perform systematic review of in vitro/ in vivo studies of neutralization for variant substitutions, 4. add more experts on VOCs to review panel, and 5. present totality of evidence to the WHO GDG for Clinical Management of COVID-19.

WHO has developed and updated 14 technical guidance documents dedicated to IPC.² Regarding VOCs, the WHO COVID-19 Infection Prevention and Control GDG advises WHO on revising, if needed, any aspect of current guidance on infection prevention and control and public health and social measures in the context of COVID-19. Based on the available evidence on the epidemiology and transmission of VOCs, as of 29 March 2021, there had been no additional changes in infection prevention and control and public health and social measures guidance. Instead, the Infection Prevention and Control GDG recommended that countries continue to support a comprehensive overall COVID-19 response, including a focus on improving adherence to public health and social measures.

² The IPC technical guidance can be accessed at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/infection-prevention-and-control/>.

Session 2:

Framework for Evidence on the SARS-CoV-2 Variants

2.1 Experience from influenza: vaccine virus selection system and risk assessment framework

Drs John McCauley (WHO Influenza Collaborating Centre, UK) and **Richard Webby (WHO Influenza Collaborating Centre, US)** provided overviews of the selection of prototype influenza vaccine viruses and the integration of the WHO TIPRA into pre-pandemic risk assessment as models for the response to SARS-CoV-2 variants.

When looking to monitoring VOCs and assessing their impact, influenza provides a model for establishing a global risk assessment and monitoring framework. Influenza circulation is largely global, and circulation is not always homogeneous; new influenza virus variants do rapidly emerge, and the Global Influenza Surveillance and Response System, a global network of laboratories, including National Influenza Centres and Collaborating Centres, is constantly monitoring the situation and rapidly, timely, and open sharing clinical samples, viruses, and genetic sequence data. Twice a year, WHO makes recommendations on the composition for trivalent and quadrivalent egg-, cell-, and recombinant-based seasonal influenza vaccines. The recommendation for each component of the vaccine is guided by two questions: Are there new viruses in circulation? Is the current vaccine the best that is available? For the first question, new viruses are assessed to see if they are antigenically different from those viruses seen previously. The viruses are assessed by post-infection ferret antisera and post-vaccination human sera, and if the new virus is antigenically different, a new vaccine recommendation is likely. For the second question, vaccine effectiveness studies are conducted by independent groups around the

world, including through the Global Influenza Vaccine Effectiveness Network, to look at past performance of the vaccine. There are similarities in the problems faced between COVID-19 and SARS-CoV-2 and influenza and influenza viruses, including: the use of genetic sequence data to detect and monitor variants; the need for viruses and reagents for antigenic characterization; the need for predictive models; vaccine effectiveness studies to inform vaccine performance; and an established framework of collaborators, including the scientific community, industry, and regulators, with recognized responsibilities.

In addition to the process for selecting prototype vaccine viruses, the development and use of the WHO TIPRA can inform the global risk monitoring and assessment framework for SARS-CoV-2 VOCs. The TIPRA is part of a comprehensive package for influenza assessments and supports a timely and updatable hazard risk assessment for influenza viruses with pandemic potential. Additionally, the TIPRA helps identify knowledge gaps, prompts further investigations for research and surveillance, facilitates information sharing, and helps identify and prioritize viruses for human vaccine seed development and testing. The TIPRA is built on nine expert-defined elements: human infection, disease severity, population immunity, geographical distribution in animals, infection in animals, receptor binding properties, transmission in animal models, susceptibility to antiviral treatment, and genomic characterization. While the TIPRA is designed for pre-pandemic purposes, it does provide considerations for a SARS-CoV-2 framework: WHO is the overall convener for conducting a TIPRA exercise; such an exercise requires a sustained period of expert input and communications; a diverse array of data inputs is required along with an understanding of how these data impact risk.

2.2 Building a framework of evidence for the monitoring and assessment of vaccines in the context of SARS-CoV-2 variants

Dr Philip Krause (US FDA) provided an overview of the considerations for building a framework of evidence for the monitoring and assessment of COVID-19 vaccines and the potential process to inform COVID-19 vaccine design.

The overall process for monitoring and assessment of vaccines in the context of SARS-CoV-2 variants is comprised of three main steps: 1. evaluate existing vaccines against VOCs to determine if a new antigen is needed, 2. decide what the new antigen should be, and 3. evaluate modified and new vaccines efficacy against VOCs.

Deciding if a new antigen is needed should consider epidemiology and virology of the VOCs, predicted loss of protection with existing vaccine antigen (i.e., it may be unacceptable to wait for actual loss of protection before investigating new antigens), potential for better protection from the new antigen, and effect on vaccination programmes (i.e., if the previous vaccine can be replaced with a new one). The totality of available evidence that can inform decisions. Potential data sources include epidemiological data (including variant-specific data), molecular and immunological studies (which have roles in predicting loss of effectiveness and selecting new antigens), animal studies, and clinical endpoint studies (including randomized and observational studies).

When evaluating existing vaccines' efficacy against variants, study endpoints (e.g., severe disease versus mild disease) should be considered, vaccine schedules can be randomized during deployment, and observational studies can be performed to estimate variant-specific vaccine effectiveness. When deciding what a new antigen should be, it is important to consider if the antigen can cover multiple emerging variants as well as those predicted to emerge.

For the evaluation of modified vaccines against variants, regulators have defined immunogenicity-based approaches, potentially with support from animal models, and have made recommendations for safety data. For evaluating new vaccines against variants, ideally this would be done in randomized placebo or active control trials (or hybrid) with clinical endpoints plus preclinical and phase 1-2 data. If supported by additional data, immunogenicity bridging could be considered.

To inform the overall process, WHO is working globally to reduce duplication; improve accuracy, efficiency, and reliability; and provide access and tools to analyse data through a global data repository on vaccines and variants. The repository will equip decision-makers with clear, timely information, and insights.

WHO is proposing a process to inform COVID-19 vaccines design and evaluation leveraging the expertise of a multidisciplinary, independent group of experts to develop recommendations. WHO will facilitate the global response, including research methods and evidence needs, the establishment of a global data repository, the composition for modified or new vaccines (if needed), and regulatory convergence.

Dr Kanta Subbarao (WHO Influenza Collaborating Centre, Australia) led a structured debate with nine experts on the development of the framework of evidence for the monitoring and assessment of vaccines in the context of SARS-CoV-2 variants. The experts included: **Dr Jakob Kramer (CEPI)**, **Dr Paul Fine (LSHTM, UK)**, **Dr Thomas Fleming (Univ of Washington, USA)**, **Dr Alan Khoo (International Medical Univ, Malaysia)**, **Dr Ira Longini (Univ of Florida, USA)**, **Dr Cesar Muñoz-Fontela (WHO)**, **Dr Richard Neher (Univ of Basel, Switzerland)**, **Dr Jerome Singh (Univ of KwaZulu-Natal, South Africa)**, and **Dr David Wentworth (CDC, USA)**. Some of the expert opinions included:

- Despite evidence that current vaccines are effective against severe disease and death, new vaccines may be pursued to help address the pandemic and emerging variants, but more data will be needed to inform the decisions.
- Secondary vaccine failures are occurring and need to be closely monitored. Observational studies, including test-negative designs and prospective and retrospective cohort studies, will be useful for providing the evidence to inform decision-making. It is important that this evidence be brought together, such as through the proposed global data repository, to inform decision-making.
- Rather than deciding if a change in antigen is needed, it may be important to consider what variant vaccine could be applied in different parts of the world should there be variability in the distribution of variants that could be evidenced.
- When thinking of the threshold of evidence for triggering changes, there needs to be greater understanding of correlates of protection and where

results are coming from (e.g., effectiveness data, interim data, final clinical trial data).

- It will be important that any next generation of COVID-19 vaccines, which may be based on various VOCs, be tested and used in the areas where those VOCs are dominant.
- Several points should be considered when thinking through vaccine reformulation, including significant reduction of virus neutralization and other antibody functions, changes in immunodominant epitopes, loss of protection against disease in animal models, and loss of effectiveness of blocking transmission.

Session 3:

Impact on Public Health Decision-Making

3.1 Interplay between vaccine supply, vaccine performance, and emergence of SARS-CoV-2 variants

COVID-19 vaccine supply rollout, equity and pace

Dr Soumya Swaminathan (WHO/SCI) provided the landscape for COVID-19 vaccine supply rollout, equity, and pace. COVID-19 vaccine supply is highly dynamic and unequal. However, the situation is very complex with wide variations in vaccine distribution and coverage around the world, based on the economic status of countries and also their manufacturing capacities. Additionally, the public health impact of VOCs – which is likely to vary by product – is most likely going to be inequitably felt, as well as the ability for countries to pivot manufacturing capacities, or book doses of new or modified vaccines in advance. This is one of the reasons why the COVAX Facility – which had already delivered over 33 million vaccine doses in more than 69 participants as of 29 March 2021 – is of critical importance to ensure that the right vaccines are allocated throughout the world.

Evolution of SARS-CoV-2 and considerations for vaccination

Dr Sarah Cobey (University of Chicago) provided an overview of the evolution of SARS-CoV-2 and considerations for vaccination. Like all pathogens, SARS-CoV-2 faces strong evolutionary selective pressures that enhance transmission and increase fitness, including escape from immune responses. Vaccine induced immunity can accelerate the evolution of immune escape. However, it will probably not be the case for partially effective, or “imperfect”, COVID-19 vaccines because within-host selection for SARS-CoV-2, which leads to the generation and amplification of new variants, looks to be inefficient since most transmissions occur a few days after infection and before strong adaptive immune responses.

Based on the above rationale, the argument was made that a widespread administration of a single dose and the detriment of a timely administration of the second dose would be of public health benefit. Imperfect vaccination will probably not accelerate immune escape because within-host selection is inefficient, and reduced transmission from higher vaccination coverage should slow the rate of adaptation. Hence, vaccinating to minimize the global incidence of SARS-CoV-2 could slow the evolution of the virus and prolong the usefulness of current vaccines.

Vaccines & VOC: evidence availability & policy perspectives

Dr Annelies Wilder-Smith (WHO/IVB) provided an overview of the available evidence and policy perspectives in relation to COVID-19 vaccines and SARS-CoV-2 variants.

A COVID-19 vaccine working group has been established within the Strategic Advisory Group of Experts on Immunization (SAGE) to provide evidence-based vaccination policy recommendations for COVID-19. The quantity and quality of evidence is appraised and documented by SAGE in its policy recommendations. However, despite the growing body of evidence on COVID-19 vaccine performance, data on the impact of VOCs on vaccine performance is still scarce, particularly for clinical infection and severe illness. To limit variability across studies, there is a need for better standardized protocols (for studies in both human and animal models), case definitions, clinical endpoints, and assays including for humoral and cellular immunity. As standards such as those developed through the R&D Blueprint are already available, it is now important to implement them in studies so that comparisons can be made, and differences can be assessed.

Overall, there is an urgent need for generating better and more comprehensive evidence based on each of the VOCs across disease, infection, immunogenicity, and vaccines to build policy recommendations on more robust data, and to equip countries with means for decision-making. To foster the development of policies to maximize the impact of vaccination strategies in light of VOCs, SAGE will focus on key questions:

- What evidence and framework should be used for assessing data on VOCs and vaccine recommendations?
- What degree of performance reduction should influence policy?
- Should vaccine access and alternatives be a consideration in policy recommendations?
- What research is needed (by product, by VOC, for disease and asymptomatic infection outcomes)?

3.2 Perspectives from regulators and developers

An important consideration, as various scenarios are considered to address the potential impact of SARS CoV-2 variants on COVID-19 vaccines, is to understand the perspectives from both regulators and product developers. Regulatory perspectives were summarized by **Dr Phil Krause (US FDA)**, with commentaries from **Drs B Semete (South Africa Health Products Regulatory Agency)** and **VG Somani (CDSCO, India)**. A perspective from developers was provided by **Dr Adam Hacker (CEPI)**.

Regulators have rapidly developed guidance on evaluation of changes, if needed, to COVID-19 vaccines with established vaccine efficacy. As of 29 March 2021, the US Food and Drug Administration (FDA), the European Medicines Agency (EMA) and the ACCESS consortium (Australia, Canada, Singapore, Switzerland, UK) had published guidance on regulatory evaluation of modified vaccines, and WHO has published guidance for prequalification /emergency use listing assessments. There is a high level of alignment between regulators on key features for situations where an existing parent vaccine has been granted marketing authorization and where a near identical manufacturing process (except for antigens), with reliance on original control strategy, will be used for the modified vaccine. New non-clinical data may not be required to support testing of the modified vaccine. Appropriate manufacturing data however will be needed to support/confirm consistency for critical quality attributes, and stability. For a vaccine

with established clinical efficacy, neutralizing immune responses may be used to bridge responses from the original efficacy trials to the modified vaccine. Safety and other immune responses should also be studied. The primary immunization series will need to be tested, as well as the effect of a booster dose. Immune responses with modified vaccines will likely need to be evaluated against several different SARS CoV-2 variants, as well as the original virus against which the parent vaccine was developed.

An additional consideration is that loss of neutralizing responses to vaccine antigens may not necessarily mean there is loss of clinical efficacy, especially against severe disease. To assist interpretation of such data, the need for standards to enable comparisons of the immune responses to COVID-19 vaccines and for standard protocols for studies in animal models was stressed. There will also be an important role for post-authorization studies on vaccine effectiveness, and here too guidance on standard protocols will be valuable.

Current regulatory guidance doesn't address authorization of completely new vaccines against variants. As reliable information on vaccine safety and efficacy will be needed to support confidence in such vaccines, randomized clinical endpoint strategies are likely to be required to allow direct evaluation of vaccine protection against variants. Regulators have not proposed immunogenicity-based strategies in this setting. It was recognized that there is a need for additional guidance from regulators for new COVID-19 vaccines that, without compromising the quality of regulatory reviews, enables timely regulatory decision-making, as has been achieved so far.

From a developer's perspective, speed is critical. Vaccine development in 300 days, as happened with COVID-19 vaccines, was unprecedented but needs to be further accelerated if control of the disease is to be achieved. The infrastructure and decision-making that is in place to determine influenza vaccine strain changes provides an important model. Whilst it is acknowledged that there are differences between seasonal influenza and COVID-19, not least that COVID-19 is rapidly evolving and the epidemiology of the infection is not yet well understood, the rapid declaration of a VOC will considerably accelerate the development process.

However, an analysis of the critical steps in the development and evaluation of modified COVID-19 vaccines found that for a vaccine targeting the new variant to rapidly enter the clinic and generate data to support authorization based on the new regulatory

guidance, development needs to be initiated at risk even before a VOC is declared. Real-time surveillance and analytics with continuous sharing of information regarding VOI and VOC with developers is a solution that will enable developers to initiate work at risk well before a VOC is declared.

Developers were urged to be ready to progress to obtain final data and registration as soon as a VOC is declared. Regulators were encouraged to continue to rapidly review submissions and, as data emerge, establish further guidance to leverage evolving knowledge. In the longer term, and by analogy with the influenza vaccine strain change model, progress toward elimination of clinical requirements could be foreseen when more is understood about the development and evaluation of COVID-19 vaccines.

3.3 Impact on public health decision-making

Drs David Heymann (Chair, STAG-IH) and **Alejandro Cravioto (Chair, SAGE)** provided their perspectives on the impact of SARS-CoV-2 variants on public health decision-making.

The global community faces five critical challenges to understand the complexity of the COVID-19 pandemic and design the way forward in making better recommendations:

- Fill the gaps in knowledge by getting technologies and training, particularly on genetic sequencing, to people working in laboratories around the world. This would allow us to set up a global system to generate vital information and data.
- Ensure standardization of research and information, including for naming the VOCs, so that the global community as a whole “speak the same language” for better collaboration and coordination.
- Transfer the flow of information to regulators and developers in a swift manner.
- Ensure continued equitable access to vaccines through specific mechanisms such as the COVAX Facility.
- Pull together stakeholders to develop a coordinated framework for diagnostic, therapeutics, and vaccines with clear standards roles and responsibilities – including for recommending changes in vaccine composition – to monitor and assess the impact of the VOCs on public health interventions.

The world must pull together and address these critical issues. SAGE and STAG-IH will work to ensure close relationship between WHO Departments working on COVID-19, notably by developing a framework for policy decision for SARS-CoV-2 variants to have clear information channel with researchers, regulators, and developers, and foster better evidence generation for policy recommendations.

At the same time, the goal is that other stakeholders involved in the current pandemic preparedness and response worldwide will link with this network within WHO to create one global network, and provide urgent information necessary to address SARS-CoV-2.

Conclusion

COVID-19 is a new disease that calls for new frameworks and new ways of thinking, including for decision-making. By bringing the relevant stakeholders around the table, this global consultation was the first step to ensure timely sharing of information on SARS CoV-2 variants and their impact on public health interventions, including with Member States, regulators, and developers. WHO will continue to work with its partners to refine the global risk monitoring and assessment framework for SARS-CoV-2 variants to ensure that processes, roles, and responsibilities are well-defined.

There is an urgent need to increase communication among the global community to ensure that we move at the same pace and as fast as possible and, above all, increase communication for the public to establish and maintain trust in evidence and decisions-makers.

Annex 1:

Consultation Agenda

Chair: Sylvie Briand

TIME	TOPIC	SPEAKERS
13:00-13:05	Opening remarks	Mike Ryan
13:05-13:10	WHO framework for monitoring & assessing SARS-CoV-2 variants	Sylvie Briand
SESSION 1: FOCUS ON SARS-COV-2 VARIANTS		
13:10-13:55	Epi update on SARS-CoV-2 variants of concern Status of assessment of mutations, VOI and VOC in terms of understanding transmissibility, severity and potential impact on countermeasures How WHO assesses knowledge and knowledge gaps and develops advice and guidance <i>Moderator: Maria Van Kerkhovea</i>	Boris Pavlin Frank Konings Volker Thiel Janet Diaz April Baller
13:55-14:00	Break	
SESSION 2: FRAMEWORK OF EVIDENCE FOR THE SARS-COV-2 VARIANTS		
14:00-14:20	Experience from influenza: vaccine virus selection system and risk assessment framework <i>Moderator: Wenqing Zhang</i>	John McCauley Richard Webby
14:20-14:40	Building a framework of evidence for the monitoring and assessment of vaccines in the context of SARS-CoV-2 variants <i>Moderator: Ana Maria Henao Restrepo</i>	Philip Krause
14:40-15:00	Structured Debate introduced by Ana Maria Henao Restrepo <i>Moderator: Kanta Subbarao</i>	Jakob Cramer Paul Fine Thomas Fleming Alan Khoo Ira Longini Cesar Muñoz-Fontela Richard Neher Jerome Singh David Wentworth
15:00-15:05	Break	
SESSION 3: IMPACT ON PUBLIC HEALTH DECISION-MAKING		
15:05-15:35	Interplay between vaccine supply, vaccine performance, and emergence of SARS-CoV-2 variants <i>Moderator: Katherine O'Brien</i>	Soumya Swaminathan Sarah Cobey Annelies Wilder-Smith
15:35-16:00	Perspectives from regulators and developers <i>Moderator: Rogerio Gaspar</i>	Philip Krause Adam Hacker Boitumelo Semete VG Somani
16:00-16:20	Impact on public health decision-making	David Heymann Alejandro Cravioto
16:20-16:30	Conclusion and next steps	Sylvie Briand

Annex 2:

List of Speakers and Moderators

Dr April Baller

Medical Officer
Infection Prevention and Control
World Health Organization

Dr Sylvie Briand

Director
Department of Global Infectious Hazards Preparedness
World Health Organization

Dr Sarah Cobey

Associate Professor of Ecology and Evolution
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Dr Jakob Cramer

Head of Clinical Development
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Dr Alejandro Cravioto

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WHO Strategic Advisory Group of Experts on
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Dr Janet Diaz

Lead
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Health Care Readiness
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Dr Paul Fine

Professor of Communicable Disease Epidemiology
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Dr Thomas Fleming

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Executive Director
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