



## Key Messages

As addressed by Dr Tedros at the opening of the World Health Assembly on 24<sup>th</sup> May, all Member States are asked to support to vaccinate at least 10% of the population of every country by September and a “Drive to December” to achieve WHO’s goal of vaccinating at least 40% by the end of the year, followed by 70% by the middle of next year.

As of 28<sup>th</sup> June, over 2.928 billion vaccine doses have been administered world wide and about 66 countries and territories have fully vaccinated more than 10% of their populations. COVAX has shipped 89.4 million doses to 133 participants, but that covers just nearly 1% of their combined population and 5 countries and territories have not yet started their vaccination programme. Much more support is needed for 250 million people in low- and middle-income countries in the next four months.

With the Delta variant spreading to 98 countries as of 2<sup>nd</sup> July, Dr Tedros recommended “two ways for countries to push back against new surges. First, public health and social measures. Second, the world must equitably share protective gear, oxygen, tests, treatments and vaccines” at the Press Briefing on 2<sup>nd</sup> July.

## Highlights and main issues

- A WHO consultation heard that while current SARS CoV-2 variants of concern (VOCs) show antigenic distance from vaccine immunogens, the current vaccines are still effective at protecting against severe disease and hospitalization.
- A newly formed WHO Technical Advisory Group on vaccine composition (TAG-COVAC) will monitor vaccine effectiveness, review evidence as it becomes available, and provide recommendations on vaccine modifications, if needed.
- WHO and its COVAX partners are working with a South African consortium comprising Biovac, Afrigen Biologics and Vaccines, a network of universities and the Africa Centres for Disease Control and Prevention (CDC) to establish its first COVID mRNA vaccine technology transfer hub.
- Strengthening regulatory capacity was agreed as an essential component of any plans to strengthen local production at the first ever World Local Production Forum, which convened countries, partners and other stakeholders to discuss strategies to promote local production to improve access to health products during the current pandemic and beyond.
- Observations of working stocks of SARS-CoV-2 suggest that sequential propagation in Vero cells leads to critical changes in the region of the furin cleavage site, which significantly reduce the value of the working stock for critical research studies. A recent WHO publication provides guidance on mitigation of this risk.
- WHO held a technical symposium on COVID-19 vaccine supply chain and Regulatory Transparency to identify lessons learned and explore potential solutions to overcome

bottlenecks

- A WHO Webinar was held on 29<sup>th</sup> June 2021 in order to present and explain the main principles of the WHO Good Regulatory Practices and WHO Good Reliance Practices, one of the key principles of efficient and effective regulatory system. Reliance concept has been successfully applied for regulatory authorization of COVID-19 vaccines in many of non-vaccine producing countries.

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## Virus variants

### Four major priorities for the global response to variants of concern

As new variants of concern emerge and spread quickly, the modification of sequences targeted by a vaccine require careful and coordinated actions. Vaccine development, vaccine modification, and vaccine deployment should be viewed as international enterprises, with international coordination by the WHO helping benefits to accrue throughout the world.

Decision making about which antigens should be included in vaccines against SARS-CoV-2 will need to involve epidemiologic data, data from evolutionary biology, and clinical, animal, and in vitro data that are pertinent to immune responses and to continued vaccine efficacy in the face of changing viral sequences and the possible waning of vaccine-induced immunity. Meeting these challenges efficiently will require enhanced surveillance with continued sharing of data (including viral sequences and corresponding antigens that are linked to clinical and epidemiologic information) and samples (including new viral variant isolates and serum samples obtained from vaccinated persons). It will also require the use of standardized reference reagents and models to evaluate viruses and modified vaccines.

With collaborative, open discussion of results, this data sharing will help foster consistent and thoughtful public communications about new variants and help maintain appropriate confidence in vaccines and in the processes used to develop, test, and deploy them.

On the basis of WHO consultations held since the early 2021, four major vaccine-related priorities for WHO to help the global control SARS CoV-2 virus variants have been identified and published. These are to:

- Determine whether existing vaccines are losing efficacy against variants,
- Decide whether modified or new vaccines are warranted to restore efficacy against variants,
- Reduce the likelihood that variants of concern will emerge, and
- Coordinate international research and the response to new variants, both in general and in relation to vaccines

These priorities have informed the global response to SARS CoV-2 variants that is being coordinated by WHO.

SARS-CoV-2 Variants and Vaccines ([NEJM, 23 Jun 2021](#))

### 2<sup>nd</sup> WHO Global Consultation on SARS-CoV-2 VOC

On 10<sup>th</sup> June, WHO convened a second Global Consultation on SARS-CoV-2 Variants of Concern

(VOCs) and their Impact on Public Health Interventions, as part of its efforts to coordinate the global response to SARS-CoV-2. Global stakeholders came together to present the existing evidence on VOCs, review information needs and decision-making processes, and outline potential decision-making processes for modifying COVID-19 vaccine composition.

According to experts, continued SARS-CoV-2 evolution is expected and requires strengthening epidemiological and genomic surveillance. In response, the WHO SARS-CoV-2 Virus Evolution Working Group (VEWG), which is in the process of being formalized as the Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE), was established to monitor new mutations and variants, assess their potential public health impact, and rapidly identify and coordinate the filling of research gaps related to transmissibility, severity and neutralization of specific mutations and variants.

In addition to increased transmissibility, SARS-CoV-2 evolution may result in changes that allow for increased disease severity, escape from immune responses, decreased effectiveness of antiviral treatment or infection in a new animal host. While current VOCs show antigenic distance from vaccine immunogens (the part of the virus gene that the vaccines targets), the current vaccines are still effective at protecting against severe disease and hospitalization. Experience from multiple countries with extensive transmission of the four VOCs has demonstrated that proven public health and social measures (PHSM), including infection prevention and control (IPC) measures in health facilities, remain effective in controlling VOCs and VOIs.

As several vaccines are in use and under development, coordinated decision-making on vaccine modification and administration is required. A newly-formed Technical Advisory Group on vaccine composition (TAG-CO-VAC) will review available evidence and provide recommendations on vaccine modifications if needed; specific considerations include appropriate antigen selection for broad protection, using broadly protective variant-specific vaccines in non-immune individuals, and balanced timing of booster vaccinations to ensure continued efficacy while avoiding extra vaccination if previous vaccination is still protective.

From the perspective of vaccine regulators and 11 vaccine developers that shared their plans during the consultation, there is ongoing work to assess the need to boost current vaccines. If/when this becomes necessary, it will be important that the regulatory community continues to work collaboratively. Moreover, whichever strategy is used (a booster dose of prototype vaccines or a variant-specific vaccine), should induce broad protection. Given the differential prevalence of variants, vaccine availability and vaccination rates, implementation of a 'mix and match' vaccination approach may be necessary.

Summary of the Global Consultation ([Weekly Epidemiological Update, 22 Jun 2021](#))

[Recording](#) (passcode: m#t9b!TI)

## Epidemiological Update

WHO, in collaboration with national authorities, institutions and researchers, routinely assesses if variants of SARS-CoV-2 result in changes in transmissibility, clinical presentation and severity, or if they result in changes in public health and social measures (PHSM) implementation by national health authorities. Systems have been established to detect "signals" of potential VOCs or VOIs and assess these based on the risk posed to global public health.

In the past week, the number of new COVID-19 cases remained similar to the previous week, and the number of new deaths continued to decrease, with over 2.6 million new cases and 57'000 new deaths reported globally. This is the lowest weekly mortality figure since those recorded in early November 2020. Globally, COVID-19 incidence remains very high, with an average of over 370'000 cases reported each day over the past week. The cumulative number of cases reported globally now exceeds now 180 million and the number of global deaths is almost 4 million.

This week, the African region recorded a sharp increase in incidence (33%) and mortality (42%) when compared to the previous week. All Regions, with the exception of the African Region,

reported a decline in the number of new deaths in the past week.

In this edition, a special focus update on the variants is provided, along with the geographical distribution of VOCs Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1) and Delta (B.1.617.2). This edition also includes an overview of current challenges in the context of the COVID-19 pandemic, as well as a summary of the WHO global conference on communicating science during health emergencies.

[The latest epidemiological update](#) (29 Jun 2021)

## Summary of phenotypic impacts of VOCs

WHO publishes generalized findings on the phenotypic impacts of VOCs as compared to previously / co-circulating variants. These findings are based on emerging evidence, including non-peer-reviewed preprint articles and reports, and all subject to ongoing investigation and revision. The findings cover transmissibility; diseases severity; risk of reinfection; impacts on diagnostics; impacts on vaccine efficacy / effectiveness; and impacts, disaggregated by each vaccine, on neutralization capacity induced by full immunization.

[Weekly Epidemiological Update](#) (22 Jun 2021)

## VOI – Lambda (lineage C.37)

On 14 June 2021, a variant assigned to Pango lineage C.37, GISAID clade GR/452Q.V1, NextStrain clade 20D, was designated as a global VOI, and assigned the WHO label “Lambda”. This variant has been monitored as an alert for an extended period, and upon more information and updated assessments, is now considered as meeting the VOI working definition based upon evidence of continued emergence and suspected phenotypic implications.

Lambda has been associated with substantive rates of community transmission in multiple countries, with rising prevalence over time concurrent with increased COVID-19 incidence. The earliest sequenced samples were reported from Peru in August 2020.

Lambda carries a number of mutations with suspected phenotypic implications, such as a potential increased transmissibility or possible increased resistance to neutralizing antibodies. It is characterized by mutations in the spike protein, including G75V, T76I, del247/253, L452Q, F490S, D614G and T859N; however, there is currently limited evidence on the full extent of the impact associated with these genomic changes, and further robust studies into the phenotypic impacts are needed to better understand the impact on countermeasures and to control the spread.

[Weekly Epidemiological Update](#) (15 Jun 2021)

## COVAX

[COVAX](#), the vaccines pillar of the ACT-Accelerator, is convened by [CEPI](#), [GAVI](#) and [WHO](#), with the ambition of contracting enough volumes to equitably deliver 2 billion doses of safe, effective and quality vaccines by the end of 2021. Vaccines included in the [COVAX Facility](#) portfolio have been selected from the COVAX R&D portfolio and other clinical candidates.

## First COVID mRNA vaccine technology transfer hub

WHO and its COVAX partners are working with a South African consortium comprising Biovac, Afrigen Biologics and Vaccines, a network of universities and the Africa Centres for Disease Control and Prevention (CDC) to establish its first COVID mRNA vaccine technology transfer hub.

Technology transfer hubs are training facilities where the technology is established at industrial scale and clinical development performed. Interested manufacturers from low- and middle-income countries can receive training and any necessary licenses to the technology. WHO and partners

will bring in the production know-how, quality control and necessary licenses to a single entity to facilitate a broad and rapid technology transfer to multiple recipients. The technology transfer hub will benefit from the Medicines Patent Pool's (MPP's) experience of intellectual property (IP) management and issuing of IP licenses. MPP is also assisting WHO to negotiate with technical partners and supporting in the governance of the hubs.

WHO's April call for expressions of interest has so far generated 28 offers to either provide technology for mRNA vaccines or to host a technology hub or both. There have been 25 expressions of interest from low- and middle-income country respondents who could receive the technology to produce mRNA vaccines. Over the coming weeks, WHO will continue the rolling evaluation of other proposals and identify additional hubs, as needed, to contribute to health security and equity in all regions. Through the COVAX partnership, WHO will continue its assessment of potential mRNA technology donors and will launch subsequent calls for other technologies, such as viral vectors and proteins, in coming months.

[WHO supporting South African consortium to establish first COVID mRNA vaccine technology transfer hub](#) (21 Jun 2021)

## **G7 pledge of 870 million COVID-19 vaccine doses**

In a landmark agreement at the G7 summit, held in Cornwall, the United Kingdom of Great Britain and Northern Ireland, global leaders have pledged to share COVID-19 vaccine doses internationally, in support of global equitable access and to help end the acute phase of the pandemic. The G7 countries committed to share at least 870 million doses of COVID-19 vaccines directly, with the aim to deliver at least half by the end of 2021. They also reaffirmed their support for COVAX as “the primary route for providing vaccines to the poorest countries.”

COVAX will work with the G7 and other countries that have stepped up to share doses as rapidly and equitably as possible. This will help address short-term supply constraints currently impacting the global response to COVID-19 and minimize the prospect of future deadly variants.

[G7 announces pledges of 870 million COVID-19 vaccine doses, of which at least half to be delivered by the end of 2021](#) (13 Jun 2021)

## **WHO's other COVID-19-related work**

### **Access to medical technologies worldwide to tackle the COVID-19 pandemic**

The Directors General of WHO, WIPO and the WTO have agreed to enhance and focus support in the context of the pandemic through two specific initiatives.

First, the three agencies will collaborate on the organization of practical, capacity-building workshops to enhance the flow of updated information on current developments in the pandemic and responses to achieve equitable access to COVID-19 health technologies. The aim of these workshops will be to strengthen the capacity of policymakers and experts in member governments to address the pandemic accordingly. The first workshop in the series will be a workshop on technology transfer and licensing, scheduled for September. The workshop will help our members update their knowledge and understanding of how intellectual property, know-how and technology transfer work in practice.

Secondly, the agencies will implement a joint platform for tripartite technical assistance to countries relating to their needs for COVID-19 medical technologies, providing a one-stop shop that will make available the full range of expertise on access, IP and trade matters provided by the organizations, and other partners, in a coordinated and systematic manner.

[Directors General of WHO, WIPO and the WTO agree on intensified cooperation in support of access to medical technologies worldwide to tackle the COVID-19 pandemic](#) (24 Jun 2021)

## The WHO BioHub System for Preparedness and Response

A proposed WHO BioHub System will allow Member States to share biological materials with epidemic or pandemic potential (BMEPP) on a voluntary basis with one of the trusted WHO BioHub Facilities under pre-agreed conditions.

The COVID-19 pandemic, along with other recent outbreaks and epidemics, has underscored the importance of rapid and broad sharing of emerging pathogens for effective characterization, surveillance, and the timely development of diagnostic products, devices, therapeutics, and vaccines. Currently, a great deal of pathogen sharing is done bilaterally and on an *ad hoc* basis. However, this process – which is often slow – is leaving some countries behind and may not be sufficient to address the global needs that are arising during acute disease outbreaks.

It is proposed to use a stepwise, phased approach to build the new System. Given the appearance of several variants of SARS-CoV-2, and following proposals from several WHO Member States, the first WHO BioHub Facility will be set up in 2021 to receive, store, grow, sequence, and share SARS-CoV-2 BMEPP. The first pilot phase will allow the rapid operationalization of the WHO BioHub System. Subsequently, in a second phase, the aim will be to expand the scope and user base of the WHO BioHub System to other pathogens and commercial qualified entities, as well as to connect the System with existing repositories or laboratory networks by the end of 2022.

Draft Concept note: [The WHO BioHub System for Preparedness and Response to Epidemics and Pandemics](#)

## World Local Production Forum

Member State requests for WHO's support in strengthening local production have been increasing in recent years. The COVID-19 pandemic has only served to highlight even more the urgent need for enhancing quality manufacturing capacity in all regions of the world, including for innovative, highly effective health products such as mRNA technologies. Such capacity is necessary to address or even avert future public health emergencies and to improve access to health products in general through stronger health systems.

WHO held the first ever World Local Production Forum from 21-25 June. Delegates from over 100 countries, international partners, civil society groups, industry associations, and major investors joined WHO, WTO, UNIDO, UNICEF and UNCTAD to highlight the challenges facing local production and the steps required to address them, as well as the range of opportunities for the sector.

Vaccine production was a central theme at the Forum, as were the role of new technologies and generation of flexible manufacturing strategies to develop sustained production capacity in low- and middle-income countries. Technology transfer and licensing were seen as key to scaling up production. Sharing intellectual property and know-how will be essential, along with facilitation of voluntary licensing and effective technology transfer. It will also be vital to create a favorable environment for technology transfer. Key elements will include good governance; a skilled workforce; good access to market information and careful assessment of local capacity to receive and absorb the transferred technology.

A very strong case was made during the Forum that strengthening regulatory capacity was an essential component of any plans to strengthen local production. National regulators, and local manufacturers, can drive quality-compliant local production and facilitate faster access to health technologies during pandemics and beyond. To do that, they need continued training, support and resources.

[At Local Production Forum, WHO and partners highlight key steps to improve access to health technologies](#) (25 Jun 2021)

[World Local Production Forum: Enhancing access to medicines and other health technologies](#)

## Launch on WHO Good Regulatory Practices and Good Reliance Practices

WHO has recently published two critical documents for countries' regulatory system strengthening activities, namely the WHO Good Regulatory Practices and Good Reliance Practices.

The Good Regulatory Practices document provides advice to establish and implement sound, affordable, efficient regulation of medical products as an important part of health system performance and sustainability. The Good Reliance Practices document presents the overarching principles of regulatory reliance in the field of regulation of medical products. This principle allows leveraging the output of other regulators whenever possible while placing a greater focus at national level on value-added regulatory activities.

[Recording](#) of the Launch webinar (29 Jun 2021)

[WHO Publishes new guidance to promote Strong, Efficient and Sustainable Regulatory Systems](#)

## Ethical Framework for WHO's work in the ACT-Accelerator

The Access to COVID-19 Tools Accelerator (ACT-A) was formed in 2020 by the WHO and partners, under the guiding principle that "No one is safe until everyone is safe." To this end, the ACT-A has brought together numerous stakeholders to end the pandemic as soon as possible. Four pillars form the foundation of the ACT-A's efforts, corresponding to particular categories of 'COVID-19 tools': diagnostics, therapeutics, vaccines and health systems.

Ending the pandemic is not simply a public health goal. Obligations to end the pandemic are underpinned by and in some cases turn on crucial considerations of ethics. For example, under the vaccines pillar, what is the fairest way to determine which subpopulations should receive vaccines first? Under the therapeutics pillar, how much risk is acceptable in accelerated authorization pathways for novel therapeutics? Under the diagnostics pillar, how should diagnostic tools be distributed across countries in light of vulnerabilities and epidemiology? And under the health systems pillar, to what extent should health systems resources be diverted from other priority areas in order to address this pandemic?

This framework has been developed in order to assist stakeholders in navigating ethical issues and dilemmas, and more broadly make value-informed decisions, arising from efforts to respond to the pandemic through the use of COVID-19 tools.

[Ethical Framework for WHO's work in the ACT-Accelerator](#) (01 Jul 2021)

## Policy considerations for implementing a risk-based approach to international travel

Countries across the world are facing diverse epidemiological situations with varying response capacities and access to life saving tools. The World Health Organization (WHO) recommends that national authorities continue to apply a risk-based approach when implementing measures related to COVID-19 and international travel while respecting the dignity, human rights and fundamental freedoms of travellers. This approach should consider the risk posed by travel for the importation and exportation of cases in the context of the evolving epidemiology, including the emergence and circulation of virus variants of concern; the expansion of the COVID-19 vaccination roll-out; and lessons learned while responding to the pandemic, including on the early detection and management of cases and the application of public health and social measures.

This document summarizes WHO policy considerations for national authorities to continue the adjustment of international travel in the context of the COVID-19 pandemic, addressing:

- Proof of COVID-19 vaccination or recovery in the context of international travel
- Testing and quarantine of international travelers
- Other key considerations for travel-related measures

This document should be read in conjunction with its annex, the updated WHO interim guidance

Technical considerations for implementing a risk-based approach to international travel in the context of COVID-19 (6). WHO encourages countries to continue analyzing the public health effectiveness and broader impact of all public health and social measures, including international travel-related ones, to inform their response to the unfolding COVID-19 pandemic.

[Policy considerations for implementing a risk-based approach to international travel in the context of COVID-19](#) (02 Jul 2021)

## Technical considerations for a risk-based approach to international travel

This updated interim guidance document provides national authorities with key considerations for establishing their policies for international travel via air, sea or land between countries, territories or sub-national areas. It is divided into three main sections: risk assessment, risk mitigation and risk communication. The document aims to support countries as they gradually increase the volume of international travel with the objective of reducing travel-associated exportation, importation and onward transmission of SARS-CoV-2.

The document is an update to the original interim guidance document entitled 'Considerations for implementing a risk-based approach to international travel in the context of COVID-19', which was published on 16 December 2020. The original document was the result of extensive consultations across all relevant departments and Regional Offices of WHO, as well as with the members of the Strategic and Technical Advisory Group for Infectious Hazards (STAG-IH) and of an ad-hoc Technical Advisory Group for the development of a risk-based approach to the gradual increase of international travel in the context of COVID-19.

Key points:

During the COVID-19 pandemic, international travel should always be prioritized for essential purposes, including emergency and humanitarian missions, travel of essential personnel, repatriations, and cargo transport of essential supplies.

- As countries gradually resume or readjust non-essential international travel, the introduction of risk mitigation measures aiming to reduce travel-associated exportation, importation and onward transmission of SARS-CoV-2 should be based on thorough risk assessments conducted systematically and routinely.
- The application of a precautionary approach is warranted in the presence of scientific uncertainties such as emergence of VOCs or VOIs.
- Proof of COVID-19 vaccination should not be required as a condition of entry to or exit from a country.
- National authorities implementing testing or quarantine as a condition for entry of international travellers may consider individualized approaches to exempting them from these measures based on acquired immunity from vaccination or previous SARS-CoV-2 infection.
- Adherence to personal protective measures such as mask use and physical distancing must continue to be respected by all international travellers, both while on board conveyances and at points of entry.
- International travellers should not be considered by default as suspected COVID-19 cases or contacts or as a priority group for testing.
- The overall health and well-being of communities should be at the forefront of considerations when deciding on and implementing international travel-related measures, which should be communicated publicly and in a timely manner.

[Technical considerations for implementing a risk-based approach to international travel in the context of COVID-19](#) (02 Jul 2021)

## Interim guidance for quarantine of contacts of COVID-19 cases

This document is an update of interim guidance entitled Considerations for quarantine of contacts

of COVID-19 cases, published on 19 August 2020. The scope of this fourth version is restricted to the use of quarantine for contacts of individuals with confirmed or probable SARS-CoV-2 infection. Considerations for the use of restricted movement of travellers (often termed “quarantine” for travellers) is covered in [the interim WHO guidance published in December 2020](#). This version provides updated guidance for the implementation of quarantine, including considerations for health authorities considering shortening the quarantine period, and updates on the care of children in quarantine. The update is informed by feedback from Member States on experience implementing quarantine of contacts for COVID-19 and is based on evidence on controlling the spread of SARS-CoV-2, the virus that causes COVID-19, and scientific knowledge of the virus.

Key message:

For all contacts of individuals with confirmed or probable SARS-CoV-2 infection, WHO continues to recommend quarantine in a designated facility or in a separate room in the household for a duration of 14 days from the last contact with the confirmed or probable case to minimize risk of onward transmission.

WHO continues to recommend that quarantine should be supported. This includes individuals in quarantine receiving adequate food, water, protection, hygiene, and communication provisions, including access to education for children and paid leave or remote work options from jobs; adequate ventilation and infection prevention and control (IPC) measures are implemented and maintained; and the requirements for monitoring the health of quarantined persons can be met during quarantine period.

[Interim guidance: Considerations for quarantine of contacts of COVID-19 cases](#) (25 Jun 2021)

## **Alignment of approaches by regulators**

### **ICMRA-WHO joint statement COVID-19 vaccines regulation**

This joint International Coalition of Medicines Regulatory Authorities (ICMRA) and WHO statement aims to help healthcare professionals answer questions about the role of regulators in the oversight of COVID-19 vaccines. It explains regulatory authorities evaluate COVID-19 vaccines through robust scientific evaluation to ensure quality, safety and efficacy, and as part of post-approval commitment, safety is closely and continually monitored after approval.

[ICMRA-WHO joint statement for healthcare professionals: How COVID-19 vaccines are regulated for safety and effectiveness](#) (11 Jun 2021)

## **In vitro diagnostics**

### **WHO EUL and Listing Update**

The WHO Prequalification Unit is assessing products for Emergency Use Listing (EUL) for candidate in vitro diagnostics (IVDs) to detect SARS-CoV-2. The following IVDs are eligible for EUL submission:

- EUL applications for SARS-CoV-2 antigen detection tests
- EUL applications for SARS-CoV-2 nucleic acid detection tests intended to be used at a point of care.

WHO EUL submissions

Manufacturers who are interested in an EUL submission for assays to detect SARS-CoV-2 are invited to contact [diagnostics@who.int](mailto:diagnostics@who.int), to arrange a pre-submission meeting / videoconference / phone conversation.

# 36<sup>th</sup> WHO Regulatory Update on COVID-19

As of 2<sup>nd</sup> July, 28 products have been listed as eligible for WHO procurement among a total of 148 expressions of interest (64 for NAT assays, 41 for antibody detection assays and 43 for antigen detection RDTs) have been received. 39 products are recommended not to be used.

[EUL listed IVDs](#) (30 Apr 2021)

[IVDs not accepted for EUL listing](#) (29 Jun 2021)

[Status of each EUL application](#) (29 Jun 2021)

## Technical specifications for selection of essential IVDs

Technical specifications for IVDs constitute a set of predefined criteria and baseline requirements to ensure good quality, safety, performance and efficacy. The specifications are companions to the WHO Model List of Essential In Vitro Diagnostics (EDL) and are provided to help Member States, donor agencies and nongovernmental organizations select specific products within each test category of the EDL and guide procurement decisions.

The present publication defines the basic generic technical characteristics of IVDs for SARS-CoV-2 listed in WHO EDL 3. WHO will review and update this document periodically.

[Technical specifications for selection of essential IVDs for SARS-CoV-2](#) (14 Jun 2021)

## WHO Facilitated procedure for accelerating national listing/authorization

WHO has introduced risk-based mechanism for WHO Emergency Use Listed in vitro diagnostics similar to the WHO Collaborative Registration Procedure (CRP). As part of pandemic preparedness, emergency approval and/or expedited fast-track regulatory pathways should be considered by the National Regulatory Authorities (NRAs) to fast-track their national approval and accelerate introduction of the needed tests. Recognition and/or reliance on the WHO prequalification/ EUL programme, the decisions of stringent regulatory authorities (SRA) or WHO-Listed Authority (WLA), are regulatory options available to expedite regulatory decision by NRAs.

A Webinar to introduce and raise awareness the Procedure to NRAs was held on 15 June 2021. NRAs taking part in the webinar indicated interest to participate in the mechanism and WHO will continue to provide technical support to all interested NRAs to ensure smooth implementation so that NRAs, manufacturers and other stakeholders benefit from this innovative mechanism.

[WHO-EUL-Facilitated Procedure for IVDs for SARS-CoV-2](#)

For more information, contact [diagnostics@who.int](mailto:diagnostics@who.int)

## IVDs listed by NRAs in IMDRF jurisdictions

To help countries, WHO publishes links to emergency lists, together with contact details, on IVDs authorized for use in the International Medical Device Regulators Forum ([IMDRF](#)) jurisdictions along with other useful information on policies and guidance.

[IVDs listed by IMDRF NRAs](#) (02 Jun 2021)

*Note:* WHO does not endorse any of the lists provided by NRAs. The information is provided exclusively to assist stakeholders with identifying the links to the various lists.

## Therapeutics

### Tocilizumab:

The US FDA have issued an emergency use authorization (EUA) for tocilizumab for the treatment of hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation,

or extracorporeal membrane oxygenation (ECMO). Tocilizumab is a monoclonal antibody that reduces inflammation by blocking the interleukin-6 receptor.

The data supporting the EUA are based on four clinical trials. These included one randomized-controlled-open-label-platform trial [Randomized Evaluation of COVID-19 Therapy (RECOVERY)] and three randomized-double-blind-placebo-controlled trials (EMPACTA, COVACTA and REMDACTA).

[FDA Authorizes Drug for Treatment of COVID-19](#) (24 Jun 2021)

## Convalescent Plasma

A fourth review of evidence on convalescent plasma has been published by the Cochrane Database of Systematic Reviews. The authors found about 130 ongoing, unpublished and recently published studies. They are very confident that convalescent plasma has no benefits for the treatment of people with moderate to severe COVID-19. The authors are uncertain about the effects of convalescent plasma for treating people with mild COVID-19 or who have no symptoms. The review will be updated with evidence from the ongoing studies as soon as possible. New evidence may answer the remaining questions.

[Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review](#), Cochrane Review (20 May 2021)

<https://doi.org/10.1002/14651858.CD013600.pub4>

## Vaccines

### WHO COVID-19 Vaccines Dashboard

As of 28th June, over 2.928 billion vaccine doses have been administered worldwide ([dashboard](#)), and about 66 countries and territories have fully vaccinated more than 10% of their populations. COVAX has shipped 89.4 million doses to 133 countries and economies, but that covers just nearly 1% of their combined population and 5 countries and territories have not yet started their vaccination programme.

More than half of all high and upper-middle income countries and economies have now administered enough doses to fully vaccinate at least 20% of their populations while just three out of 79 low- and middle-income countries have reached the same level.

To see the data, choose “Vaccination” from the dropdown menu on the left-hand side of the map.

[WHO Coronavirus \(COVID-19\) Dashboard](#)

### Pfizer BioNTech tozinameran

#### WHO SAGE Recommendations:

Updated interim recommendations for use of the vaccine have been published after an extraordinary meeting of SAGE on 27 May 2021. Updates were made to recommendations on: considerations for deferring the second dose in settings with limited vaccine supply; interchangeability between vaccine products and platforms; paediatric age indication; children and adolescents below the age of 16 years; pregnant and lactating women; role of vaccines among other preventive measures; SARS-CoV-2 variants; and vaccination logistics.

[Interim recommendations for use of the Pfizer–BioNTech COVID-19 vaccine, BNT162b2, under EUL](#) (15 Jun 2021)

## **FDA:**

A suggested increased risks of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the tissue surrounding the heart) following vaccination is reflected in revisions to the patient and provider fact sheet. A warning has been added that reports of adverse events suggest increased risks of myocarditis and pericarditis, particularly following the second dose and with onset of symptoms within a few days after vaccination. Vaccine recipients should seek medical attention right away if they have chest pain, shortness of breath, or feelings of having a fast-beating, fluttering, or pounding heart after vaccination. The FDA and CDC are monitoring the reports, collecting more information, and will follow-up to assess longer-term outcomes over several months.

[FDA Coronavirus \(COVID-19\) Update](#) (25 Jun 2021)

## **EMA:**

EMA granted extension of the existing indication from "individuals 16 years of age and older" to "individuals 12 years of age and older". Accordingly, the Package Leaflet is updated.

[Assessment report on variation](#) (30 Jun 2021)

Two additional manufacturing sites have been approved for manufacture. One site, located in Reinbek, Germany, is operated by Allergopharma GmbH & Co. KG. The other in Stein, Switzerland, is operated by Novartis Pharma. The sites will perform finished product manufacturing steps at different stages of the process.

[Two additional manufacturing sites](#) (22 Jun 2021)

A regular safety update from EMA notes that reports of inflammation of the heart muscle (myocarditis) and membrane (pericarditis) in a small number of people after vaccination continue to be assessed under an accelerated timetable.

[EMA COVID-19 vaccine safety update](#) (18 Jun 2021)

## **Moderna (mRNA 1273) elasomeran**

### **WHO SAGE Recommendations:**

Updated interim recommendations for use of the vaccine have been published after an extraordinary meeting of SAGE on 27 May 2021. Updates were made to recommendations on: Considerations for deferring the second dose in settings with limited vaccine supply; pregnant and lactating women; role of vaccines among other preventive measures; and, SARS-CoV-2 variants.

[Interim recommendations for use of the Moderna mRNA-1273](#) (15 Jun 2021)

[Latest GRADE and ETR tables](#)

[Background document on the mRNA-1273 vaccine \(Moderna\) against COVID-19](#)

## **FDA:**

A suggested increased risks of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the tissue surrounding the heart) following vaccination is reflected in revisions to the patient and provider fact sheet. A warning has been added that reports of adverse events suggest increased risks of myocarditis and pericarditis, particularly following the second dose and with onset of symptoms within a few days after vaccination. Vaccine recipients should seek medical attention right away if they have chest pain, shortness of breath, or feelings of having a fast-beating, fluttering, or pounding heart after vaccination. The FDA and CDC are monitoring the reports, collecting more information, and will follow-up to assess longer-term outcomes over

several months.

[FDA Coronavirus \(COVID-19\) Update](#) (25 Jun 2021)

## **EMA:**

Reports of inflammation of the heart muscle (myocarditis) and membrane (pericarditis) in a small number of people after vaccination continue will be assessed under an accelerated timetable. There are no updates to the product information. COVID-19 Vaccine Moderna is effective in preventing COVID-19.

[COVID-19 vaccine safety update Moderna](#) (18 Jun 2021)

[EU Risk Management Plan for COVID-19 mRNA vaccine](#) (18 Jun 2021)

EMA's committee for human medicines ([CHMP](#)) has approved a new manufacturing site for the production of Moderna COVID-19 vaccine finished product. The site, operated by Recipharm, is located in Monts, France. In addition to the new manufacturing facility for this vaccine, the [CHMP](#) has also given a positive opinion for the addition of several alternative sites responsible for batch control/testing.

[Additional manufacturing capacity for Moderna's COVID-19 vaccine](#) (11 Jun 2021)

## **AstraZeneca (ChAdOx1-S) [recombinant]**

### **EMA:**

The EMA's safety committee (PRAC) has concluded that people who have previously had capillary leak syndrome must not be vaccinated with Vaxzevria (formerly COVID-19 Vaccine AstraZeneca). The Committee also concluded that capillary leak syndrome should be added to the product information as a new side effect of the vaccine, together with a warning to raise awareness among healthcare professionals and patients of this risk. The Committee carried out an in-depth review of 6 cases of capillary leak syndrome in people who had received Vaxzevria. Most of the cases occurred in women and within 4 days of vaccination. Three of those affected had a history of capillary leak syndrome and one of them subsequently died.

As of 27 May 2021, more than 78 million doses of Vaxzevria had been administered in the EU/EEA and the UK. People who have been vaccinated with Vaxzevria should seek immediate medical assistance if they experience rapid swelling of the arms and legs or sudden weight gain in the days following vaccination. These symptoms are often associated with feeling faint (due to low blood pressure).

[EMA advises against use in people with history of capillary leak syndrome](#) (11 Jun 2021)

## **Janssen (Ad26.COVS-2-S) [recombinant]**

### **WHO SAGE Recommendations:**

Updated interim recommendations for use of the vaccine have been published after an extraordinary meeting of SAGE on 27 May 2021. Updates were made to recommendations on: precautions and pregnancy.

[Interim recommendations for the use of the Janssen Ad26.COVS-2.S](#) (15 Jun 2021)

[Latest GRADE and ETR tables](#)

[Background document on the Janssen Ad26.COVS-2.S \(COVID-19\) vaccine](#)

## US FDA:

On 11 June, FDA published a memorandum with assessment of certain Janssen COVID-19 vaccine batches manufactured at the Emergent BioSolutions facility, summarizing relevant events and findings at the Emergent BioSolutions facility that led to FDA's decision to authorize batches GMP 2 and 4 and/or vaccine manufacturers from these batches and not a combination of other batches that includes batches GMP 5 through 9 or any other batches not authorized under the EUA.

[US FDA Memorandum to Janssen COVID-19 Vaccine EUA 27205](#) (11 Jun 2021)

## EMA:

EMA stated that the batches of the vaccine released in the EU are not affected by the cross contamination. However, as a precaution and to safeguard the quality of vaccines, the supervisory authorities have recommended not releasing vaccine batches containing the active substance made at around the same time that the contamination occurred.

[Authorities in EU take steps to safeguard vaccine quality](#) (11 Jun 2021)

EMA's committee for human medicines (CHMP) has approved an additional manufacturing site to produce the Janssen COVID-19 Vaccine, located in Anagni, Italy, operated by Catalent Anagni SRL. The site will perform finished product manufacturing.

EMA's CHMP has also approved a scale-up of the active substance manufacturing process at Janssen Biologics B.V, located in Leiden, the Netherlands, producing all active substance for the manufacture of the EU supply of COVID-19 Vaccine Janssen.

[Increased manufacturing capacity for COVID-19 Vaccine Janssen](#) (02 Jul 2021)

[Additional manufacturing site for COVID-19 Vaccine Janssen](#) (25 Jun 2021)

[Updated summary of product characteristics](#) (30 Jun 2021)

[COVID-19 vaccine safety update](#) (18 Jun 2021)

## CureVac candidate COVID-19 vaccine CVnCoV – zorecimeran

CureVac announced results on 16 June of the second interim analysis of its international pivotal Phase 2b/3 study in approximately 40,000 subjects (the HERALD study) of its first-generation COVID-19 mRNA vaccine candidate, zorecimeran. The HERALD study, conducted by CureVac in conjunction with Bayer, enrolled approximately 40,000 participants in ten countries in Latin America and Europe. The second interim analysis included 134 cases, occurring at least two weeks after administration of the second dose. In the context of at least 13 variants circulating within the study population subset assessed at this interim analysis, zorecimeran demonstrated an interim vaccine efficacy of 47% against COVID-19 disease of any severity which does not meet the criteria defined by WHO Target Product Profile nor EUL.

Initial analyses suggest age and strain dependent efficacy. Available data were communicated with the European Medicines Agency (EMA). The Data Safety Monitoring Board (DSMB) confirmed a favourable safety profile for zorecimeran. The study is continuing to the final analysis and the totality of the data will be assessed for the most appropriate regulatory pathway.

[CursVac provides update on Phase 2b/3 trial of first-generation COVID-19 vaccine candidate, CVnCoV](#) (16 Jun 2021)

# 36<sup>th</sup> WHO Regulatory Update on COVID-19

## Status Update: WHO EUL/PQ evaluation

WHO has placed into the public domain the status of COVID-19 vaccines for which an expression of interest has been received by WHO/PQ. The information shared includes the National Regulatory Authority (NRA) of record for each vaccine; whether the expression of interest has been accepted; if a pre-submission meeting has been held; if the dossier has been accepted for review; the status of the assessment; and the anticipated decision date.

Please visit the site regularly for the latest updated version. Below is version 02 July 2021.

Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process

	Manufacturer / WHO EUL holder	Name of Vaccine	NRA of Record	Platform	EOI accepted	Pre-submission meeting held	Dossier accepted for review*	Status of assessment**	Decision date***
1.	<b>pfizer</b>	BNT162b2/COMIRNATY Tozinameran (INN)	EMA	Nucleoside modified mRNA	✓	✓	✓  ✓	Finalized  Finalized: - Baxter Oncology GmbH Germany (DP)  Diluent suppliers: - Pfizer Perth, Australia - Fresenius Kabi, USA	31/12/2020  30/06/2021  18 June 2021 18 June 2021
							Additional sites, awaited: • Polymun Scientific, Austria (DP) • Pharmacia & Upjohn, Kalamazoo (DP) • mibe (Dermapharm), Germany (DP)	• Submission awaited • Submission awaited • Submission awaited	• As submitted • As submitted • As submitted
2.	<b>AstraZeneca</b>	AZD1222	EMA	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	✓	Core data finalized	16 April 2021
							Data for Covax sites expected in April 2021 onwards	Finalized: SK-Catalent Wuxi (DS) Chemo Spain	16 April 2021 30 April 2021 04 June 2021
							Other sites	As submitted	As submitted
3.	<b>AstraZeneca</b>	AZD1222	MFDS KOREA	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	✓	Finalized	15 Feb 2021
4.	<b>BEIJING INSTITUTE OF BIOLOGICAL PRODUCTS CO LTD</b>	Covishield (ChAdOx1_nCoV-19)	DCGI	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	✓	Finalized	15 Feb 2021
5.	<b>Janssen</b>	Ad26.COV2.S	EMA	Recombinant, replication- incompetent adenovirus type 26 (Ad26) vectored vaccine encoding the (SARS-CoV-2) Spike (S) protein	✓	✓	✓	Core data finalized (US +NL sites)	12 March 2021
							Additional sites: - Aspen RSA (DP) - Catalent Agnini Italy (DP) - Merck, Durham, UK (DS) - Merck, West Point/PA (DP)	- Finalized - Ongoing - Future submission - Future submission	-25 June 2021 - 02 July 2021 - As submitted - As submitted
6.	<b>moderna</b>	mRNA-1273	EMA	mRNA-based vaccine encapsulated in lipid nanoparticle (LNP)	✓	✓	✓	Finalized	30 April 2021
							Additional sites, awaited: - ModernaTx, Norwood (DS) - Catalent Indiana, LLC (DP) - Lonza Biologics, Inc. Portsmouth, USA (DS) - Baxter, Bloomington, USA (DP)	- Ongoing - Ongoing - Ongoing - Ongoing	- As submitted - As submitted - As submitted - As submitted
7.	<b>SinoPharm / BIBP</b>	SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV)	NMPA	Inactivated, produced in Vero cells	✓	✓	✓	Finalized	07 May 2021
8.	<b>SINO VAC</b>	COVID-19 Vaccine (Vero Cell), Inactivated/ Coronavac™	NMPA	Inactivated, produced in Vero cells	✓	✓	✓	Finalized	01 June 2021
9.	<b>THE GAMALEYA NATIONAL CENTER</b>	Sputnik V	Russian NRA	Human Adenovirus Vector-based Covid-19 vaccine	Additional information submitted	Several meetings have been and continue to be held.	"Rolling" submission of clinical and CMC data has started.	Additional data (Non-CLIN, CLIN, CMC) Required. Following up on inspection observations.	Anticipated date will be set once all data is submitted and follow- up of inspection observations completed.
10.	<b>AstraZeneca</b>	AZD1222	Japan MHLW/PMDA	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	Submission from AZ received on 15 June. MHLW submitted review and GMP reports on 16 June 2021 and June 22.	Several meetings held separately with AZ and MHLW/PMDA	✓	Ongoing	Anticipated date: Week of 05 July
11.	<b>AstraZeneca</b>	AZD1222	Australia TGA	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	Submission from AZ received on 11 June	Several meetings held separately with AZ and TGA	✓	Ongoing	Anticipated date: Week of 05 July
12.	<b>CansinoBio</b>	Ad5-nCoV	NMPA	Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector)	✓	✓	✓	Rolling data starting July 2021	
13.	<b>Bharat Biotech, India</b>	SARS-CoV-2 Vaccine, Inactivated (Vero Cell)/ COVAXIN	DCGI	<b>Whole-Virion Inactivated Vero Cell</b>	✓	✓	✓	Rolling data starting July 2021	
14.	<b>NOVAVAX</b>	NVX-CoV2373/Covovax	EMA	Recombinant nanoparticle prefusion spike protein formulated with Matrix-M™ adjuvant.	✓	✓	✓		
15.	<b>SinoPharm / WIBP</b>	Inactivated SARS-CoV-2 Vaccine (Vero Cell)	NMPA	Inactivated, produced in Vero cells	✓	✓	✓		
16.	<b>CUREVAC</b>	Zincimeran (INN) concentrate and solvent for dispersion for injection; Company code: CVnCoV/CV07050101	EMA	mRNA-based vaccine encapsulated in lipid nanoparticle (LNP)	✓	Planned for 28 July 2021			
17.	<b>Sanofi Pasteur</b>	CoV2-preS dTM-AS03 vaccine	EMA	Recombinant, adjuvanted	✓	Planned for 9 July 2021			
18.	<b>Vector State Research Centre of Virology and Biotechnology</b>	EpiVacCorona	Russian NRA	Peptide antigen	Letter received not EOI. Reply sent on 15/01/2021				
19.	<b>Zhifei Longcom, China</b>	Recombinant Novel Coronavirus Vaccine (CHO Cell)	NMPA	Recombinant protein subunit	Response to 2 <sup>nd</sup> EOI sent 29 Jan 2021. Additional information requested.				
20.	<b>IMBCAMS, China</b>	SARS-CoV-2 Vaccine, Inactivated (Vero Cell)	NMPA	Inactivated	Not accepted, still under initial development				
21.	<b>Clover Biopharmaceuticals</b>	SCB-2019	EMA	Novel recombinant SARS-CoV-2 Spike (S)-Trimer fusion protein	In discussion on submission strategy and timelines				
22.	<b>BioCubaFarma - Cuba</b>	Soberana 01, Soberana 02, Soberana Plus Abdala	CECMED	SARS-CoV-2 spike protein conjugated chemically to meningococcal B or tetanus toxin or Aluminum	Awaiting information on strategy and timelines for submission.				

1. Beijing Institute of Biological Products Co Ltd  
2. Wisan Institute of Biological Products Co Ltd

\* Dossier Submission dates: more than one date is possible because of the rolling submission approach. Dossier is accepted after screening of received submission.

\*\* Status of assessment: 1. Under screening; 2. Under assessment; 3. Waiting responses from the applicant; 4. Risk-benefit decision; 5. Final decision made

\*\*\* Anticipated decision date: this is only an estimate because it depends on when all the data is submitted under rolling submission and when all the responses to the assessors' questions are submitted.

# 36<sup>th</sup> WHO Regulatory Update on COVID-19

Please send any questions you may have to: [WHOEUL@who.int](mailto:WHOEUL@who.int)

## WHO guidance on evaluation of the quality, safety and efficacy of mRNA vaccines

WHO held a meeting on 20-22 April 2021 to:

- 1) Review the global development of mRNA prophylactic vaccines for infectious diseases;
- 2) Exchange experiences and perspectives regarding aspects relevant to the quality, safety and efficacy of the mRNA vaccines,
- 3) Review the second draft of a WHO document, discussing key issues identified during a public consultation on aspects of standardization of mRNA vaccines; and
- 4) Reach consensus where possible and to propose improvements towards finalizing the WHO mRNA vaccine document for submission to the Expert Committee on Biological Standardization in July 2021.

Good consensus was reached on further development of the WHO regulatory considerations document and the final version will be available for a second-round of public consultation on the WHO website from July to September. The document will then be reviewed by the ECBS at its meeting during 18-22 October 2021 for advice regarding the next steps.

[Executive Summary WHO informal consultation on regulatory considerations for evaluation of the quality, safety and efficacy of RNA-based prophylactic vaccines for infectious diseases Virtual meeting, 20-22 April 2021](#)

## EMA Guidance update on variation addressing variants

EMA published updated procedural guidance on submitting a variation application to address SARS-CoV-2 variants by updating the composition of an authorized COVID-19 vaccine, including recommendations on how to name the variant vaccine.

[Procedural guidance for variant strain\(s\) update to vaccines intended for protection against Human coronavirus](#) (28 Jun 2021)

## FDA data requirements of COVID-19 vaccines for use in pediatric populations

The US FDA held a Vaccines and Related Biological Products Advisory Committee (VRBPAC) meeting on 10 June to discuss, in general, data needed to support authorization and/or licensure of COVID-19 vaccines for use in pediatric populations.

[Vaccines and Related Biological Products Advisory Committee June 10, 2021 Meeting Announcement](#)

[Recording: Vaccines and Related Biological Products Advisory Committee](#) (10 Jun 2021)

## COVAX Regulatory Advisory Group (RAG)

The COVAX RAG is co-chaired by WHO and CEPI and its members, as of April 2021, include Regulatory Agencies from Argentina, Australia, Brazil, Canada, Europe (EMA & EDQM), Ghana, Japan, Singapore, UK and USA. Regulatory Agencies from the Republic of Korea and India joined the RAG starting from the May 2021 meeting.

The RAG was set up to give feedback on regulatory science questions of an agnostic nature raised by the COVAX SWAT teams in order to promote regulatory preparedness among COVID-19 vaccine developers. Feedback from the RAG is published in the form of a Technical Brief, for the benefit of all COVID-19 vaccine developers and for the wider community of regulatory authorities.

Topics discussed in the May meeting were:

- Evaluation of vaccines against variants: immunobridging within same vaccine platform – endpoints and trial population

Technical Briefs [Jun 2021](#), [May 2021](#), [April 2021](#)

For any questions, contact [COVAX-Reg@who.int](mailto:COVAX-Reg@who.int)

## WTO Symposium on COVID-19 Vaccine Supply Chain and Regulatory Transparency

On 29th June, WTO held a technical symposium to gather lessons learned and bottlenecks in supplying COVID-19 vaccines around the world with representatives from the different field.

Sessions covered 1) mapping vaccine manufacturing and trade, 2) mapping cross-border movement of vaccines, 3) Promoting transparency and convergence in the regulatory landscape and 4) Mapping other COVID-19 essential health technologies and trade.

Speakers in session 3 included June Raine (MHRA), Rogerio Gaspar (WHO), Yasuhiro Fujiwara (PMDA), Delese Darko (Ghana FDA) and others, discussed the approaches used to expedite the regulatory processes, international cooperation to quickly and safely manufacture, approve and disseminate needed vaccines, therapeutics and diagnostics, and importance of transparency in the regulatory approval processes, regulatory areas to be strengthened for future pandemics, among others.

[Recoding](#) (29 Jun 2021)

## Safety of COVID-19 Vaccines

### WHO GACVS reviews cases of mild myocarditis

The COVID-19 subcommittee of the WHO GACVS is reviewing reports of a small number of cases of myocarditis reported in individuals vaccinated with the COVID-19 mRNA vaccines. The subcommittee noted that in most of the reported cases, the individuals have recovered. The subcommittee is soliciting and monitoring for additional information to assess for any relationship to COVID-19 vaccination.

Myocarditis is an inflammation of the heart muscle and pericarditis is an inflammation of the lining that surrounds the heart. While it can cause serious illness, it is frequently mild and responds well to conservative treatment.

[COVID-19 subcommittee of the WHO GACVS reviews cases of mild myocarditis reported with COVID-19 mRNA vaccines](#) (26 May 2021)

### Updated EMA coreRMP19 guidance v2.0

The EMA "[Pharmacovigilance Plan of the EU Regulatory Network for COVID-19 Vaccines](#)" provides an overview of the monitoring activities to be carried out in the EU for COVID-19 vaccines, including the roles, responsibilities and interactions of the stakeholders involved. Experience gained from interactions between EMA, NCAs, and the vaccine manufacturers have identified the need to develop further guidance on RMP requirements for COVID-19 vaccines. The coreRMP19 document addresses the planning for post-marketing surveillance for COVID-19 vaccines in the context of marketing authorization in the EU.

EMA also published updated guidance on risk management plans (RMPs) for COVID-19 vaccines, together with guidance on Risk management plans and Good pharmacovigilance practices, which apply to all medicines.

[Consideration on core requirements for RMPs of COVID19 vaccines coreRMP19 guidance v2.0](#) (15 Jun 2021)

[Risk management plans](#)

## [Good pharmacovigilance practices](#)

### **WHO surveillance protocols**

In December 2020, WHO has published the COVID-19 vaccines: safety surveillance manual to guide the processes for collecting, analysing and sharing safety data and information on COVID-19 vaccines within and across countries. To accompany this manual and to facilitate conducting safety surveillance studies, WHO published surveillance protocols on 1<sup>st</sup> July.

#### **Protocol template for hospital case-based sentinel surveillance studies:**

Sentinel surveillance is an active safety surveillance study design that can be used for signal detection and evaluation. Sentinel surveillance is based on an active safety surveillance study design that can be used for signal detection and evaluation. The present protocol template describes study designs for hospital case-based monitoring of pre-defined adverse events of special interest (AESIs) following COVID-19 vaccination in all age groups.

[Protocol template to be used as template for observational study protocols for sentinel surveillance of adverse events of special interest \(AESIs\) after vaccination with COVID-19 vaccines](#) (01 Jul 2021)

#### **Protocol template for cohort event monitoring (CEM) studies:**

The present template protocol is for CEM studies of COVID-19 vaccines for the purpose of safety signal detection, developed under the guidance of a scientific committee including former and current GACVS committee members.

[Protocol template for observational study for CEM for safety signal detection after vaccination with COVID-19 vaccines](#) (01 Jul 2021)

## **WHO Assays Working Group**

Data from a widely used sensitive and specific IgG binding assay were presented in the 16 June meeting comparing immune responses between SARS-CoV-2 vaccines; on potential correlates of protection; and on variant immunity. The calibration of the assay with the WHO International Standard (IS) for SARS CoV-2 antibodies was readily achieved. This provides proof of principle supporting calls for assay harmonization using the WHO IS, which should lead to improved comparability of antibody responses between laboratories, between vaccines, between populations and for calibration of antibody correlates of protection. A good relationship between IgG binding titres to SARS CoV-2 spike/RBD, expressed relative to the IS, and vaccine efficacy was demonstrated. Data were also presented to suggest serological techniques can distinguish infection with variants and may contribute to an understanding of a threshold that protects against re-infection.

Note: WHO considers data on correlates of protection for COVID-19 vaccines to be limited and incomplete. Further work is needed.

## **WHO Animal Models Working Group**

Progress with a correlates of protection (CoP) study in rhesus macaques for SARS-CoV-2 Vaccine candidates was reported in the 17 June meeting. Initial natural history studies indicated the most robust endpoints for vaccine evaluations were determined to be bronchioalveolar lavage and nasal swabs. Challenge virus stocks were certified against quality control criteria, including in vivo testing in hamsters.

The CoP study design is to evaluate dose down of lead SARS CoV-2 vaccine candidates, covering

mRNA, adeno vectors, and subunit spike platforms until virus breakthrough is obtained. The study is designed to be complimentary to human clinical correlates analysis. The study is currently in progress with read-outs expected over the next few months.

The Working Group was also informed of a publication based on the work of the group. An array of SARS-CoV-2 virus variants have been isolated, propagated and used in in vitro assays, in vivo animal studies and human clinical trials. Observations of working stocks of SARS-CoV-2 suggest that sequential propagation in Vero cells leads to critical changes in the region of the furin cleavage site, which significantly reduce the value of the working stock for critical research studies. Serially propagating SARS-CoV-2 in Vero E6 cells leads to rapid increases in genetic variants while propagation in other cell lines (e.g. Vero/hSLAM) appears to mitigate this risk thereby improving the overall genetic stability of working stocks. From these observations, investigators are urged to monitor genetic variants carefully when propagating SARS-CoV-2 in Vero cells.

[A cautionary perspective regarding the isolation and serial propagation of SARS-CoV-2 in Vero cells](#), npj Vaccines 6, Article number: 83 (2021) (17 Jun 2021)

## Supply Chain

### Transportation backlogs

Continued diligence in planning is advised due to ongoing disruptions in countries with severe impact of COVID19. Ocean freight movement is also affected, including problems with port handling equipment and insufficient availability of maintenance staff. Export restrictions in some countries are compounding the problem of ports with freight backlogs.

### Supply chain of ultracold products

Care should be taken to avoid transfers of large cold chain shipments through the same airport at the same time due to limited cold chain space. Repacking of cold chain products is not possible in certain connecting airports and transport plans should verify in advance.

### Traceability

UNICEF has released an RFP for a Global Trust Repository, which is a database that countries can use to perform basic validation of bar codes. This is consistent with the guidance from WHO to include 2D data matrix codes with serialization on secondary packaging of vaccines. For countries with limited capacity to uptake data and make use of bar codes, the repository will facilitate basic activities while countries scale up to use traceability systems in medicines supply chains.

### Newly added or reconfirmed shortages

The following medicines are appearing as multi-country shortages (5 or more reports) from WHO sources. Medicines on the watch list are added to this list if they move to a confirmed shortage in more than 5 countries. They also remain on the watch list.

Of note on this list:

- Animal-derived insulin is reported as a shortage in a single country, however, given the limited manufacturing base of this product, supply could be highly constrained;
- Morphine granules are also only reported in a single country. Substitutions are available, but options are limited for paediatric palliative care
- Antifungal medicines to treat Mucormycosis remain in shortage.

Other items listed are:

- antifungal:
  - voriconazole
  - amphotericin B
- anti-pyretics

- ibuprofen
- Anti-ulcer
  - Omeprazole
- Anti-psychotics
  - Risperidone
  - Haloperidol
- Muscle relaxants
  - Atracurium
- Opioids, anesthesia, preoperative medicines:
  - Fentanyl
  - Oxycodone
  - Hydromorphone
  - Morphine sulfate, morphine capsules
- Diabetes
  - Metformin
  - Animal-derived insulin

## Shortage watch list

The following medicines are of concern considering the high demand and should be watched carefully. Hoarding and speculative procurement should be avoided. Care should be used to ensure the best use of available national inventories.

- Antibiotics: azithromycin, levofloxacin, metronidazole, amoxiclav, piperacillin, tazobactam
- Atracurium Injection
- epinephrine and norepinephrine
- Benzodiazepine sedatives: midazolam and lorazepam
- Nonbenzodiazepine sedatives: propofol
- Antipsychotics: haloperidol
- Neuromuscular relaxants: succinylcholine, atracurium, or vecuronium.
- Opioids: morphine and fentanyl
- Malaria treatments: hydroxychloroquine, chloroquine, artemether-lumafantrine, artemisinin-based combination therapies, sulfadoxine-pyrimethamine + amodiaquine)
- NCD: Metformin and insulin
- Anticoagulants: heparin and new generation oral anticoagulants
- Corticosteroids: dexamethasone
- Antipyretics: paracetamol (aka acetaminophen)
- PPE
- Oxygen and related equipment
- Ventilators

## Upcoming events

### Expert Network: Monitoring new threats to medical products of human origin

The WHO has a collaborating centre agreement with the Italian National Transplant Centre for the development of a database on adverse events and reactions related to transplantation and other medical products of human origin (MPHO), including blood and reproductive cells. Building on the COVID-19 experience and the threats it poses to the supply and safety of all MPHOs, it has been decided to establish a network for monitoring Emerging Infectious Diseases and to provide information and guidance where available. The network will include representatives from the European Commission, the ECDC, the US CDC, regulators from Member State authorities and experts from the relevant technical and clinical sectors. An agreement has been reached with the WHO mechanism for Epidemic Intelligence from Open Sources (EIOS) that will host the newly established community.

For more information, contact Mr. Efstratios Chatzixiros at [chatzixirose@who.int](mailto:chatzixirose@who.int)

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## ICMRA workshop on “Enabling Manufacturing Capacity in the COVID-19 pandemic” 7 July 12:00 – 15:00 CET.

Please register: <https://www.eventbrite.com/e/enabling-manufacturing-capacity-in-the-covid-19-pandemic-day-1-tickets-161659743645>

**ICMRA-Industry Virtual Workshop on  
Enabling Manufacturing Capacity in the COVID-19 Pandemic**  
Wednesday, July 7, 2021  
**6:00-9:00 EST | 12:00-15:00 CEST AGENDA**

EST	
6:00 - 6:05	<b>ICMRA Chair Welcome</b> <i>Emer Cooke, EMA and Chair ICMRA</i>
6:05 - 6:10	<b>Industry perspective</b> <i>Greg Perry, IFPMA</i>
6:10 - 6:25	<b>Regulatory Presentation: “Regulatory flexibilities to support the rapid increase in manufacturing capacity for COVID-19 therapeutics &amp; vaccines”</b> <i>Sean Barry, HPRA, and Evdokia Korakianiti, EMA</i>
6:25 - 6:40	<b>Industry Presentation: “Science and Risk-based Approaches to Enable the Rapid Increase of Manufacturing Capacity for COVID-19 Therapeutics and Vaccines”</b> <i>Connie Langer, Pfizer (presenting on behalf of Industry)</i>
6:40 - 6:55	<b>Discussion</b> <i>Moderated by Emer Cooke, EMA, and Theresa Mullin, FDA</i> Panelists: <ul style="list-style-type: none"> <li>▪ Sean Barry, HPRA, and Evdokia Korakianiti, EMA</li> <li>▪ Connie Langer, Pfizer</li> </ul>
6:55 – 7:10	<b>Regulatory Case Studies</b> <i>Stelios Tsinontides, FDA, and Karl Cogan, HPRA</i>
7:10 – 7:25	<b>Industry Case Studies</b> <i>Matt Popkin, GSK, Boris Zimmermann, Genentech/Roche, and Graham Cook, Pfizer</i>
7:25 – 7:35	<b>Break</b>
7:35 – 8:50	<b>Panel discussion --</b> featuring three 25-minute panel discussions
	<b>Panel 1 – Priority Regulatory Mechanisms and Flexible CMC Approaches Lessons Learned, Moderated by Sau “Larry” Lee, FDA</b> <b>Panelists: Regulators</b> <i>Stelios Tsinontides, FDA</i> <i>Karl Cogan, HPRA</i> <i>Raphael Sanches Pereira, ANVISA</i> <i>Maria Baca-Estrada, HC</i>
	<b>Panelists: Industry</b> <i>Matt Popkin, GSK</i> <i>Boris Zimmermann, Genentech/Roche</i> <i>Graham Cook, Pfizer</i> <i>Connie Langer, Pfizer</i>
	<b>Panel 2 – Lifecycle Management – Tools, Challenges, and Key Learnings During the COVID-19 Pandemic, Moderated by Markus Goese, Roche (EFPIA)</b> <b>Panelists: Regulators</b> <i>Evdokia Korakianiti, EMA</i> <i>Patricia Aprea, ANMAT*</i> <i>Raphael Sanches Pereira, ANVISA</i> <i>Maria Baca-Estrada, HC</i> <i>Mohammed A. AlMuteri, SFDA</i>
	<b>Panelists: Industry</b> <i>Thierry Gastineau, Sanofi Pasteur (Vaccines Europe)</i> <i>Diane Wilkinson, Astra Zeneca (Vaccines Europe)</i> <i>Suresh Jadhav, Serum Institute of India (DCVMN)</i>
	<b>Panel 3 – Inspections, Alternative Tools, and Reliance Practices During the COVID-19 Pandemic</b> <i>Moderated by Lorraine Nolan, HPRA</i> <b>Panelists: Regulators</b> <i>Derek Smith, FDA</i> <i>Brendan Cuddy, EMA</i> <i>Mohammed Alaqeel, SFDA</i> <i>Paula Walker, MHRA</i>
	<b>Panelists: Industry</b> <i>Rajiv Desai, Lupin Ltd. (IGBA)</i> <i>Steve Mendivil, Amgen (PhRMA)</i> <i>Caroline Bell, Kindeva Drug Delivery (PBOA)</i>
8:50 – 8:55	<b>Industry Concluding Remarks, David Jefferys, IFPMA</b>
8:55 – 9:00	<b>ICMRA Chair Concluding Remarks, Emer Cooke, EMA and Chair, ICMRA</b>