



Key Messages

The global number of confirmed COVID-19 cases and deaths reported to WHO has passed over 220 million cases and 4.5 million deaths. The situation is very different from region to region, country to country, province to province and town to town. Some regions and countries continue to see steep increases in cases and deaths, while in others they are declining. Getting vaccinated, maintaining physical distancing, cleaning hands, avoiding crowded and closed spaces, and wearing a mask are 'anti-lockdown measures': they can prevent the spread of disease without having to shut down large parts of society. However, the inequitable distribution of the tools which assist in mitigating transmission or save lives - including diagnostics, oxygen, PPE and vaccines- is driving a two-track pandemic. This inequity will prolong the acute stage of this pandemic for years when it could be over in a matter of months. If this virus is circulating anywhere, it's a threat everywhere.

Highlights and main issues

- The most recent summary of vaccine performance against variants of concern (VOC), from four studies, provides evidence for the maintenance of high levels of protection against severe COVID-19 disease due to the Delta SARS CoV-2 VOC.
- The SARS CoV-2 variant, B.1.621 was classified as a new WHO Variant of Interest (VOI) on 30 August 2021 and given the WHO label "Mu". The Mu variant has a constellation of mutations that indicate potential properties of immune escape. More studies are required to understand the phenotypic and clinical characteristics of this variant. The epidemiology of the Mu variant in South America, particularly with the co-circulation of the Delta variant, will be closely monitored.
- WHO has announced the next phase in its Solidarity trial: Solidarity PLUS will enrol hospitalized patients to test three new drugs - artesunate, imatinib and infliximab - in COVID-19 patients. These therapies are already used for other indications: artesunate for severe malaria, imatinib for certain cancers, and infliximab for diseases of the immune system such as Crohn's Disease and rheumatoid arthritis. These drugs were donated for the trial by their manufacturers.
- WHO opens Hub for Pandemic and Epidemic Intelligence in Berlin with a mission to provide the world with better data, analytics and decisions to detect and respond to health emergencies.
- India's drug regulator has granted emergency use approval for Zydus Cadila's COVID-19 vaccine, the world's first DNA vaccine against the coronavirus, in adults and children aged 12 years and above. The vaccine is administered in three doses and using a needle-free applicator as opposed to traditional syringes.

Contents

Key Messages.....	1
Highlights and main issues.....	1
Virus variants.....	3
Epidemiological Update.....	3
New WHO Variant of Interest (VOI) Mu.....	3
Guidance for surveillance of SARS-CoV-2 variants.....	4
Summary of phenotypic impacts of VOCs.....	4
Call for experts: Scientific Advisory Group for the Origins of Novel Pathogens.....	4
The Unity Studies: WHO Sero-epidemiological Investigations Protocols.....	5
ACT-Accelerator.....	6
Urgent US\$ 7.7 billion appeal to stem surge of dangerous variants and save lives.....	6
Unitaid and WHO Joint Statement on availability of tocilizumab.....	7
ACT-Accelerator Quarterly Update Q2: 1 April - 30 June 2021.....	7
COVAX.....	8
Addressing the vaccine inequity crisis.....	8
COVAX Supply Forecast for 2021 and early 2022.....	8
WHO's other COVID-19-related work.....	9
Guidance for issuing digital certificates for vaccination against COVID-19.....	9
New WHO Hub for Pandemic and Epidemic Intelligence in Berlin.....	9
WHO compendium of innovative health technologies.....	10
Infodemic Signal Detection during the COVID-19 pandemic.....	10
WHO report on AI in health and six guiding principles for its design and use.....	11
Alignment of approaches by regulators.....	11
ICMRA Innovation Network report on AI.....	11
ICMRA recommendations on CTD for track and trace systems for medical products.....	12
Evaluation of the quality, safety and efficacy of mRNA vaccines.....	12
WHO-Listed Authorities: Operational guidance on evaluation and designation.....	13
In vitro diagnostics.....	13
WHO EUL and Listing Update.....	13
Therapeutics.....	14
WHO's Solidarity clinical trial enters a new phase with three new candidate drugs.....	14
Additional information on clinical trials.....	14
Vaccines.....	15
WHO COVID-19 Vaccines Dashboard.....	15
COVID-19 vaccine booster doses.....	15
Dose-sparing strategies for COVID-19 vaccines (fractionated vaccine doses).....	18
Heterologous priming for COVID-19 vaccines.....	18
WHO Workshop on correlates of protection for COVID-19 vaccines.....	19
Pfizer BioNtech tozinameran (COVID-19 mRNA vaccine).....	19
Moderna (mRNA 1273) elasomeran.....	20
AstraZeneca COVID-19 vaccine (ChAdOx1-S) [recombinant].....	20
Janssen COVID-19 Vaccine (Ad26.COV2-S [recombinant]).....	21
ZyCoV-D (ZyCoV-D) DNA vaccine.....	21
Status Update: WHO EUL/PQ evaluation.....	21
Vaccination guidance and policy updates.....	23
COVID-19 immunization in refugees and migrants: principles and key considerations.....	23
WHO SAGE Updates.....	23
COVID-19 vaccine post-introduction evaluation (cPIE).....	24

38th WHO Regulatory Update on COVID-19

Guidance on vaccination costing and budgeting: WHO-ECHO webinars	25
Standards for measurement of antibody responses	25
COVAX Enabling Science workshop:.....	25
WHO Measurement standards	25
Other Covid-19 vaccine information:	26
IMF-WHO Covid-19 vaccine supply tracker	26
Interactives maps on VE studies	26
COVID-19 vaccine tracker and landscape	26
Substandard and falsified products	27
Alert N°4/2021: Falsified remdesivir identified in the Americas	27
Alert N°5/2021: Falsified COVISHIELD vaccine	27
WHO Assays Working Group	28
Supply Chain	29
Medical Devices	30
Upcoming events.....	30
Extraordinary International Conference of Drug Regulatory Authorities (ICDRA)	30
Call for nomination: WHO 3 rd Global infodemic manager training	31
GVIRF Webinar: mRNA Vaccine Technologies for Global Health.....	31
WHO Virtual cGMP Training Marathon for Vaccine Manufacturing.....	31

Virus variants

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 Variants of Concern (VOCs) or Variants of Interest (VOIs) and assess these based on the risk posed to global public health.

As surveillance activities to detect SARS-CoV-2 variants are strengthened at national and subnational levels, including through the expansion of genomic sequencing capacities, the number of countries/areas/territories (hereafter countries) reporting VOCs continues to increase. This distribution should nonetheless be interpreted with due consideration of surveillance limitations, including differences in sequencing capacities and sampling strategies between countries.

Edition 55 of the Weekly Epidemiological update provides a special focus on SARS-CoV-2 VOCs: Alpha, Beta, Gamma and Delta which includes updates on the geographic distribution as well as a description of a newly classified VOI, Mu.

[Weekly epidemiological update on COVID-19, Ed 55](#) (31 Aug 2021)

New WHO Variant of Interest (VOI) Mu

Based on the latest round of assessments, B.1.621 was classified as a VOI on 30 August 2021 and given the WHO label “Mu”. This includes the descendent Pango lineage B.1.621.1. This variant is known as 21H in Nextstrain nomenclature.

The Mu variant has a constellation of mutations that indicate potential properties of immune escape. Preliminary data presented to the WHO Virus Evolution Working Group show a reduction in neutralization capacity of convalescent and vaccinee sera similar to that seen for the Beta variant, but this needs to be confirmed by further studies. Since its first identification in Colombia in January 2021, there have been a few sporadic reports of cases of the Mu variant and some larger outbreaks have been reported from other countries in South America and in Europe. As of

29 August, over 4'500 sequences (3'794 sequences of B.1.621 and 856 sequences of B.1.621.1) have been uploaded to GISAID from 39 countries.

Although the global prevalence of the Mu variant among sequenced cases has declined and is currently below 0.1%, the prevalence in Colombia (39%) and Ecuador (13%) has consistently increased. The reported prevalence should be interpreted with due consideration of sequencing capacities and timeliness of sharing of sequences, both of which vary between countries. More studies are required to understand the phenotypic and clinical characteristics of this variant. The epidemiology of the Mu variant in South America, particularly with the co-circulation of the Delta variant, will be monitored for changes.

[Weekly epidemiological update on COVID-19, Ed 55](#) (31 Aug 2021)

Guidance for surveillance of SARS-CoV-2 variants

Interim WHO guidance that aims to describe a minimum set of surveillance activities recommended at the national level to detect and monitor the relative prevalence of SARS-CoV-2 variants and outline a set of activities for the characterization and assessment of risk posed by these variants has been published. A set of indicators is also provided to standardize monitoring and public reporting of variant circulation.

[Guidance for surveillance of SARS-CoV-2 variants: Interim guidance](#) (09 Aug 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. The findings, together with the geographic distribution of VOCs, are updated in each Epidemiological Update.

A summary of vaccine performance against variants of concern is also regularly collated and summarized. The most recent information, from four studies, provides evidence for the maintenance of high levels of protection against severe COVID-19 disease due to the Delta. While there is some evidence that vaccine effectiveness (VE) against SARS-CoV-2 infection and non-severe disease may be reduced with Delta, it is currently not possible to separate the effect of Delta from the effect of potential waning immunity, differential risk of exposure profiles between vaccinated and unvaccinated populations, spuriously low VE due to increasing levels of natural immunity in the unvaccinated population, or other potential confounding factors.

[Weekly epidemiological update on COVID-19, Ed 56](#) (07 Sept 2021)

Call for experts: Scientific Advisory Group for the Origins of Novel Pathogens

Call for experts - Deadline extended to 17 September 2021

WHO has issued an open call for experts to serve as members of the new WHO Scientific Advisory Group for the Origins of Novel Pathogens (SAGO).

The SAGO will advise WHO on technical and scientific considerations regarding the origins of emerging and re-emerging pathogens of epidemic and pandemic potential and will be composed of a wide range of experts acting in their personal capacity. SAGO will also guide WHO on next steps for understanding the SARS-CoV-2 origins.

There have been an increasing number of high threat pathogens emerging and re-emerging in recent years with, for example, SARS-CoV, MERS-CoV, Lassa, Marburg, Ebola, Nipah, avian

influenza, the latest being SARS-CoV-2. There is a clear need for robust surveillance and early actions for rapid detection and mitigation efforts, as well as systematic processes to study the emergence of these pathogens and routes of transmission from their natural reservoirs to humans. This is critical to helping WHO, Member States and partner institutions to prepare for future spillover threats and to minimize the risk of a disease outbreak growing into a pandemic.

From SARS-CoV-2, which continues to wreak havoc around the world, to the next "Disease X", this global framework to study the emergence of new and known high threat pathogens needs to be comprehensive and coordinated based on a One Health approach. It should also encompass biosafety and biosecurity, and needs to be scientific, transparent, comprehensive, rapid and inclusive.

Functions of SAGO

In its capacity as an advisory body to WHO, the SAGO will have the following functions:

1. To advise WHO on the development of a WHO global framework to define and guide studies into the origins of emerging and re-emerging pathogens of epidemic and pandemic potential;
2. To advise WHO on prioritizing studies and field investigations into the origins of emerging and re-emerging pathogens of epidemic and pandemic potential, in accordance with the WHO global framework described in point (1) above;
3. To provide information and views to assist the WHO Secretariat in the development of a detailed work plan of the SAGO;
4. In the context of SARS-CoV-2 origins:
 - To provide the WHO Secretariat with an independent evaluation of all available scientific and technical findings from global studies on the origins of SARS-CoV-2;
 - To advise the WHO Secretariat regarding developing, monitoring and supporting the next series of studies into the origins of SARS-CoV-2, including rapid advice on WHO's operational plans to implement the next series of global studies into the origins of SARS-CoV-2, as outlined in the 'Joint WHO-China Global Study of Origins of SARS-CoV-2: China Part' report published on 30 March 2021 and advise on additional studies as needed; and
5. To provide additional advice and support to WHO, as requested by the WHO SAGO Secretariat, which may include participation in future WHO-international missions to study the origins of SARS-CoV-2 or for other emerging pathogens.

More information can be found on the [Terms of Reference of the SAGO](#).

Who can express interest?

The SAGO will be multidisciplinary, with members who have a range of technical knowledge, field experience, skills and experience relevant to emerging and re-emerging pathogens. Up to 25 experts may be selected.

WHO welcomes expressions of interest from individuals with significant expertise in one or more technical disciplines outlined in the [call for experts](#) in order to ensure a One Health approach.

[Call for experts to join Scientific Advisory Group for the Origins of Novel Pathogens](#) (20 Aug 2021)

The Unity Studies: WHO Sero-epidemiological Investigations Protocols

Unity Studies is a global sero-epidemiological standardization initiative, which aims at increasing the evidence-based knowledge for action. WHO, in collaboration with technical partners, has developed several standardized generic epidemiological investigation protocols branded as UNITY studies. These studies aim to support national public health and social measures, promote the

38th WHO Regulatory Update on COVID-19

international comparability of research and address gaps in current knowledge regarding the COVID-19 pandemic.

The emergence of a new virus means that our understanding of the transmission patterns, immunity, severity, clinical features, and risk factors for infection is still limited. The WHO UNITY Studies can be adapted to local settings and implemented rapidly to collect robust data on key epidemiological parameters to understand, respond and control the COVID-19 pandemic.

The UNITY Studies promote standardized epidemiological, molecular and serological methods to facilitate international comparisons so that both countries and the global community can collectively address knowledge gaps and inform an evidence-based COVID-19 response.

Finally, UNITY Studies enable countries, regardless of their resource setting, to conduct local investigations and are thus an invaluable tool for research equity.

Unity studies: Early Investigational Protocols

For more information, contact: EarlyInvestigations-2019-nCoV@who.int

List and access to individual protocols:

Population-based age-stratified sero-epidemiological investigation protocol for COVID-19 infection:	Access the protocol
Measuring COVID-19 vaccines effectiveness	
Cohort study to measure COVID-19 vaccine effectiveness among health workers:	Access the protocol
COVID-19 vaccine effectiveness against severe acute respiratory infections (SARI) hospitalizations (test-negative case-control design)	Access the protocol
The First Few X (FFX) cases and contact investigation protocol for COVID-19 infection:	Access the investigation protocol
Household transmission investigation protocol for COVID-19 infection	Access the investigation protocol
Assessment of risk factors for COVID-19 in health workers (HW):	
Protocol for a prospective study of a cohort of HW:	Access the protocol
Protocol for a case-control study:	Access the protocol
Schools and other educational institutions transmission investigation protocol for coronavirus disease 2019 (COVID-19)	Access the protocol
A prospective cohort study investigating maternal, pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2:	Access the protocol
Surface sampling of coronavirus SARS-CoV-2: A practical “how to” protocol for health care and public health professionals:	Access the protocol

WHO Science in 5 on Delta variant

What do we know about the Delta variant so far? How can we assess our risk? What strategies should we apply to protect ourselves whether we are in a low vaccination or high vaccination setting? WHO's Dr Maria Van Kerkhove explains in Science in 5.

[WHO Science in 5: Episode #45 - Delta variant](#) (05 Jul 2021)

ACT-Accelerator

Urgent US\$ 7.7 billion appeal to stem surge of dangerous variants and save lives

The Delta SARS CoV-2 variant is on track to become the dominant strain worldwide as surges in this highly transmissible variant increases the urgency for vaccinating large numbers of vulnerable people. Rising infection rates globally are resulting in increased hospitalizations which are

overwhelming health systems and leaving many countries in urgent need of life-saving oxygen. COVID-19 testing rates in much of the world are too low, especially in low- and lower-middle-income countries – leaving much of the world blind to how the disease is evolving and vulnerable to new variants.

Funding the Rapid ACT-Accelerator Delta Response (RADAR) urgent appeal for US \$7.7 billion would enable: significantly increased testing and better surveillance to detect and protect against new variants; more oxygen to treat the seriously ill and save lives; vital personal protective equipment to protect health workers; the rolling out of emergency response and delivery support for the effective delivery and deployment of COVID-19 tools, including in humanitarian contexts; and continued research and development so that tools remain effective.

The US\$ 7.7 billion is not an additional funding need but is part of the ACT-Accelerator's overall 2021 budget, which is needed urgently within the next four months.

[ACT-Accelerator launches urgent US\\$ 7.7 billion appeal to stem surge of dangerous variants and save lives everywhere](#) (16 Aug 2021)

Unitaid and WHO Joint Statement on availability of tocilizumab

Tocilizumab, an IL6 inhibitor WHO recommended in June for use as a treatment for severe COVID-19 cases, can play a key role in decreasing mortality and reducing need for invasive mechanical ventilation among severely ill patients, when delivered alongside oxygen and corticosteroids.

While we welcome and acknowledge that Roche has announced measures to address the shortage, WHO and Unitaid, on behalf of ACT-Accelerator, call on the company to ensure equitable allocation of current stocks of this medicine for all countries, including low- and middle-income countries and strongly encourage Roche to facilitate technology transfer and knowledge and data sharing to broaden access to this important treatment.

The ACT-A partnership Access to COVID-19 Tools (ACT) Accelerator partners are working with Roche to set up channels for distribution of tocilizumab in places where it is not yet in use, as part of their effort to support roll-out of effective new therapeutic products for COVID-19.

WHO has also issued a call for Expression of Interest to its Prequalification programme to expand the number of quality-assured manufacturers of the drug and thus to increase global supplies.

WHO and Unitaid remain committed to ensuring equitable access to medicines for treating patients with severe COVID-19 as a vital element of the effort to fight the pandemic everywhere and save lives.

[Joint Statement from Unitaid and the World Health Organization \(on behalf of the Access to COVID-19 Tools Accelerator\) regarding availability of tocilizumab](#) (18 Aug 2021)

[Therapeutics and COVID-19: living guideline](#) (06 Jul 2021)

[Prequalification call for Expression of Interest](#): Tocilizumab products, Tocilizumab IV 20 mg/mL and Sarilumab products, Sarilumab 200 mg/1.14 mL and Sarilumab 150 mg/1.14 mL, all products for further dilution prior to intravenous infusion.

ACT-Accelerator Quarterly Update Q2: 1 April - 30 June 2021

The update provides an overview of the progress made, during April to June 2021, in bringing life-saving COVID-19 tools to countries around the world, and highlights the efforts made to ensure health systems are able to receive and fully optimize the use of COVID-19 countermeasures. It shows how investments made to the ACT-Accelerator have driven results and impact in the fight against COVID-19.

Increased global discourse and new initiatives echo the imperative to achieve equity in the fight

against the pandemic. In just over 15 months, by 9th August 2021, donors had stepped up and provided US\$ 17.8 billion of the ACT-Accelerator's US\$ 38.1 billion funding needs. This unprecedented generosity has driven the fastest and most coordinated effort in history to develop tools to protect global health security, and to deliver impact where it is most needed.

[ACT Accelerator: Quarterly Update Q2: 1 April - 30 June 2021](#) (04 Aug 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.

Addressing the vaccine inequity crisis

The global rollout of COVID-19 vaccines is progressing at two alarmingly different speeds. Less than 2% of adults are fully vaccinated in most low-income countries compared to almost 50% in high-income countries. These countries, the majority of which are in Africa, simply cannot access sufficient vaccine to meet even the global goals of 10% coverage in all countries by September and 40% by end 2021, let alone the African Union's goal of 70% in 2022.

This **crisis of vaccine inequity** is driving a dangerous divergence in COVID-19 survival rates and in the global economy.

Effectively tackling this acute vaccine supply shortage in low- and lower middle-income countries, and fully enabling African Vaccine Acquisition Trust (AVAT) and COVAX, requires the urgent cooperation of vaccine manufacturers, vaccine-producing countries, and countries that have already achieved high vaccination rates.

To ensure all countries achieve the global goals of at least 10% coverage by September and 40% by end-2021, the heads of the WHO, the International Monetary Fund, the World Bank Group and the World Trade Organization have issued a statement calling for four things to address the current global vaccine inequity:

1. Countries that have contracted high volumes of vaccines to swap near-term delivery schedules with COVAX and AVAT.
2. Vaccine manufacturers to immediately prioritize and fulfil their contracts to COVAX and AVAT, and to provide regular, clear supply forecasts.
3. G7 and all dose-sharing countries to fulfil their pledges urgently, as barely 10% of nearly 900 million committed doses have so far been shipped.
4. All countries to eliminate export restrictions and any other trade barriers on COVID-19 vaccines and the inputs involved in their production.

[Joint Statement of the Multilateral Leaders Taskforce on Scaling COVID-19 Tools](#) (27 Aug 2021)

COVAX Supply Forecast for 2021 and early 2022

COVAX has already achieved significant progress: more than US\$10 billion has been raised; legally-binding commitments for up to 4.5 billion doses of vaccine; 240 million doses have been delivered to 139 countries in just six months. Yet the global picture of access to COVID-19 vaccines is unacceptable as only 20% of people in low- and lower-middle-income countries have received a first dose of vaccine compared to 80% in high- and upper-middle income countries.

According to its latest Supply Forecast, COVAX expects to have access to 1.425 billion doses of vaccines in 2021 in the most likely scenario and in the absence of urgent action by producers and high-coverage countries to prioritize COVAX.

Of these doses, approximately 1.2 billion will be available for the lower income economies participating in the COVAX Advance Market Commitment (AMC). This is enough to protect 20% of the population, or 40% of all adults, in all 92 AMC economies, except for India. Over 200 million doses will be allocated to self-financing participants.

The key COVAX milestone of two billion doses released for delivery is now expected to be reached in the first quarter of 2022.

[Joint COVAX Statement on Supply Forecast for 2021 and early 2022](#) (06 Sept 2021)

[COVAX Global Supply forecast](#) (08 Sept 2021)

WHO's other COVID-19-related work

Guidance for issuing digital certificates for vaccination against COVID-19

The guidance is part of a series of planned documents on digitalization of COVID-19 certificates and will, amongst other things, support Member States in adopting digital tools for documenting COVID-19 vaccination status for the purposes of effective health care, and proof of vaccination should it be needed for other purposes. The minimum requirements for implementing digital documentation in countries around the world allow Member States the greatest possible flexibility to build a solution that is appropriate not just for their needs, but the diverse needs of individuals around the world.

The guidance was developed in collaboration with a multi-disciplinary group of experts to ensure that it will be useful to governments and implementing partners who have built or who are currently developing systems for issuing or verifying digital vaccination certificates. Technical assistance will be provided to countries and implementing partners to assist with aligning existing products to WHO specifications.

[Digital documentation of COVID-19 certificates: vaccination status: technical specifications and implementation guidance](#) (27 Aug 2021)

[Annex A: DDCC:VS core data dictionary](#) (27 Aug 2021)

[Annex B: Technical Briefing in PowerPoint](#) (27 Aug 2021)

New WHO Hub for Pandemic and Epidemic Intelligence in Berlin

To better prepare and protect the world from global disease threats, the new WHO Hub was launched with its mission to provide the world with better data, analytics and decisions to detect and respond to health emergencies. It aims to harness broad and diverse partnerships across many professional disciplines, and the latest technology, to link the data, tools and communities of practice so that actionable data and intelligence are shared for the common good.

The WHO Hub will support the work of public health experts and policy-makers in all countries with the tools needed to forecast, detect and assess epidemic and pandemic risks so they can take rapid decisions to prevent and respond to future public health emergencies. Dr Chikwe Ihekweazu, currently Director-General of the Nigeria Centre for Disease Control, has been appointed to lead the WHO Hub.

The WHO Hub is currently operating from a centre provided by the [Charité - Universitätsmedizin](#) in Berlin. It will soon move to a permanent campus at the heart of Berlin, Kreuzberg, that will provide a collaborative work environment for the Hub's staff who will represent a wide range of disciplines.

[WHO, Germany open Hub for Pandemic and Epidemic Intelligence in Berlin](#) (01 Sept 2021)

38th WHO Regulatory Update on COVID-19

Event recording is available at: [Inauguration of the WHO Hub for Pandemic and Epidemic Intelligence](#) (01 Sept 2021)

Other international initiatives:

- [Prezode](#), France: an international One Health initiative supporting emergence risk reduction strategies for zoonotic infectious diseases
- [Pandemic Prevention Institute](#), USA: expanding genomic sequencing and data sharing capacity across the world, collaborating across sectors, and partnering with existing and emerging global surveillance systems to give communities everywhere the tools they need to be effective first-responders in an outbreak.
- Pandemic Institute: to be launched soon in Liverpool

WHO compendium of innovative health technologies

Health technologies, specially [medical devices](#) are essential for a functioning health system. The response to the global COVID-19 pandemic crisis has exacerbated the need for rapid evidence based assessments of [innovative health technologies](#) to ensure safe and appropriate use.

Thus, the objectives of the 2021 compendium are to:

1. Select innovative technologies that can have an immediate or future impact on the COVID-19 preparedness and response, have the potential to improve health outcomes and quality of life, and/or offer a solution to an unmet medical/health technology need by evaluating their appropriateness, quality, and safety;
2. Shed light on advantages and challenges associated with the adoption of innovative health technologies in low-resource settings;
3. Acknowledge some success stories and, at the same time, raise awareness of the pressing need for appropriate and affordable solutions and encourage more innovative efforts in the field;
4. Encourage greater interaction among Ministries of Health, procurement offices, donors, technology developers, manufacturers, clinicians, academics and the general public to ensure greater investment in appropriate health technology and a move toward universal access to essential health technologies;
5. Support informed procurement decisions by NGOs, governments, and other stakeholders.

[WHO releases new compendium of innovative health technologies for COVID-19 and other priority diseases](#) (31 Aug 2021)

[WHO compendium of innovative health technologies for low-resource settings 2021: COVID-19 and other health priorities](#) (31 Aug 2021)

Infodemic Signal Detection during the COVID-19 pandemic

A new WHO paper, in the new journal JMIR Infodemiology, describes the development of a social listening public health taxonomy for COVID-19 and how a developed methodology is applied to identify relevant points of confusion, harmful narratives, and key questions from public online conversations. It also outlines how the approach can be easily adapted to other health topics and can be used to navigate the information overload that can occur during an infodemic.

Rather than only reacting to viral rumours, this approach gives decision-makers relevant information quickly and helps experts more quickly spot information voids so they can be addressed more proactively before such vacuums become filled with rumours when time is of the essence during a health emergency.

The [WHO Early AI-Supported Response with Social Listening \(EARS\) platform](#) builds on this

taxonomy to move from a weekly analysis to daily automated classification of publicly shared questions and concerns for 25 pilot countries.

[Infodemic Signal Detection During the COVID-19 Pandemic](#) (18 Aug 2021)

[Watch the interview about the paper](#) presented by Tim Nguyen and Dr Jennifer Joe

[Early AI-supported Response with Social Listening](#)

WHO report on AI in health and six guiding principles for its design and use

The WHO guidance on Ethics & Governance of Artificial Intelligence (AI) for Health is the product of eighteen months of deliberation amongst leading experts in ethics, digital technology, law, human rights, as well as experts from Ministries of Health. While new technologies that use artificial intelligence hold great promise to improve diagnosis, treatment, health research and drug development and to support governments carrying out public health functions, including surveillance and outbreak response, such technologies, according to the report, must put ethics and human rights at the heart of its design, deployment, and use.

The report identifies the ethical challenges and risks with the use of AI of health, six consensus principles to ensure AI works to the public benefit of all countries.

Six consensus principles are as follows:

1. Protect autonomy
2. Promote human well-being, human safety and the public interest
3. Ensure transparency, explainability and intelligibility
4. Foster responsibility and accountability
5. Ensure inclusiveness and equity
6. Promote AI that is responsive and sustainable

It also contains a set of recommendations that can ensure the governance of AI for health maximizes the promise of the technology and holds all stakeholders – in the public and private sector – accountable and responsive to the healthcare workers who will rely on these technologies and the communities and individuals whose health will be affected by its use.

WHO's report cautions against overestimating the benefits of AI for health, especially when this occurs at the expense of core investments and strategies required to achieve universal health coverage and points out that opportunities are linked to challenges and risks, including unethical collection and use of health data; biases encoded in algorithms, and risks of AI to patient safety, cybersecurity, and the environment.

[WHO issues first global report on Artificial Intelligence \(AI\) in health and six guiding principles for its design and use](#) (28 June 2021)

[Ethics and governance of artificial intelligence for health](#) (28 June 2021)

Alignment of approaches by regulators

ICMRA Innovation Network report on AI

Recommendations to help regulators to address the challenges that the use of artificial intelligence (AI) poses for global medicines regulation have been published by ICMRA. AI technologies are increasingly applied in medicines development. Opportunities to apply AI occur across all stages of a medicine's lifecycle: from target validation and identification of biomarkers to annotation and analysis of clinical data in trials, pharmacovigilance and clinical use optimization. This range of applications brings with its regulatory challenges, including the transparency of the algorithms themselves and their meaning, as well as the risks of AI failures and the wider impact these would

have on its uptake in pharmaceutical development and ultimately on patients' health.

To elucidate some of the challenges AI use poses for global medicines regulation, two hypothetical case studies were developed by ICMRA members. These examples were then used to 'stress test' the regulatory systems of ICMRA members to discover the areas where change may be needed. This report details the methods used and the findings.

[ICMRA Horizon Scanning Assessment Report – Artificial Intelligence](#) (16 Aug 2021)

ICMRA recommendations on CTD for track and trace systems for medical products

ICMRA has published recommendations on Common Technical Document (CTD) to facilitate the use of track and trace systems for medical products at a global level. The recommendations emphasize that the interoperability of track and trace systems for medical products helps to protect public health by improving information sharing in case of quality defects, reducing shortages, contributing to the fight against falsified medicines and supporting pharmacovigilance activities. A common understanding of these potential benefits of interoperability is fundamental to promoting global planning and implementation of interoperable systems for medicines. Technical features which would allow national/regional systems to be interoperable are discussed including identifiers of products, standards, data elements, data carriers, transitional and master data, traceability, and information exchange.

Development of these recommendations was carried out in parallel to the development of a policy paper on national traceability systems for medical products by WHO. ICMRA and WHO have worked in close cooperation in developing their respective documents, which include common parts (e.g. glossary).

[ICMRA Recommendations on common technical denominators for track and trace systems to allow for interoperability](#) (06 Aug 2021)

Evaluation of the quality, safety and efficacy of mRNA vaccines

Comments by 17 Sept 2021

Following the virtual WHO informal consultation meeting held on 20-22 April 2021 on regulatory evaluation of mRNA vaccines, a drafting group has further developed the document taking into consideration the discussions at the meeting. As a next step, the 2nd round of public consultation is now open for public comments.

This document provides information and regulatory considerations regarding key aspects of the manufacture and quality control, and nonclinical and clinical evaluation, of preventive mRNA vaccines for human use. Although the most advanced vaccines in this class are COVID-19 vaccines and are used as examples in the text, the document should not be taken as providing guidance specific only to COVID-19 vaccines. However, in light of the current COVID-19 pandemic and corresponding speed of mRNA vaccine development, the document is intended to provide special considerations for this class of preventive mRNA vaccine as rapidly as possible.

It should nevertheless be noted that there remain knowledge gaps in the scientific understanding of the pathogenesis of COVID-19 and of precisely what level of immunogenicity is needed for a successful, broadly relevant and durable COVID-19 vaccine. These knowledge gaps are currently being addressed by ongoing research and development efforts.

The comments received will be reviewed by the Expert Committee on Biological Standardization at its meeting during 18-22 October 2021 for advice regarding the next steps.

[Evaluation of the quality, safety and efficacy of messenger RNA vaccines for the prevention of infectious diseases: regulatory considerations](#) – comments by 17 Sep 2021

[Comment form](#)

Please send comments to Tiequn Zhou, at: zhout@who.int.

WHO-Listed Authorities: Operational guidance on evaluation and designation

Comments by 19 Sept 2021

The benefits of a robust, transparent, evidence-based, global system for recognizing regulatory excellence serve the interests of a variety of stakeholders that are committed to promoting access to safe, effective, and quality medical products.

To meet this need, the introduction of a framework for designating and publicly listing a regulatory authority as a WHO-listed authority (WLA) is proposed to provide a transparent and evidence-based pathway for regulatory authorities to be globally recognized as meeting WHO and other international recognized standards and practices.

[Policy brief: Evaluating and publicly designating regulatory authorities as WHO listed authorities](#) (21 Jun 2021)

[Arabic](#), [Chinese](#), [French](#), [Russian](#), [Spanish](#)

A draft guideline that describes the process for evaluating and publicly designating regulatory authorities and regional regulatory systems as WLAs has been published for comment.

[Operational guidance: evaluating and publicly designating regulatory authorities as WHO-listed authorities](#) (330 pages) – comments by 19 Sep 2021

[Table for comments](#)

Comments to be sent to Hiiti Sillo silloh@who.int with Cc to Anna Laura Salvati salvatia@who.int

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.

IVDs eligible for EUL submission

Currently, the following IVDs are eligible for EUL submission:

- assays for the detection of SARS-CoV-2 nucleic acid (multiplex assays, detecting more than one viral target)
- rapid diagnostic tests for the detection of SARS-CoV-2 antigens; other platforms to detect SARS-CoV-2 antigen will be considered on a case-by-case basis.

Applicants are asked to submit their applications for assessment based on WHO instructions and requirements for NAT and Ag detection RDTs:

[Instructions and requirements for EUL Submission: IVDs detecting SARS-CoV-2 nucleic acid or antigen](#)

As of 7th September, 28 products have been listed as eligible for WHO procurement among a total of 154 expressions of interest received (65 for NAT assays, 41 for antibody detection assays and 48 for antigen detection RDTs); 44 products were not accepted under WHO Emergency Use Listing for SARS-CoV-2.

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

[IVDs not accepted for EUL listing](#) (04 Aug 2021)

[Status of each EUL application](#) (07 Sept 2021)

Therapeutics

WHO's Solidarity clinical trial enters a new phase with three new candidate drugs

WHO has announced the next phase in its Solidarity trial: Solidarity PLUS will enroll hospitalized patients to test three new drugs in COVID-19 patients. These therapies - artesunate, imatinib and infliximab – were selected by an independent expert panel for their potential in reducing the risk of death in hospitalized COVID-19 patients. They are already used for other indications: artesunate is used for severe malaria, imatinib for certain cancers, and infliximab for diseases of the immune system such as Crohn's Disease and rheumatoid arthritis. These drugs were donated for the trial by their manufacturers.

The Solidarity PLUS trial is a platform trial that represents the largest global collaboration among WHO Member States. It involves thousands of researchers in over 600 hospitals in 52 countries, 16 more countries than the first phase of trials. This allows the trial to assess multiple treatments at the same time using a single protocol, recruiting thousands of patients to generate robust estimates on the effect a drug may have on mortality--even moderate effects.

Artesunate is derivative of artemisinin, a drug extracted from the herb *Artemisia annua*, and is used to treat malaria. The WHO COVID-19 Therapeutics Advisory Group recommended evaluating the anti-inflammatory properties of artesunate. In the trial, it will be administered intravenously for 7 days, using the standard dose recommended for the treatment of severe malaria.

Imatinib is a small molecule tyrosine kinase inhibitor used to treat certain cancers. A randomized clinical trial performed in the Netherlands reported that imatinib might confer clinical benefit in hospitalized COVID-19 patients, in the absence of safety issues. In the trial, it will be administered orally, once daily, for 14 days. The dose used is the standard maintenance dose, which is at the lower end of the dose patients with haematological malignancies are given over extended periods.

Infliximab is a TNF alpha inhibitor, a chimeric monoclonal antibody that recognizes human TNF alpha and is used to treat diseases of the immune system. In the trial, it will be administered intravenously as a single dose. The dose used is the standard dose that patients with Crohn's Disease are given over extended periods.

[WHO's Solidarity clinical trial enters a new phase with three new candidate drugs](#) (11 Aug 2021)

[SOLIDARITY TRIAL PLUS: An international randomized trial of additional treatments for COVID-19 in hospitalized patients who are all receiving the local standard of care](#) (trial registry)

Additional information on clinical trials

[International Clinical Trials Registry Platform](#) (ICTRP)

Information on clinical trials and trial registration. Clinical trials registered with the ICTRP platform can be searched and details of COVID-19 clinical trials can be downloaded in csv and xml formats.

[Mapping and systematic review of Covid-19 trials](#) (COVID-19 - living NMA initiative)

A real-time monitoring and mapping of new evidence for treating and preventing COVID-19, with living mapping of trials and living synthesis of published trials.

[Global Coronavirus COVID-19 Clinical Trial Tracker](#) (Cytel)

An interactive dashboard of clinical trials on COVID-19 that can be explored by type of product, trial status and country.

Vaccines

WHO COVID-19 Vaccines Dashboard

As of 08 September, nearly 5.5 billion vaccine doses have been administered. However, 80% of vaccines have been administered in high and upper-middle income countries. COVAX has shipped over 243 million doses to 139 countries and economies.

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

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

COVID-19 vaccine booster doses

WHO calls for global moratorium on booster doses

Although over 5.5 billion vaccine doses have now been administered, 80% of these doses are used in high- and upper-middle income countries. On average, WHO African region has managed to vaccinate only 3% of population with at least one dose and 2% with full doses. For this reason, WHO calls for an extension of the moratorium on booster doses at least till end of 2021 to ensure every country to vaccinate at least 40% of its population.

[WHO Director-General's opening remarks at the media briefing on COVID-19 - 8 September 2021](#) (08 Sept 2021)

WHO consultation on COVID-19 vaccines research – 13 August 2021

In continuation to the scientific discussions on COVID-19 vaccines research, WHO R&D Blueprint organized a consultation on the state of the art and best research methods to evaluate existing, modified and new COVID-19 vaccines. The objectives of this consultation were to review the available evidence on the efficacy and effectiveness of vaccines being deployed in terms of:

- Emerging variants effect on protection levels
- Duration of protection
- Safety of booster vaccines
- Research to evaluate various delivery strategies

During the consultation, experts debated the methodological strengths and limitations of existing data and the potential designs to generate additional data leading to evidence-based decisions. More than 2000 participants worldwide heard expert presentations and discussions on:

- Available randomized and non-randomized data on COVID-19 vaccine efficacy and effectiveness against different variants, and initial assessment of risk of bias and confounding.
- Available randomized and non-randomized data on COVID-19 vaccines' duration of protection and methodological challenges with its interpretation.
- Vaccine developers update about their current progress and plans to generate evidence to inform discussions on the need and pertinence of booster vaccines.
- Opportunities and designs to be considered in the generation of additional data.

Conclusions:

Despite rapid development of effective vaccines, there is still a worldwide crisis with the highly transmissible Delta variant. To date, there is no compelling evidence to suggest that vaccine effectiveness against severe hospitalization and death is waning. Key questions remain about the need for and assessment of booster doses related to the immune response, vaccine efficacy against Delta from randomized and non-randomized studies, and the safety of booster doses. Decisions on booster doses should be based on scientific evidence and equity and should be

transparently made based on publicly available data.

The WHO plans to review and update shortly the Target Product Profile for COVID-19 vaccines and address the questions raised during this consultation. Mass vaccination has not successfully prevented outbreaks worldwide and the need to evaluate different strategies is critical. Implementation of a coordinated research agenda will allow us all, working together, to bring the world closer to ending the pandemic for everybody.

[Report](#) with links to presentations

[Agenda and presentations](#)

SAGE interim statement (points to consider) on additional vaccine dose

The SAGE COVID-19 Vaccines Working Group is reviewing the emerging evidence on the need for and timing of an additional vaccine dose (booster dose) for the currently available COVID-19 vaccines which have received Emergency Use Listing (EUL).

The introduction of booster doses should be firmly evidence-driven and targeted to the population groups in greatest need. The rationale for implementing booster doses should be guided by evidence on waning vaccine effectiveness, in particular, a decline in protection against severe disease in the general population or in high-risk populations, or due to a circulating VOC. The rationale for booster doses may differ by vaccine product, epidemiological setting, risk group, and vaccine coverage rates. To date, the evidence remains limited and inconclusive on any widespread need for booster doses following a primary vaccination series.

The interim statement outlines the data required to assess the need for booster doses; to assess the performance of booster doses; and additional considerations such as global vaccine supply and global and national equity.

WHO is carefully monitoring the situation and will continue to work closely with countries to obtain the data required for policy recommendations.

[Interim statement on COVID-19 vaccine booster doses](#) (10 Aug 2021)

WHO Science in 5 on booster shots

What does evidence say so far about safety and effectiveness of booster shots? Are there groups who may need them? Should the world be considering booster shots at this stage of the pandemic? Dr Katherine O'Brian explains in Science in 5 this week.

[WHO Science in 5: Episode #53 - COVID-19: Booster Shots](#) (11 Sept 2021)

Medicines and Healthcare products Regulatory Agency (MHRA), UK

The MHRA has issued a statement that the COVID-19 vaccines made by Pfizer and AstraZeneca can be used as safe and effective booster doses. The current supply of these COVID-19 vaccines in the UK has been authorised on an emergency use basis by the MHRA under Regulation 174 of the Human Medicine Regulations 2012 and changes have been made to the Regulation 174 Product Information only. Both vaccines are also authorised under Conditional Marketing Authorisations (CMAs) but changes to these would follow a different procedure. Vaccines covered by CMAs can also be used as part of a deployment programme via "off-label" use under a prescriber's direction.

[MHRA statement on booster doses of Pfizer and AstraZeneca COVID-19 vaccines](#) (09 Sept 2021)

EMA

In a joint statement with the ECDC, the EMA consider there is no urgent need for the

administration of booster doses of vaccines to fully vaccinated individuals in the general population. Evidence on vaccine effectiveness and duration of protection shows that all vaccines authorized in the EU/EEA are currently highly protective against COVID-19-related hospitalization, severe disease and death, while about one out of three adults in the EU/EEA over 18 years is still currently not fully vaccinated. In this situation, the priority now should be to vaccinate all those eligible individuals who have not yet completed their recommended vaccination course.

The EMA advise it is important to distinguish between booster doses for people with normal immune systems and additional doses for those with weakened immune systems. Some studies report that an additional vaccine dose can improve the immune response in immunocompromised individuals, such as organ transplant recipients whose initial responses to vaccination were low. In such cases, the option of administering an additional dose should be considered already now. Consideration could also be given to providing an additional dose, as a precautionary measure, to older frail individuals, in particular those living in closed settings such as residents of long-term care facilities.

[ECDC and EMA highlight considerations for additional and booster doses of COVID-19 vaccines](#) (02 Sept 2021)

[EMA Regular press briefing on COVID-19](#) (09 Sept 2021), including statements on booster doses / additional doses and update on evaluation status of treatments

Ministry of Health, Israel

The administration of the third vaccine dose of Pfizer-BioNTech COVID-19 Vaccine tozinameran BNT162b2 to adults aged 30 and older in Israel was approved following the recommendation by the Israel's COVID-19 Vaccination Advisory Board and the Pandemic Response Team as well as the recommendation by the members of the Vaccine Safety and Effectiveness Surveillance Committee.

The Ministry of Health Pharmaceutical Administration (the NRA) extended their Emergency Use Authorization to enable the use of the vaccine for this purpose.

[Third Dose of the COVID-19 Vaccine – Now Also for Everyone 30 Years of Age and Older](#) (24 Aug 2021)

US FDA

The US FDA has amended the emergency use authorizations (EUAs) for both the Pfizer-BioNTech COVID-19 Vaccine and the Moderna COVID-19 Vaccine to allow for the use of an additional dose in certain immunocompromised individuals, specifically, solid organ transplant recipients or those who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise. People who are immunocompromised in a manner similar to those who have undergone solid organ transplantation have a reduced ability to fight infections and other diseases, and they are especially vulnerable to infections, including COVID-19. The FDA evaluated information on the use of a third dose of the Pfizer-BioNTech or Moderna Vaccines in these individuals and determined that the administration of third vaccine doses may increase protection in this population.

[FDA press announcements on additional vaccine dose for certain immunocompromised individuals](#) (12 Aug 2021)

A virtual meeting of FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC) will be held on 17 September to discuss the matter of additional doses of COVID-19 vaccines and specifically to discuss the Pfizer-BioNTech supplemental Biologics License Application for administration of a third ("booster") dose of Comirnaty (COVID-19 Vaccine, mRNA) in individuals 16 years of age and older.

Background material will be made available to the public, including the meeting agenda and committee roster, no later than two business days before the meeting.

[FDA announcement on Advisory Committee Meeting to Discuss Pfizer-BioNTech's Application for COVID-19 Booster](#) (01 Sept 2021)

FDA VRBPAC's meeting on 17 Sept 2021: [information site](#)

Dose-sparing strategies for COVID-19 vaccines (fractionated vaccine doses)

SAGE interim statement (points to consider)

The SAGE COVID-19 Vaccines Working Group is reviewing the role of fractionating doses as a dose-sparing strategy in light of global vaccine supply constraints. All current COVID-19 vaccines have undergone dose-finding studies in their clinical development. The potential for dose-reduction may depend on the individual vaccine and its platform technology (e.g., mRNA, vectored or inactivated virus). Reducing the amount of vaccine given (e.g., 1/2, 1/3 or 1/5) could theoretically be considered with various options: fractionated doses for the priming schedule, or fractionated doses for any booster doses should booster doses prove to be needed in the future. However, policy recommendations for reducing doses should only be made after an extensive evidence review in terms of immunogenicity and safety. Additional clinical studies would therefore be needed to inform policy.

Several questions that need to be addressed are outlined. SAGE encourages further research such as prospective randomized trials to assess the safety and immunologic non-inferiority of fractional versus full doses given for the priming schedule, and as a single booster vaccination in primed and unprimed subjects. In addition, vaccine effectiveness and safety studies should be instituted as part of the follow-up. Programmatic and operational considerations should be considered from the start of such research programmes.

SAGE considers there is currently insufficient evidence to recommend the use of fractional doses. Any use of a fractional dose now constitutes an off-label use of the vaccine.

[Interim statement on dose-sparing strategies for COVID-19 vaccines \(fractionated vaccine doses\)](#) (10 Aug 2021)

Heterologous priming for COVID-19 vaccines

SAGE interim statement (points to consider)

The SAGE COVID-19 Vaccines Working Group is also reviewing the emerging evidence on the use of heterologous priming schedules (also known as mix and match schedules). In a heterologous priming schedule, the second dose uses a different vaccine product than the first dose. By contrast, heterologous boosting refers to the administration of a vaccine from a different vaccine platform from the vaccine that was used to complete the primary vaccine series. The interim statement here pertains only to heterologous priming and not heterologous boosting.

The most common reason for considering a heterologous COVID-19 vaccine as second priming dose is lack of availability of the same vaccine in settings with limited vaccine supply or unpredictable supply. Interchangeability of vaccine products would therefore allow for added programmatic flexibility. There are other reasons to investigate the utility of heterologous priming such as reducing reactogenicity, increasing immunogenicity and enhancing vaccine effectiveness. Heterologous priming should only be instituted if supportive evidence is available.

In general, for COVID-19 vaccines listed for emergency use by WHO with a 2-dose primary series schedule, WHO recommends that the same vaccine product should be used for both doses. At present, mix-and-match schedules constitute off-label use of respective vaccines and as such should only be used if benefits outweigh the risks such as in situations of interrupted vaccine supply.

Many clinical studies of various vaccine combinations and schedules are currently ongoing. Studies reported so far are encouraging, but they require cautious interpretation given the limited sample sizes and lack of follow up, especially related to safety data, and the uncertain relevance of

immunological readouts in relation to clinical impact. SAGE will review these data as they become available and update the recommendations accordingly.

[Interim statement on heterologous priming for COVID-19 vaccines](#) (10 Aug 2021)

WHO Workshop on correlates of protection for COVID-19 vaccines

There is a need for robust data to help to swiftly evaluate updated versions of available vaccines against emerging strains and new vaccines against current and emerging variants. Immunobridging could contribute to the evaluation of modified vaccines, to bridge efficacy to additional populations and against variants of concern, and to better understand the duration of protection.

Continuing the [May 2021 WHO consultation held on Correlates of Protection](#), WHO R&D Blueprint organized another consultation on 3rd September to discuss emerging evidence that moves towards the establishment of correlates of protection for COVID-19 vaccines. Vaccine developers and researchers presented new data and current research plans. The consultation included deliberations on specific components of the immune response that may be correlated with clinical protection and trial and statistical methods to generate and analyze available evidence.

A regulatory session covered views of regulatory agencies on whether emerging data will allow increased reliance on vaccine immune responses for regulatory decision-making.

Conclusions:

Despite the complexity of the immune system, there has been a substantial advancement in identifying immune markers that predict protection for many vaccines. Randomized trials showed variable effectiveness against beta and delta variants, generally lower than against previous variants in the same studies, but data show that vaccines are still effective against these variants. Observational studies are subject to important biases, but in general support the conclusion that vaccines are effective against the delta variant, both for symptomatic and for severe disease. Efficacy of existing vaccines against severe disease is high and it is greater than against symptomatic disease, regardless of variants, type of vaccines, time since vaccination.

If vaccines are made available using immune biomarkers, safety data and post-deployment confirmation of effectiveness and safety data are required. More investigation is needed for relevance of quantitative antibody response vs. qualitative response, protection from infection vs. severe disease, relevance for targeted recommendations, duration of protection, animal studies. Additional clinical data could also help to support use of correlates in heterologous boosting situation.

Practical aspects of Immunobridging – availability and selection of comparator vaccines, criteria for comparisons, must be considered. Additional supportive data may be needed to support some decisions that may be made based on neutralizing antibody responses. Key considerations include variants, duration of immunity, severity of disease, assay standardization. Importance of post-authorization confirmatory studies.

A meeting report will be available shortly.

[Agenda](#) and [presentations](#)

Pfizer BioNtech tozinameran (COVID-19 mRNA vaccine)

WHO EUL:

WHO has extended its EUL recommendation for individuals 12 through 15 years old.

Updated information will be made available on the [WHO Prequalification Covid-19 vaccines website](#) in the week of 13th September 2021.

US FDA:

The U.S. Food and Drug Administration approved the Pfizer-BioNTech COVID-19 Vaccine, Comirnaty, for the prevention of COVID-19 disease in individuals 16 years of age and older. The approval builds on the extensive data and information previously submitted that supported an Emergency Use Authorization (EUA), such as preclinical and clinical data and information, as well as details of the manufacturing process, vaccine testing results to ensure vaccine quality, and inspections of the sites where the vaccine is made. The agency conducts its own analyses of the information in the submission from the manufacturer to make sure the vaccine is safe and effective and meets the FDA's standards for approval.

The vaccine also continues to be available under EUA for individuals 12 through 15 years of age and for the administration of a third dose in certain immunocompromised individuals.

[FDA Approves First COVID-19 Vaccine](#) (23 Aug 2021)

EMA:

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) continuously monitors and assesses emerging worldwide safety data and regularly provide updates to the public. No new updates to the product information are currently recommended as of 8th September.

PRAC has started assessments to determine whether erythema multiforme (a hypersensitivity (allergic) reaction with characteristic round skin lesions which may also affect mucous membranes in internal body cavities) and of glomerulonephritis (inflammation of filters in the kidneys) and nephrotic syndrome (kidney disorder causing the kidneys to leak too much protein in the urine) to establish whether they may be side effects of tozinameran.

Further data and analyses have been requested from the marketing authorization holder to support the ongoing assessment by PRAC.

[EMA COVID-19 vaccine safety update, COMIRNATY](#) (08 Sept 2021)

Moderna (mRNA 1273) elasomeran

EMA:

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) continuously monitors and assesses emerging worldwide safety data and regularly provide updates to the public. No new updates to the product information are currently recommended as of 8th September.

PRAC has started assessments to determine whether erythema multiforme (a hypersensitivity (allergic) reaction with characteristic round skin lesions which may also affect mucous membranes in internal body cavities) and of glomerulonephritis (inflammation of filters in the kidneys) and nephrotic syndrome (kidney disorder causing the kidneys to leak too much protein in the urine) to establish whether they may be side effects of tozinameran.

Further data and analyses have been requested from the marketing authorization holder to support the ongoing assessment by PRAC.

[EMA COVID-19 vaccine safety update, SPIKEVAX Moderna Biotech Spain, S.L.](#) (08 Sept 2021)

AstraZeneca COVID-19 vaccine (ChAdOx1-S) [recombinant]

EMA:

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) continuously monitors and assesses emerging worldwide safety data. Safety updates are regularly provided to the public. As a result of the latest review, Guillain-Barré syndrome (GBS) has been added to the product information as a very rare side effect. Pain in legs and arms or stomach and influenza-like

symptoms have also been included in the product information as side effects.

[EMA COVID-19 vaccine safety update VAXZEVRIA AstraZeneca AB](#) (08 Sept 2021)

Janssen COVID-19 Vaccine (Ad26.COV2-S [recombinant])

EMA:

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) continuously monitors and assesses emerging worldwide safety data. Safety updates are regularly provided to the public. As a result of the latest review, PRAC finalized updates to the product information to include swollen lymph nodes, unusual or decreased feeling in the skin, tinnitus, diarrhoea and vomiting as side effects.

[EMA COVID-19 vaccine safety update JANSSEN Janssen-Cilag International NV](#) (08 Sept 2021)

In its August update, Guillain-Barré syndrome (GBS) was added to the product information as a very rare side effect and also recommended updating the product information to include immune thrombocytopenia (ITP), dizziness and tinnitus as side effects.

Although cases of GBS after vaccination with COVID-19 Vaccine Janssen have been reported very rarely, healthcare professionals should be alert to signs and symptoms of GBS, in view of the seriousness of this condition, to allow for early diagnosis, supportive care and treatment.

ITP is a condition in which the immune system mistakenly attacks and destroys blood cells called platelets that are needed for normal blood clotting. Over 21 million people had received the vaccine globally. A total of 120 worldwide cases of suspected ITP were reported, by 18 June 2021, of which 27 cases were reported from clinical trials and 93 spontaneously from vaccination campaigns; of these, 4 cases had a fatal outcome.

PRAC concluded that dizziness and tinnitus (ringing or other noises in one or both ears) should be added to the product information as side effects of COVID-19 Vaccine Janssen based on an analysis of 1,183 worldwide cases of dizziness identified from spontaneous reports received through 31 May 2021. Regarding tinnitus, 6 cases observed in clinical trials and 108 worldwide cases identified by the marketing authorisation holder, reported through 18 May 2021, during monitoring spontaneous reports were investigated.

[EMA COVID-19 vaccine safety update JANSSEN Janssen-Cilag International NV](#) (11 Aug 2021)

Zyklus Cadila (ZyCoV-D) DNA vaccine

Central Drugs Standard Control Organization (CDSCO), India's drug regulator, has granted emergency use authorization for Zyklus Cadila's COVID-19 vaccine, the world's first DNA vaccine against the coronavirus, in adults and children aged 12 years and above. Unlike most COVID-19 vaccines, which need two doses or even a single dose, ZyCoV-D is administered in three doses. The vaccine is administered using a needle-free applicator as opposed to traditional syringes. The authorization of ZyCoV-D was based on an efficacy rate of 66.6% in a clinical trial in India of over 28,000 volunteers nationwide.

[CDSCO Tweet on emergency use approval of ZyCoV-D](#) (20 Aug 2021)

[Phase III clinical trial registry Zyklus Cadila](#)

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

38th WHO Regulatory Update on COVID-19







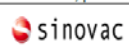
been accepted; if a pre-submission meeting has been held; if the dossier has been accepted for review; the status of the assessment; and the anticipated decision date.

Please visit the site regularly for the [latest updated version](#).

Below is version 08 September 2021.

• Vaccines	Guidance document 08 September 2021
------------	--

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

#	Manufacturer / WHO EUL holder Name / platform	EUL Assessment			Post-EUL activities
		NRA of Record	Status of assessment	Decision date	Other EUL commitments/changes
1.	 BNT162b2/Comirnaty Tozinameran (INN) Nucleoside modified mRNA	EMA	Core data finalized	31 Dec 2020	<ul style="list-style-type: none"> Clinical and CMC updates Extension of storage conditions at 2-8°C from 5 days to 31 days. New indication (12-15 y): EUL recommended on 08 Sept 2021 (Update to be issued in week 13 Sept)
		EMA	Baxter Oncology, Germany (DP) Novartis, Switzerland Mibe, Darmapharm Germany (DP)	02 Jul 2021 08 Jul 2021 16 Jul 2021	
			Diluent suppliers: Pfizer Perth, Australia Fresenius Kabi, USA	18 Jun 2021	
		US FDA	Pharmacia & Upjohn (Kalamazoo, MI) USA Hospira (McPherson, KS) USA	16 Jul 2021	
2.	 AZD1222 Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2	EMA	Core data finalized	16 Apr 2021	<ul style="list-style-type: none"> Clinical and CMC updates
			Finalized: SK-Catalent Wuxi (DS) Chemo Spain	16 Apr 2021 30 Apr 2021 04 Jun 2021	
		MFDS Korea	Finalized	15 Feb 2021	<ul style="list-style-type: none"> Clinical and CMC updates
		MHLW/PMDA Japan	Finalized	09 July 2021	
3.	TGA Australia	Finalized	09 July 2021		
4.		Finalized	09 July 2021		
5.		Finalized	09 July 2021		
6.	Canada (donation)	Finalized	27 Aug 2021		
7.	 Covishield (ChAdOx1_nCoV-19) Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2	DCGI India	Finalized	15 Feb 2021	<ul style="list-style-type: none"> Clinical and CMC updates, Extension of shelf life at 2-8°C 06 to 09 months
8.	 Ad26.COV2.S Recombinant, replication-incompetent Ad type 26 vectored Vx encoding the SARS Spike protein	EMA	Core data finalized (US +NL sites)	12 Mar 2021	<ul style="list-style-type: none"> Clinical and CMC updates New storage conditions at 2-8°C for 4.5 months – recommended New storage conditions at 2-8°C for 6 months (from US sites)
		EMA	- Aspen SVP, South Africa (DP) - Catalent Agnani, Italy (DP) - Catalent Indiana, USA (DP) - Grand River, Michigan USA (DP) - Merck, Durham, UK (DS), - West Point/PA, USA (DP)	25 Jun 2021 02 Jul 2021 02 Jul 2021 02 Jul 2021 - As submitted	
			Finalized	30 Apr 2021	
			ModernaTX, Inc (Norwood), USA	06 Aug 2021	
9.	 mRNA-1273 mRNA-based vaccine encapsulated in lipid nanoparticle (LNP)	US FDA	ModernaTX, Inc (Norwood), USA	06 Aug 2021	<ul style="list-style-type: none"> Clinical and CMC updates Support for international shipments Documentation requested by countries: Certificate of Analysis – now provided regularly.
10.	 SARS-CoV-2 Vaccine (Vero Cell) Inactivated, produced in Vero cells	NMPA China	Finalized	07 May 2021	<ul style="list-style-type: none"> Clinical and CMC updates New sites and presentation
11.	 CoronaVac Inactivated, produced in Vero cells	NMPA China	Finalized	01 Jun 2021	<ul style="list-style-type: none"> Clinical and CMC updates New sites, presentation, indication

#	Manufacturer / WHO EUL holder	NRA of Record	Status	Pre-submission meeting	Rolling data
12.	 Human Adenovirus Vector-based Covid-19 vaccine	Russian NRA	Additional information submitted	Several meetings have been and continue to be held.	"Rolling" data of clinical and CMC has started, but incomplete On hold, awaiting completion of rolling submission
13.	 CanSinoBio	NMPA China	✓	✓	Rolling data started 09 Aug 2021
14.	 Bharat Biotech, India Whole-Virion Inactivated Vero Cell	DCGI India	✓	✓	Rolling data started 06 Jul 2021
15.	 Recombinant nanoparticle prefusion spike protein formulated with Matrix-M™ adjuvant.	EMA	✓	✓	Rolling data started 20 Aug 2021
16.	 Sinopharm / WIBP ² Inactivated, produced in Vero cells	NMPA China	✓	✓	Rolling data started 23 July 2021
17.	 Sanofi Pasteur Recombinant, adjuvanted	EMA	✓	✓	Sept-Nov 2021
18.	 NOVAVAX Recombinant nanoparticle prefusion spike protein formulated with Matrix-M™ adjuvant	DCGI India	✓	✓	Rolling data starting
19.	 LureVac mRNA-based vaccine encapsulated in lipid nanoparticle (LNP)	EMA	✓	Q4 2021	

38th WHO Regulatory Update on COVID-19

20.	Clover Biopharmaceuticals	NMPA China	✓	Being planned	
21.	Vector State Research Centre of Virology and Biotechnology Peptide antigen	Russian NRA	Letter received not EOI. Reply sent on 15/01/2021	Q4 2021	
22.	Zhifei Longcom, China Recombinant protein subunit	NMPA China	Response to 2 nd EOI sent 29 Jan 2021. Additional info received.	Being planned	
23.	IMBCAMS, China Inactivated	NMPA China	Not accepted, still under initial development		
24.	BioCubaFarma - Cuba SARS-CoV-2 spike protein conjugated chemically to meningococcal B or tetanus toxoid or Aluminum	CECMED Cuba	Awaiting information on strategy and timelines for submission.		

Vaccination guidance and policy updates:

COVID-19 immunization in refugees and migrants: principles and key considerations

Although everyone is affected by the COVID-19 pandemic, the impact is not shared equally. Refugees and migrants are more likely to experience a higher burden of COVID-19 infection and be disproportionately represented in cases, hospitalizations and deaths.

This interim guidance provides information on key challenges and barriers to accessing vaccination services, such as stigma, exclusion and mistrust, resulting in low vaccine uptake and hesitancy; lack of financial means and information; fears regarding cost, safety and deportation or detention. It highlights principles such as global equity for vaccine distribution, national equity and equal respect. It also emphasizes the importance of community engagement and communication to build trust and counter misinformation, fake news and misconceptions, as well as the importance of developing innovative approaches for vaccine delivery.

According to the results of the WHO review of 104 National Deployment and Vaccination Plans (NDVPs) from February to March 2021, 72% of these NDVPs did not explicitly include migrants and only 17% explicitly included migrants in irregular situations.

Since then, significant positive development has been made and refugees and asylum seekers have begun to receive vaccinations in 101 of the 162 countries monitored by the United Nations High Commissioner for Refugees. However, coverage for migrants are far from universal, several countries reported the inclusion of regular migrants in their NDVPs and the vaccine roll out but migrants in irregular situations in many countries were not.

Although everyone is affected by the COVID-19 pandemic, the impact is not shared equally. The COVID-19 pandemic has exposed vulnerabilities and exacerbated existing inequalities within and between low- and high-income countries. These inequalities have had the biggest impact on the poorest and most vulnerable people, which may include refugees and migrants (particularly those in irregular situations). These groups often have vulnerabilities that are heightened by this pandemic.

[Covid-19-immunization in refugees and migrants: Principles and key considerations. interim guidance](#) (31 Aug 2021)

[WHO News on issuing an interim guidance on Covid-19 immunization in refugees and migrants](#) (03 Sept 2021)

[ECDC: Reducing COVID-19 transmission and strengthening vaccine uptake among migrant populations](#) (03 Jun 2021)

WHO SAGE Updates

[The Pfizer BioNTech \(BNT162b2\) COVID-19 vaccine: What you need to know](#) (02 Sept 2021)

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

[The Moderna COVID-19 \(mRNA-1273\) vaccine: what you need to know](#) (02 Sept 2021)

[SAGE Interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19](#) (15 Jun 2021)

[The Oxford/AstraZeneca COVID-19 vaccine: what you need to know](#) (02 Sept 2021)

[SAGE 19 Interim recommendations for use of the ChAdOx1-S \[recombinant\] vaccine against COVID-19 \(AstraZeneca COVID-19 vaccine AZD1222 Vaxzevria™, SII COVISHIELD™\)](#) (30 Jul 2021)

[GACVS review of latest evidence of **rare** adverse blood coagulation events with AstraZeneca COVID-19 Vaccine \(Vaxzevria and Covishield\)](#) (16 Apr 2021)

[The Janssen Ad26.COV2.S COVID-19 vaccine: What you need to know](#) (02 Sept 2021)

[SAGE Interim recommendations for the use of the Janssen Ad26.COV2.S \(COVID-19\) vaccine](#) (15 Jun 2021)

[The Sinovac-CoronaVac COVID-19 vaccine: What you need to know](#) (02 Sept 2021)

[SAGE Interim recommendations for use of the inactivated COVID-19 vaccine, CoronaVac, developed by Sinovac](#) (01 Jun 2021)

[The Sinopharm COVID-19 vaccine: What you need to know](#) (02 Sept 2021)

[SAGE Interim recommendations for use of the inactivated COVID-19 vaccine BIBP developed by China National Biotec Group \(CNBG\), Sinopharm](#) (07 May 2021)

[WHO Prioritization Roadmap \(in the context of limited supply\)](#) (16 Jul 2021)

COVID-19 vaccine post-introduction evaluation (cPIE)

Following new vaccine introduction into a routine immunization programme, the purpose of a post-introduction vaccine evaluation (PIE) is to evaluate the impact of the vaccine introduction on the country's immunization programme and to rapidly identify problems needing correction as vaccination expands in country. The evaluation, more flexible mini-cPIE in the mid- to long-term phase (between 6–18 months after introduction) followed by a classic or full COVID-19 vaccine PIE (cPIE), is recommended to improvements in the implementation of the new vaccine and overall immunization programme and to provide valuable lessons for other countries for future vaccine introductions.

The classic cPIE includes comprehensive tools to address key programmatic vaccine introduction activities at all levels of the immunization system including national, subnational and vaccination facility/site levels. Site visits that include observation of vaccination sessions, observation of vaccine storage facilities, and interviews with health workers and other priority groups receiving COVID-19 vaccine are an important component of the evaluation. As with PIEs for other vaccines, the country should review and adapt tools to the country context.

For countries interested in implementing the classic cPIE, please refer to the cPIE Guide document and the following web annexes:

[COVID-19 vaccine post-introduction evaluation \(cPIE\)](#) (25 Aug 2021)

annex A: [cPIE questionnaires](#)

annex B: [cPIE questionnaire summary tables](#)

annex C: [cPIE country presentation template](#)

annex D: [cPIE example figures for presentation](#)

Guidance on vaccination costing and budgeting: WHO-ECHO webinars

- [Costing alone is not enough: Budgets need to be planned and executed](#) (25 Aug 2021)
[Recording](#) (25 Aug 2021)
- [Where does needed COVID-19 vaccination Funding come from?](#) (01 Sept 2021)
[Recording](#) (01 Sept 2021)
- [Process of COVID-19 vaccination planning, costing and budgeting in African region](#) (08 Sept 2021)
[Recording](#) (08 Sept 2021)

French, Spanish and Russian interpretation are available in all webinars

Sign up news letter via [link](#)

Standards for measurement of antibody responses

COVAX Enabling Science workshop:

Standardization of Immune Response Assays for COVID-19 vaccines

A year's experience transferring assays to a global laboratory network was the subject of a COVAX Enabling Science workshop held on 31 August 2021. Comparing immune responses against different vaccine candidates intended for the prevention of SARS-CoV-2 is challenging.

In order to reduce some of this complexity, better assess the immunological profile of each vaccine candidate, and provide robust assays for regulatory purposes, CEPI created a Centralized Laboratory Network to test the immune response elicited by different vaccine candidates. The webinar summarized the lessons learned during technology transfer of immunological assays to a global network of laboratories to standardize the evaluation of the immune response elicited by different SARS-CoV-2 vaccines.

Presentations from the meeting and the meeting report will be available shortly.

WHO Measurement standards

Accurate tests are key to ensuring generating accurate data for studying COVID-19 disease and interventions. Currently a variety of molecular and serological assays are in use in worldwide settings for detection of SARS-CoV-2 infection and for measurement of antibody response to SARS-CoV-2 infection and to COVID-19 vaccines. In support of the global response to COVID-19, WHO has highlighted the importance of the availability of International Standards and/or reference reagents for anti-SARS-CoV-2 antibody and for SARS-CoV-2 RNA. The availability of International Standards will facilitate development, validation and assessment of the assays and allow for comparability of results from different assays, thus eventually facilitate and harmonize evaluation of diagnostics, vaccines, therapeutics and other products.

The WHO collaborating center for biological standardization, National Institute for Biological Standards and Control (NIBSC), UK, is leading the projects listed below with the support of other WHO Collaborating Centers and worldwide laboratories.

Development of the 1st WHO International Standard and Reference Panel for anti-SARS-CoV-2 antibody

Vaccines and treatments for COVID-19 are rapidly being developed and reliable assays are needed for their evaluation. The availability of an International Standard for antibodies to SARS-CoV-2 would facilitate the standardization of SARS-CoV-2 serological methods and allow for comparison and harmonization of datasets across laboratories. This will help determine the antibody levels that are needed for efficacious vaccines and therapeutics, and improve our

38th WHO Regulatory Update on COVID-19

understanding of virus epidemiology. An international collaborative study has been completed in 2020 to evaluate a pool of convalescent plasma from COVID-19 recovered patients as a candidate international standard, and to assess whether the candidate material is able to harmonize the results from serological assays detecting anti-SARS-CoV-2 antibodies. Also, as part of the study, a candidate International Reference Panel for anti-SARS-CoV-2 antibody was characterized with the aim to facilitate the development and evaluation of serological assays.

[Establishment of the WHO International Standard and Reference Panel for anti-SARS-CoV-2 antibody](#) (18 Nov 2020)

At the 73rd meeting of the WHO ECBS held on 9 and 10 December 2020, the First WHO International Standard of anti-SARS-CoV-2 immunoglobulin was established by the Committee, with assigned unitage of 250 IU/ampoule (neutralizing antibody activity); the First WHO International Reference Panel of anti-SARS-CoV-2 immunoglobulin was established with no assigned units.

[Main outcomes of the meeting of the WHO Expert Committee on Biological Standardization held from 9 to 10 December 2020](#) (15 Dec 2020)

[WHO International Standard for anti-SARS-CoV-2 immunoglobulin \(human\), NIBSC code: 20/136.](#)

[WHO International Reference Panel for anti-SARS-CoV-2 immunoglobulin, NIBSC code: 20/268](#)

[WHO International Standard for SARS-CoV-2 RNA, NIBSC code: 20/146](#)

Other Covid-19 vaccine information:

IMF-WHO Covid-19 vaccine supply tracker

The IMF-WHO COVID-19 Vaccine Supply Tracker providing updated weekly with the number of vaccine doses secured by countries through different channels.

[IMF-WHO COVID-19 vaccine supply tracker](#) (launched on 02 Aug 2021)

Interactives maps on VE studies

[COVID-19 VIEW-hub by IVAC](#)

[Vaccine tracker and efficacy trial map](#)

COVID-19 vaccine tracker and landscape

As of 7th September 2021, 299 candidate vaccines are in the pipeline.



The COVID-19 vaccine tracker:

- Provides summary tables of COVID-19 vaccine candidates in both clinical and pre-clinical development;
- Provides analysis and visualization for several COVID-19 vaccine candidate categories;
- Tracks the progress of each vaccine from pre-clinical, Phase 1, Phase 2 through to Phase 3 efficacy studies and including Phase 4 registered as interventional studies;
- Provides links to published reports on safety, immunogenicity and efficacy data of the

vaccine candidates;

- Includes information on key attributes of each vaccine candidate and
- Allows users to search for COVID-19 vaccines through various criteria such as vaccine platform, schedule of vaccination, route of administration, developer, trial phase and clinical endpoints.

[Covic-19 vaccine tracker and landscape](#) (07 Sept 2021)

Substandard and falsified products

Alert N°4/2021: Falsified remdesivir identified in the Americas

The WHO Medical Product Alert refers to two batches of falsified remdesivir injection 100mg/20ml (5mg/ml) identified in the WHO Region of the Americas and reported to WHO in July 2021. These products claim to be manufactured by GILEAD. However, GILEAD has confirmed that the remdesivir products listed in this alert are falsified and were not manufactured by them. These falsified products have been reported at the patient level (including at a hospital) in Mexico and are illicitly supplied on the internet.

The products identified in this alert are confirmed as falsified on the basis that they deliberately / fraudulently misrepresent their identity, composition, or source. The composition of the vials is currently unknown and laboratory analyses are to be conducted.

- Batch EN2005A2-B: the batch number and the expiry date (06/2023) do not correspond to any remdesivir manufactured by GILEAD.
- Batch EN2009D7-Q: the batch number does not correspond to any remdesivir manufactured by GILEAD.

Advice to regulatory authorities and the public

WHO requests increased vigilance within the supply chains of countries and regions likely to be affected by these falsified products. Increased vigilance should include hospitals, clinics, health centers, wholesalers, distributors, pharmacies, and any other suppliers of medical products.

All medical products must be obtained from authorized/licensed suppliers. The products' authenticity and physical condition should be carefully checked. Seek advice from a healthcare professional in case of doubt.

If you are in possession of the above products, please do not use them.

If you have used these products, or you suffered an adverse reaction/event having used these products, you are advised to seek immediate medical advice from a qualified healthcare professional and to report the incident to the National Regulatory Authorities/National Pharmacovigilance Centre.

National regulatory / health authorities are advised to immediately notify WHO if these falsified products are discovered in their country. If you have any information concerning the manufacture, distribution, or supply of these products, please contact rapidalert@who.int

Alert N°5/2021: Falsified COVISHIELD vaccine

The WHO Medical Product Alert refers to falsified COVISHIELD (ChAdOx1 nCoV-19 Corona Virus Vaccines (Recombinant)) identified in the WHO African Region, and the WHO South-East Asia Region. The falsified products were reported to WHO in July and August 2021. The genuine manufacturer of COVISHIELD (Serum Institute of India Pvt. Ltd.) has confirmed that the products listed in this alert are falsified. These falsified products have been reported at the patient level in Uganda, India and Myanmar.

38th WHO Regulatory Update on COVID-19

Genuine COVISHIELD vaccine is indicated for active immunization of individuals 18 years or older for the prevention of coronavirus disease caused by the SARS-CoV-2 virus. The use of genuine COVID-19 vaccines should be in accordance with official guidance from national regulatory authorities.

Falsified COVID-19 vaccines pose a serious risk to global public health and place an additional burden on vulnerable populations and health systems. It is important to detect and remove these falsified products from circulation to prevent harm to patients.

The products identified in this alert are confirmed as falsified on the basis that they deliberately / fraudulently misrepresent their identity, composition or source:

- Batch 4121Z040 - the expiry date (10.08.2021) on this product is falsified
- COVISHIELD 2ml - the genuine manufacturer does not produce COVISHIELD in 2ml (4 doses).
- Batch 4126Z079 - the batch number on this product is falsified and the product name: COVISHIELD (incorrect spelling).

Products subject of WHO Medical Product Alert N°5/2021

Stated Product name	COVISHIELD, ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant)		COVISHIELD ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombination)
Stated manufacturer	Serum Institute of India Pvt. Ltd.		
Stated dose	5ml (10 doses)	2ml (4 doses)	5ml (10 doses)
Batch	4121Z040	Not stated	4126Z079
Mfg. date	Not stated	Not stated	08.05.2021
Exp. date	10.08.2021	Not stated	07.1 1.2021
Packaging language	English	English	English
Identified in	Uganda	India	Myanmar

[Medical Product Alert N°5/2021: Falsified COVISHIELD vaccine \(Update\)](#) (31 Aug 2021)

Request for vigilance and reporting by national regulatory authorities

Regulatory authorities should continue to be vigilant for Substandard and Falsified (SF) versions of Covid-19 related therapies, vaccines and in vitro diagnostics and must report these to the WHO Global Surveillance and Monitoring System: rapidalert@who.int.

It is essential to report such products early on, regardless if they are only suspected or fully confirmed. National focal points from regulatory authorities are encouraged to use their dedicated portal (updated access is being given to all regions) to verify any pre-existing records of substandard / falsified medical products: [WHO Secure Portal](#).

WHO Assays Working Group

The changing antigenic anatomy of the SARS CoV-2 spike protein was described in a presentation on 11 August. Whilst there is much that we do not yet understand in the relationship between structure and function, the analysis suggested that there is considerable scope for further antigenic variation in the receptor binding domain of the spike protein.

The correlation between several serological assays and neutralizing antibody titre was examined in a presentation in the 11 August meeting. Factors which affected the correlation of some, but not all, assays included time from infection and variation in the spike protein.

The evolution of a beta variant in a long-term SARS-CoV-2 shedder with advanced HIV was described in the 25 August meeting. More than 6 months of shedding of infectious virus was documented which was terminated after a change in HIV treatment which also suppressed HIV replication in the individual. Molecular changes in the virus during the period of prolonged replication occurred in a manner reminiscent of quasi-species evolution seen with other viruses. Implications for vaccine composition were discussed in the context of changes in the neutralization capacity for virus from the patient of human plasma collected from different waves of infection with the ancestral strain, the beta and delta variants.

The discovery of pan-sarbecovirus neutralizing antibodies was described in the 25 August meeting. Sarbecovirus is the virus family to which SARS CoV-2 belongs, which includes SARS CoV-1 and several viruses that are present in animals but not in humans. Using a surrogate neutralizing antibody test, pan-sarbecovirus neutralizing antibodies were detected in 8/8 individuals who were survivors of SARS CoV-1 infection and, years later, had been immunized with SARS CoV-2 vaccine. These individuals had a broader antibody repertoire in terms of neutralizing different viruses of the sarbovirus family compared to SARS CoV-2 infected or immunized individuals. The successful isolation of highly-potent pan-sarbecovirus human neutralizing monoclonal antibodies was reported and discussed as a possible future therapeutic option. The potential to use a cocktail of these human neutralizing monoclonal antibodies as a future WHO International Standard antibody preparation was proposed and is being followed-up by the WHO Collaborating Centre at NIBSC, UK. Finally, the implications for future vaccine design are already being discussed with vaccine developers.

Supply Chain

Export and transportation restrictions

Concerns are increased regarding potential export restrictions on vaccines and therapeutics related to prevention and treatment of COVID 19. While export restrictions are not a favored solution, if they are used, advance notice and planning with affected countries is key. Transportation routes also continue to experience backlogs, in part due to port handling constraints, limited route availability and changes at some ocean ports related to the return of empty containers.

Supply chain of ultracold products

No change since August 2021. 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

The Global Trust Repository is moving forward. UNICEF has released an RFP for a Global Trust Repository, which is a data base that countries can use to perform basic validation of bar codes in line with guidance from WHO to include 2D data matrix codes with sterilization on secondary packaging of vaccines. The scope of the GTR outside of COVID19 vaccines is under discussion. Country feedback is under discussion through a regulatory mechanism.

Newly added or reconfirmed shortages

There are concerns regarding potential shortages of syringes, particularly the size and type used for the COVID19 vaccines. WHO will be issuing a policy brief that includes information on injection safety, recognizing that lack of supply can lead to unsafe practice. Advance planning is particularly important with injection equipment. They are voluminous to store and take longer to transport;

however, they must be available at the point of care with or prior to the vaccines. This is especially important noting that the shelf life of the vaccine is limited.

- 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
- Neuromuscular relaxants: succinylcholine, atracurium, or vecuronium.
- Opioids: morphine
- Malaria treatments: hydroxychloroquine, chloroquine, artemether-lumefantrine, artemisinin-based combination therapies, sulfadoxine-pyrimethamine + amodiaquine)
- Anticoagulants: heparin and new generation oral anticoagulants
- Corticosteroids: dexamethasone
- Antipyretics: paracetamol (aka acetaminophen)
- PPE
- Oxygen and related equipment
- Ventilators
- AD syringes for immunization

Medical Devices

Global Atlas of Medical Devices

Comment by 24 Sept 2021

After many months of surveys, more than 1,000 email communications and desk reviews, WHO presents the Draft 2021 Global Atlas of Medical Devices for final consultation.

Comments are requested **by 24 September 2021**.

[Draft Global atlas of medical devices](#)

Upcoming events

Extraordinary International Conference of Drug Regulatory Authorities (ICDRA)

“Smart Regulation: Timely Delivery of Quality Assured Medical Products for All during the Global Pandemic” 20-24 Sept 2021, 13:00 – 15:00 CET

This virtual conference provides the opportunity to the global regulatory community and other key stakeholders to exchange information, best practices and collaborative approaches related to

regulation of medical products, especially important during the current challenging times of the COVID-19 pandemic.

[Programme overview](#)

[Registration](#)

Call for nomination: WHO 3rd Global infodemic manager training

Nomination by sponsoring organization by 01 Oct 2021 at 17:00 CET

This is a call for nomination by sponsoring organization to provide support the online training with the following objectives:

- Build a curriculum and apply it in delivering a training of the 3rd cohort of cross-disciplinary infodemic managers that can be deployed to the field for infodemic preparedness and response
- Build skills of health authority staff and other relevant experts in infodemic management
- Offer opportunity for UN staff to learn about infodemic management
- Create a theoretical and practical foundation for future infodemic training modules.

For more details, please visit [WHO Infodemic manager training site](#)

GVIRF Webinar: mRNA Vaccine Technologies for Global Health

14 Oct 2021 15:00 – 18:00 CET

This Global Vaccine and Immunization Research Forum (GVIRF) webinar is the first in a series of events hosted by the US National Institute of Allergy and Infectious Diseases, the Bill & Melinda Gates Foundation, and the WHO. GVIRF is the central forum for research related to the WHO's Global Vaccine Action Plan (GVAP) and its successor, the Immunization Agenda 2030.

[More information about the webinar](#)

[Registration](#)

WHO Virtual cGMP Training Marathon for Vaccine Manufacturing

From 5 Oct to 11 Nov 2021, on Tuesdays and Thursdays, this training sessions will address challenges and improve compliance to cGMP and regulatory requirements by providing the wide range of cGMP topics and how to minimize interruptions to business operations. This training welcomes the participation of vaccine manufacturers, biopharmaceutical manufacturers, manufacturers intending to produce vaccines, National Regulatory Agencies and officials from related government ministries such as Ministries of Health and Ministries of Industries.

A certificate will be delivered to those passing the course requirements.

[Registration](#)

[Information flyer](#)

For more info, please contact localproduction@who.int