37th WHO Regulatory Update on COVID-19

09 August 2021

World Health Organization

Key Messages

The WHO Emergency Committee on COVID-19 in its latest meeting expressed concern that the pandemic is being mischaracterized as coming to an end even though it is nowhere near finished. It also warned about the strong likelihood for the emergence and global spread of new and possibly more dangerous variants of concern that may be even more challenging to control.

As stated by Dr Tedros on 4th August, WHO is calling for a moratorium on boosters to enable at least 10% of the population of every country to be vaccinated and all countries are asked to support this effort.

Highlights and main issues

- To increase awareness and to assist healthcare providers, WHO published an interim guidance for clinical case management of thrombosis with thrombocytopenia syndrome (TTS) in individuals vaccinated with COVID-19 non-replicant adenovirus vector-based vaccines. Knowledge about TTS following vaccination is rapidly evolving. WHO will continue to monitor the situation closely for update as needed.
- SAGE published its updated Roadmap that offers recommendations on how vaccines should be prioritized for maximum public health impact in countries with limited supply, considering the most recent evidence on COVID-19 vaccines and on the ongoing supply constraint issues faced by the COVAX Facility.
- An ICMRA workshop reached consensus that immunogenicity bridging studies may be needed if an assessment of effectiveness of 2nd generation COVID-19 vaccines in clinical endpoint efficacy studies are no longer feasible. These could be designed as non-inferiority immunogenicity studies if the comparator vaccine has demonstrated high efficacy in clinical diseases endpoint efficacy trials and/or superiority designs if the comparator vaccine has demonstrated modest efficacy.
- A milestone meeting between ICMRA and industry associations discussed enabling manufacturing capacity in the COVID-19 pandemic. Most regulatory agencies have adopted the use of regulatory flexibilities for Covid-19 products. The workshop was an opportunity for an exchange of views on what changes have worked well, what were less effective, what future changes should be prioritized, what are the major challenges over the next 12 months, and where are the regulatory bottlenecks.
- WHO has launched an expression of interest for prequalification of manufacturers of interleukin-6 (IL-6) receptor blockers. Global demand for IL-6 receptor blockers for the treatment of severe COVID-19 has been soaring since the WHO's treatment recommendation on 6 July. Prequalification of innovator and its biosimilar products aims to expand the availability of quality-assured products with reduced prices to meet urgent public health needs through increased market competition.

Contents

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.

Weekly epidemiological update on COVID-19 (27 Jul 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 are updated in each Epidemiological Update.

Table 2: Summary of phenotypic impacts* of Variants of Concern

WHO label	Alpha	Beta	Gamma	Delta
Transmissibility	Increased transmissibility and secondary attack rate[6]	Increased transmissibility[7]	Increased transmissibility[8]	Increased transmissibility and secondary attack rate[1,9,10]
Disease severity	Increased risk of hospitalization[11], possible increased risk of severity and mortality[12]	Not confirmed, possible increased risk of in-hospital mortality[13,14]	Not confirmed, possible increased risk of hospitalization[15]	Increased risk of hospitalization[3,16]
Risk of reinfection	Neutralizing activity retained,[17] risk of reinfection remains similar[18,19]	Reduction in neutralizing activity reported; T cell response elicited by D614G virus remains effective[20–23]	Moderate reduction in neutralizing activity reported[24,25]	Reduction in neutralizing activity reported[26]
Impacts on diagnostics	Limited impact – S gene target failure (SGTF); no impact on overall result from multiple target RT-PCR, No impact on Ag RDTs observed[27]	No impact on RT-PCR or Ag RDTs observed[16]	None reported to date	None reported to date

**Generalized findings as compared to previously/co-circulating variants. Based on emerging evidence, including non-peer-reviewed preprint articles and reports, all subject to ongoing investigation and revision.*

Table 2 from the Weekly epidemiological update on COVID-19 (20 Jul 2021)

Growing evidence supports the increased transmissibility of the Delta variant as compared to non-VOCs. However, the exact mechanism for the increase in transmissibility remains unclear. A recent study from China during an outbreak of the Delta variant examined the time interval from the exposure of a quarantined population to the first positive PCR result and found that the interval may be shorter for the Delta variant when compared to non-VOCs. Moreover, the viral load of the first positive test of Delta infection was over 1200 times higher than non-VOCs, suggesting that this VOC may be able to replicate faster and be more infectious during the early stages of infection.

A summary of vaccine performance against variants of concern is also regularly collated and summarized in the Weekly epidemiological update on COVID-19.

Table 3. Summary of vaccine performance against Variants of Concern

Alpha	Beta	Gamma	Delta
Efficacy/effectiveness against disease or infection (full vaccination), see key below table			
Protection retained against all outcomes	Protection retained against severe disease; possible reduced protection against symptomatic disease and infection	Unclear impact; very limited evidence	Protection retained against severe disease; possible reduced protection against symptomatic disease and infection
Severe disease			
• ↔: Moderna-mRNA-1273 (1), Moderna-mRNA-1273/Pfizer BioNTech-Comirnaty (1), Pfizer BioNTech-Comirnaty (2)[28,30–32] • ↓: AstraZeneca- Vaxzevria (1) [31]	• ↔: Janssen Ad26.COV 2.5 (1), PfizerBioNTech-Comirnaty (1)[30,33]	• No evidence	• ↔: AstraZeneca- Vaxzevria (1), Pfizer BioNTech-Comirnaty (1)[31]
Symptomatic disease			
• ↔: Moderna-mRNA-1273 (1), Moderna-mRNA-1273/Pfizer BioNTech-Comirnaty (1), Pfizer BioNTech-Comirnaty (3)[34–37] • ↔ to ↓: AstraZeneca-Vaxzevria (3)[35,36,38] • ↓: Novavax-Covavax (1)[39]	• ↔: Janssen-Ad26. COV 2.5 (1)[33] • ↓↓↓: AstraZeneca-Vaxzevria (1), Novavax-Covavax (1)[40,41]	• ↔ to ↓: Sinovac-CoronaVac (1)[42,43]	• ↔ to ↓: PfizerBioNTech-Comirnaty (3)[35–37] • ↓:Bharat-Covaxin (1)[44] • ↓↓: AstraZeneca- Vaxzevria (2)[35,36]
Infection			
• ↔: PfizerBioNTech-Comirnaty (1)[36] • ↔ to ↓: AstraZeneca-Vaxzevria (2)[36,38]	• ↔: Moderna-mRNA-1273 (1)[29] • ↓: PfizerBioNTech-Comirnaty (1)[30]	• No evidence	• ↓: AstraZeneca-Vaxzevria (1), Pfizer BioNTech-Comirnaty (1)[36]
Neutralization (full vaccination), see key below table			
• ↔: Anhui ZL-Recombinant (1), Beijing CNBG-BBIBP-CorV (1), Bharat-Covaxin (1), Gamaleya-Sputnik V (1), Novavax-Covavax (1) [45–49] • ↔ to ↓: Janssen-Ad26.COV 2.5 (3), Moderna-mRNA-1273 (9), Pfizer BioNTech-Comirnaty (27) Sinovac-CoronaVac (5)[23,45,48–84] • ↓ to ↓↓: AstraZeneca-Vaxzevria (2)[38,55]	• ↔ to ↓: Anhui ZL-Recombinant (2), Beijing CNBG-BBIBP-CorV (2)[45,85,86] • ↓: Bharat-Covaxin (1)[87] • ↓ to ↓↓: Moderna-mRNA-1273 (11), Pfizer BioNTech-Comirnaty (27), Sinovac-CoronaVac (4)[23,45,50–52,55,57–61,63,64,66–69,71,73–78,81,84,85,88–96] • ↓ to ↓↓↓: Janssen-Ad26.COV 2.5 (3)[79,80,97] • ↓↓: AstraZeneca-Vaxzevria (4), Gamaleya-Sputnik V (1)[40,47,55,68,93] • ↓↓↓: Novavax-Covavax (1)[59]	• ↔ to ↓: Pfizer BioNTech-Comirnaty, (12), Sinovac-CoronaVac (3)[51,55,57,59,61,64,74,82–84,88,99–101] • ↓: AstraZeneca-Vaxzevria (1), Janssen-Ad26.COV 2.5 (2), Moderna-mRNA-1273 (4)[55,57,73,78–80,100]	• ↔: Janssen-Ad.COV 2.5 (1)[79] • ↓: Anhui ZL-Recombinant (1), AstraZeneca-Vaxzevria (2), Bharat-Covaxin (1), Moderna-mRNA-1273 (2), SII – Covishield (1)[49,78,87,93,102–104] • ↓ to ↓↓: Pfizer BioNTech-Comirnaty (6)[71,84,93,99,102,103] • ↓ to ↓↓↓: Sinovac-CoronaVac (2)[49,81]

Arrows generalize the magnitude of reduction in VE or neutralization: "↔" <10% reduction in VE, or VE >90% with no comparator, or that there was a <2-fold reduction in neutralization; "↓" 10 to <20% reduction in VE, or 2 to <5-fold reduction in neutralization; "↓↓" 20 to <30% reduction in VE, or 5 to <10-fold reduction in neutralization; "↓↓↓" ≥30% reduction in VE, or ≥10-fold reduction in neutralization. When more than one neutralization study is available, the interquartile range (25th and 75th percentiles) of fold-reductions across all studies for specific vaccine/variant was used.
The number of studies is shown in parentheses.
"Moderna-mRNA-1273/Pfizer BioNTech-Comirnaty" indicates that both vaccines were evaluated together in study.

Table e from the Weekly epidemiological update on COVID-19 (20 Jul 2021)

Reclassification of three variants

Based upon the latest round of assessments, VOIs Epsilon (B.1.427/B.1.429), Zeta (P.2), and Theta (P.3) were reclassified as 'Alerts for further monitoring'. While all three variants carry mutations with suspected and/or established phenotypic impacts, reported detections of these variants have decreased over time, suggesting a decline in their respective incidence worldwide, and diminishing public health risks relative to other VOCs and VOIs.

WHO Tracking SARS-CoV-2 Variants for more details on VOCs, VOIs, Alerts for further monitoring

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.

As of 5th August, over **4.27 billion vaccine doses** have been administered worldwide, where 75% of all doses were administered in 10 countries. COVAX has **shipped 187.6M** doses, including donations, to **138** participants, yet 3 countries have not started vaccination programmes with different reasons. While most countries started their vaccination programme, coverage varies across WHO regions: 39 countries (out of 53) in the WHO European region vaccinated more than 20% of population whereas only 2 countries (out of 47) in the African region, 3 countries (out of 11) in the South-East Asia region and 7 countries (out of 21) in East Mediterranean region achieved the 20% or more coverage.

WHO's other COVID-19-related work

IMF-World Bank-WHO-WTO: joint forces to accelerate access

The International Monetary Fund, World Bank Group, World Health Organization and World Trade Organization have joined forces to accelerate access to COVID-19 vaccines, therapeutics and diagnostics by leveraging multilateral finance and trade solutions, particularly in low- and middle-income countries.

The aim is to vaccinate at least 40 percent of people in every country by the end of 2021, and at least 60 percent by mid-2022. The effort will track, coordinate, and advance delivery of COVID-19 vaccines, therapeutics and diagnostics, working with governments and partners at the global and local levels to address finance and trade barriers to ensure that vulnerable populations have access to these life-saving tools. It supports the goals of the ACT-Accelerator and complementary initiatives.

The Task Force members are mobilizing critical financing, with a focus on grants and concessional lending; helping to remove barriers to export and import of vaccines, therapeutics, and diagnostics; and supporting more production, including in low- and middle-income countries. The Task Force is calling on countries to share at least 1 billion vaccine doses with developing countries during 2021.

Partners include governments, regional development banks, members of the Access to COVID-19 Tools (ACT) Accelerator and its COVAX Facility, the Africa Vaccine Acquisition Task Force, pharmaceutical firms, and others in the private sector.

Task Force's priorities are Financing, Manufacturing and Trade, Coordination, Advocacy and Country delivery.

COVID-19 Task Force

International Health Regulations (2005) Emergency Committee

The eighth meeting of the Emergency Committee, convened by the WHO Director-General under the International Health Regulations (2005) (IHR) regarding the coronavirus disease (COVID-19), took place on Wednesday, 14 July 2021. The Secretariat highlighted factors driving the current situation including: VOCs, inconsistent application of public health and social measures (PHSM), increased social mobility, and highly susceptible populations due to lack of equitable vaccine distribution. The pandemic remains a challenge globally with countries navigating different health, economic and social demands.

The Committee noted that regional and economic differences are affecting access to vaccines, therapeutics, and diagnostics. Countries with advanced access to vaccines and well-resourced health systems are under pressure to fully reopen their societies and relax the PHSM. Countries with limited access to vaccines are experiencing new waves of infections, seeing erosion of public trust and growing resistance to PHSM, growing economic hardship, and, in some instances,

increasing social unrest.

The Committee unanimously agreed that the COVID-19 pandemic still constitutes an extraordinary event that continues to adversely affect the health of populations around the world, poses a risk of international spread and interference with international traffic, and requires a coordinated international response. As such, the Committee concurred that the COVID-19 pandemic remains a public health emergency of international concern (PHEIC).

> Statement on the eighth meeting of the International Health Regulations (2005) Emergency Committee regarding the coronavirus disease (COVID-19) pandemic (15 Jul 2021)

Alignment of approaches by regulators

WHO-Listed Authorities: Operational guidance on evaluation and designation

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

ICMRA COVID-19 vaccine development: future steps workshop

The objective of an ICMRA workshop held on 24 June was to brainstorm among regulators about the development of second-generation vaccines and booster doses, with a particular focus on immunobridging, the design and use of controlled trials (placebo or other controls), and correlates of immunity. The meeting highlighted the importance of a well-coordinated and convergent global response to evaluating existing vaccines and developing modified and new vaccines in the face of SARS-CoV-2 variants of concern.

Approaches to authorization of 2nd generation vaccines may include placebo controlled clinical disease endpoint trials provided they can still be ethically performed. Alternative approaches may include relative clinical disease endpoint efficacy studies and possibly human challenge trials.

There was consensus that immunogenicity bridging studies may be needed if an assessment of effectiveness of 2nd generation COVID-19 vaccines in clinical endpoint efficacy studies are no longer feasible. These could be designed as non-inferiority immunogenicity studies if the comparator vaccine has demonstrated high efficacy in clinical diseases endpoint efficacy trials and/or superiority designs if the comparator vaccine has demonstrated modest efficacy. Questions around study designs need to be further explored including from the practical aspects.

It was proposed to create a new forum through setting up an ICMRA Clinical Trials Working Group.

An ICMRA follow-up workshop will be organised after the summer to focus on development and approval of second-generation vaccines.

ICMRA COVID-19 Vaccine development: Future steps Workshop

ICMRA workshop: Enabling manufacturing capacity in the COVID-19 pandemic

A milestone meeting between ICMRA and industry associations was held on 7 July to discuss enabling manufacturing capacity in the COVID-19 pandemic. The current pandemic has necessitated significant acceleration to normal development timelines and companies have identified vaccine candidates, run clinical trials and received regulatory approval in under 12 months. This accelerated development has been crucial to timely vaccination roll outs and significant efforts have been made by regulators to implement regulatory flexibilities and new ways of working.

Most agencies have adopted the use of regulatory flexibilities for Covid-19 products. A survey of regulators was carried out to determine which regulatory tools and flexibilities are being most used. This found that multiple regulatory and scientific tools are being used with rolling submissions and frequent engagement with regulators a common feature. In general, agencies can approve products in the absence of certain data, with additional data provided post-approval. There is already sharing of information between regulatory agencies, however reliance on assessment reports from other agencies or joint assessment is somewhat less common, and this is an area for future exploration.

The workshop was an opportunity for an exchange of views on what changes have worked well, what were less effective, what future changes should be prioritized, what are the major challenges over the next 12 months, and where are the regulatory bottlenecks.

The meeting report and meeting output is expected to be available in September.

Workshop presentations

WHO good practices for research and development facilities of pharmaceutical products

In view of the need for the development of health products, including the research and development for the treatment of COVID-19 therapies, the WHO Prequalification Inspection Services Team raised the urgency for the development of lifecycle appropriate good practices text to address the manufacturing of developmental batches, pilot batches and the sequential stability data that are submitted in product applications (dossiers) for marketing authorization and the prequalification of medical products.

A draft WHO document intends to provide guidance on good manufacturing practices (GMP) to research and development facilities and aims to ensure that the correct systems are followed, ensuring appropriateness, reliability and the quality of products, processes, procedures and data.

WHO good practices for research and development facilities of pharmaceutical products – comments by 31 Aug 2021

Please send comments to Steve Estevão Cordeiro estevaos@who.int and Sinéad Jones jonessi@who.int

WHO good manufacturing practices for investigational products

This draft working document is open for comments. In view of an old publication date, and the recent need for new guidelines arising from inspections carried out for COVID-19 therapeutics, the WHO Prequalification Team -Inspection Services raised the urgency for a revision of the WHO Good manufacturing practices for investigational pharmaceutical products for clinical trials in humans.

The objective of this update is to bring the guideline in line with current expectations and trends in good practices and to harmonize the text with the principles from other related international guidelines.

WHO good manufacturing practices for investigational products – comments by 31 Aug 2021

Please send comments to Steve Estevão Cordeiro estevaos@who.int and Sinéad Jones jonessi@who.int

WHO good manufacturing practices for medicinal gases

There is an urgent need to scale-up the production of medicinal gases, in particular 'oxygen', meeting quality specifications. These specifications define the production, control, storage and distribution of oxygen and other medicinal gases so that these products are of assured quality when they reach the patients. Where the standards for medicinal gases are not followed, for example in the production and control of industrial oxygen, purity and content could be affected.

The possible contamination of industrial oxygen with viable and non-viable particulate matter, including other impurities, could result in risks to patients when applied for medicinal use. Industrial oxygen should not be used as a medicinal gas.

The WHO departments involved in the supply of oxygen and the inspection of production sites of medicinal gases raised the urgency for the preparation of the WHO good manufacturing practices for medicinal gases guidance text.

WHO good manufacturing practices for medicinal gases – comments by 31 Aug 2021

Please send comments to Steve Estevão Cordeiro estevaos@who.int and Sinéad Jones jonessi@who.int

Medicinal oxygen: for revision in the *International Pharmacopeia*

The proposed revision defines quality requirements for medicinal oxygen generated by:

- Oxygen Generation Plants and concentrators, which use Pressure Swing Adsorption or Vacuum Swing Adsorption technologies to generate 90 to 96% pure oxygen, referred to in the draft revision as "Oxygen 93%"; and/or
- Air Separation Units, which use cryogenic technology to generate 99% pure oxygen, referred to in the draft revision as "Oxygen 99%";

and to define quality requirements for these products.

Medicinal Oxygen: draft proposal for revision in the International Pharmacopoeia – comments by 10 Sep 2021

Please send comments to Herbert Schmidt schmidth@who.int and Sinéad Jones jonessi@who.int

Remdesivir and remdesivir for infusion: for the *International Pharmacopeia*

Draft quality specifications for remdesivir and remdesivir for infusion have been prepared for inclusion in the *International Pharmacopoeia.*

Remdesivir – comments by 10 Sep 2021

Remdesivir for intravenous infusion – comments by 10 Sep 2021

Please send comments to Herbert Schmidt schmidth@who.int and Sinéad Jones jonessi@who.int

Evaluation of the quality, safety and efficacy of mRNA vaccines

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.

Recommendations on regulatory processes and aspects related to the introduction of vaccines during the COVID-19 Pandemic and other emergencies

During emergency situations, WHO recommends that national regulatory authorities (NRAs) adopt agile and efficient regulatory pathways to evaluate the quality, safety, and efficacy of new vaccines, which should be based on risk-benefit assessments. It also recommends that, for each authorized vaccine, pharmacovigilance activities should be implemented, based on risk management plans. Countries should have national emergency preparedness and response plans that include streamlined regulatory pathways that allow new vaccines to be introduced following legal and orderly processes. Such regulatory preparedness is key to achieving a rapid response that does not obstruct or delay the availability of vaccines.

A situation analysis of the emergency regulatory procedures implemented by NRAs in the Americas, and based on the available information regarding existing regulatory frameworks in the Region, identified the main gaps in readiness for the introduction of COVID-19 vaccines and proposed the regulatory procedures needed to manage and reduce these gaps.

> Recommendations on Regulatory Processes and Aspects related to the Introduction of Vaccines during the COVID-19 Pandemic and Other Emergencies

In vitro diagnostics

WHO EUL and Listing Update

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

- Assays for the detection of SARS-CoV-2 nucleic acid;

- Rapid diagnostic tests and enzyme immunoassays for the detection of IgM/IgG to SARS-CoV-2; and
- Rapid diagnostic tests for the detection of SARS-CoV-2 antigens.

WHO EUL submissions

Applicants are asked to submit their applications for assessment based on WHO instructions and requirements for NAT and Ag detection RDTs and IVDs detecting antibodies to SARS-CoV-2 virus.

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

As of 29th July, 28 products have been listed as eligible for WHO procurement among a total of 151 expressions of interest (64 for NAT assays, 41 for antibody detection assays and 46 for antigen detection RDTs) have been received. So far, 43 products are recommended not to be used.

EUL listed IVDs (30 Apr 2021)

IVDs not accepted for EUL listing (04 Aug 2021)

Status of each EUL application (03 Aug 2021)

IVDs listed by National Regulatory Authorities in IMDRF jurisdictions

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

IVDs listed by IMDRF NRAs (02 Jun 2021)

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

Therapeutics

IL-6 receptor blockers

WHO has updated its patient care guidelines to include interleukin-6 receptor blockers, a class of medicines that are lifesaving in patients who are severely or critically ill with COVID-19, especially when administered alongside corticosteroids. Interleukin-6 blocking drugs – tocilizumab and sarilumab – act to suppress the overreaction of the patient's immune system. These were the findings from a prospective and a living network meta-analysis initiated by WHO, the largest such analysis on the drugs to date. Data from over 10 000 patients enrolled in 27 clinical trials were considered.

The prospective and living network meta-analyses showed that in severely or critically ill patients, administering these drugs reduce the odds of death by 13%, compared to standard care. This means that there will be 15 fewer deaths per thousand patients, and as many as 28 fewer deaths for every thousand critically ill patients. The odds of mechanical ventilation among severe and critical patients are reduced by 28%, compared with standard care. This translates to 23 fewer patients out of a thousand needing mechanical ventilation.

To increase access and affordability of these life-saving products, WHO calls on manufacturers to reduce prices and make supplies available to low- and middle-income countries, especially where COVID-19 is surging. WHO also encourages companies to agree to transparent, non-exclusive voluntary licensing agreements using the C-TAP platform and the Medicines Patent Pool, or to waive exclusivity rights.

WHO has also launched an expression of interest for prequalification of manufacturers of

interleukin-6 receptor blockers. Prequalification of innovator and its biosimilar products aims to expand the availability of quality-assured products with reduced prices to meet urgent public health needs through increased market competition.

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.

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 5th August, over **4.27 billion vaccine doses** have been administered worldwide, where 75% of all doses were administered in 10 countries. COVAX has **shipped 187.6M** doses, including donations, to **138** participants, yet 3 countries have not started vaccination programmes with different reasons. In low-income countries, only 1% of people have received at least one dose, compared with more than half of people in high-income countries.

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

WHO Coronavirus (COVID-19) Dashboard

Joint initiative: Global dashboard for vaccine equity

Safe and effective COVID-19 vaccines were developed in record time. But the virus is moving faster than the global distribution of vaccines. The vast majority have been administered in high- and upper-middle-income countries, mostly in 10 countries alone. If these doses had been distributed equitably, they would have been enough to cover all health workers and older people globally. The global failure to share vaccines equitably is taking its toll on some of the world’s poorest and most vulnerable people. New variants of concern mean that the risks of infection have increased in all countries for people who are not yet protected by vaccination.

COVID-19 vaccine inequity will have a lasting and profound impact on socio-economic recovery in low- and lower-middle income countries without urgent action to boost supply, share vaccines and ensure they’re accessible to everyone now.

The Global Dashboard for Vaccine Equity combines the latest data on the global roll-out of COVID-19 vaccines with the most recent socio-economic information to illustrate why accelerating vaccine equity is not only critical to saving lives but also to driving a faster and fairer recovery from the pandemic with benefits for all.

It provides new, actionable insights and possibilities for policy makers to dive into the implications of vaccine inequity for socio-economic recovery, jobs and welfare. Analyses can be generated and compared by country, region and globally, and organised per income group.

The Dashboard is a joint initiative of UNDP, WHO and the University of Oxford with cooperation across the UN system, anchored in the SDG 3 Global Action Plan for Healthy Lives and Well-being for All.

WHO Vaccine-equity

UNDP Vaccine-equity

Data on accessibility

Data on affordability

IMF-WHO Covid-19 vaccine supply tracker

The new IMF-WHO COVID-19 Vaccine Supply Tracker is launched and will be 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)

SAGE roadmap for the prioritisation of COVID-19 vaccines

An updated SAGE Roadmap offers recommendations on how vaccines should be prioritized for maximum public health impact in countries with limited supply, considering the most recent evidence on COVID-19 vaccines and on the ongoing supply constraint issues faced by the COVAX Facility.

It is not meant to guide the setting of coverage targets or country goals for disease control. WHO, in collaboration with its COVAX partners and key regional and national stakeholders, is currently updating its initial goals for 2021 towards a WHO Global COVID-19 Vaccination Strategy for 2021–2022. The Vaccination Strategy will consider global goals against COVID-19 and describe different strategies and resources needed to pursue the various goals. The Prioritization Roadmap and the Vaccination Strategy are two distinct documents complementary to one another.

Key changes to previous recommendations are to increase the prioritization of immunization in pregnancy, in particular pregnant women of higher age, and those with comorbidities; to clarify there is no need to discontinue breastfeeding because of vaccination; and that children and adolescents with underlying health conditions should be included in stage II of roll-out of vaccines where community transmission is high, or where there is a risk of clusters of cases forming.

WHO SAGE Roadmap For Prioritizing Uses Of COVID-19 Vaccines In The Context Of Limited Supply (16 Jul 2021)

Evaluations of the effectiveness of COVID-19 vaccines

As of 20 July 2021, six vaccine types (AstraZeneca- ChAdOx1-S, Janssen Ad26.COV 2.5, Moderna-mRNA-1273- elasomeran, Pfizer BioNTech- tozinameran, COVID-19 vaccine BIBP, and Sinovac-CoronaVac) have received WHO emergency use listing (EUL) based, in part, on vaccine efficacy results from randomized controlled trials (RCTs). In contrast to vaccine efficacy, which is estimated in the controlled clinical trial setting, vaccine effectiveness, is estimated from observational (non-randomized) studies in real-world settings.

VE study protocols

WHO has produced best practice guidance on how to undertake VE studies, and provides links to

VE study protocols.

> Interim guidance on conducting vaccine effectiveness evaluations in the setting of new SARS-CoV-2 variants: Addendum to Evaluation of COVID-19 vaccine effectiveness (23 Jul 2021)

Guidance to estimate COVID-19 vaccine effectiveness against severe acute respiratory infections (SARI) hospitalizations associated with laboratory-confirmed SARS-CoV-2: an evaluation using the test-negative design was published in May 2021. This guidance proposes enhanced data collection within existing SARI surveillance systems and describes how existing hospital-based surveillance systems for SARI can be adapted to collect data to inform estimates of vaccine effectiveness against COVID-19 in persons of all ages. It outlines methods for collecting and analyzing data on vaccinated and unvaccinated patients based on a case control "test negative design".

> Estimating COVID-19 vaccine effectiveness against severe acute respiratory infections (SARI) hospitalizations associated with laboratory-confirmed SARS-CoV-2: an evaluation using the test-negative design (May 2021)

Cohort study protocol to measure COVID-19 vaccine effectiveness among health workers was published in March 2020, outlining the methods of a prospective cohort study to evaluate the effectiveness of the COVID-19 vaccine in the health workers (HWs), with a focus on hospital-based HWs. HWs should be enrolled ideally prior to or simultaneous with the implementation of the COVID-19 vaccination campaign.

> Cohort study to measure COVID-19 vaccine effectiveness among health workers (Mar 2020)

VE studies in the real-world settings

As of 20 July 2021, there have been over 90 VE studies made publicly available in peer-reviewed or pre-print literature, though the quality of these studies varies considerably. The evidence base to date has been skewed, with 62% (58/93) of studies coming from three countries with early introduction of vaccination campaigns (i.e. Israel, the United Kingdom and the United States of America); and 71% (66/93) reporting on VE of only two vaccines - Pfizer BioNTech-tozinameran and AstraZeneca-ChAdOx1-S.

In general, symptomatic disease efficacy results from these studies, for fully vaccinated individuals, have been similar to the results of the randomized clinical trials that informed the WHO EUL decision. Overall, VE against severe disease, hospitalization and death has been higher than against non-severe symptomatic disease, with VE estimates for these more serious outcomes to be above 80% for AstraZeneca-ChAdOx1-S, Moderna-mRNA-1273-elasomeran, Pfizer BioNTech-tozinameran, and Sinovac- CoronaVac.

> Weekly Epidemiological Update 50: with the latest update on VE against VOCs (27 Jul 2021)

> Landscape of observational study designs on the effectiveness of COVID-19 vaccination (22 Jul 2021)

Interactives maps on VE studies

> COVID-19 VIEW-hub by IVAC

> Vaccine tracker and efficacy trial map

Pfizer BioNtech tozinameran – COVID-19 mRNA vaccine

WHO EUL:

Pfizer site at Novartis Switzerland is now listed for EUL on 08 July 2021

https://extranet.who.int/pqweb/vaccines/who-recommendation-covid-19-mrna-vaccine-nucleoside-modified-comirnaty

Drug products manufactured at Mibe (Darmapharm) in Germany, Pharmacia & Upjohn (Kalamazoo, Michigan) and Hospira Inc. (McPherson, Kansas) in the USA are also listed for EUL on 16 July 2021.

https://extranet.who.int/pqweb/vaccines/who-recommendation-biontech-tozinameranus-fda-covid-19-mrna-vaccine-nucleoside-modified

US FDA and EMA:

Myocarditis and pericarditis can occur in very rare cases following vaccination and have been added in the product information as new side effects, together with a warning to raise awareness among healthcare professionals and people taking these vaccines.

US FDA Pfizer-BioNTech COVID-19 Vaccine

EMA COVID-19 vaccine safety update (14 Jul 2021)

Meeting highlights from the Pharmacovigilance Risk Assessment Committee (5-8 Jul 2021)

EMA direct healthcare professional communication on risk of myocarditis and pericarditis (19 Jul 2021)

Moderna COVID-19 vaccine (mRNA 1273) elasomeran

WHO EUL:

ModernaTX, Inc (Norwood, USA) is now listed for EUL (06 Aug 2021).

https://extranet.who.int/pqweb/vaccines/who-recommendation-modernatx-incusfda-covid-19-mrna-vaccine-nucleoside-modified

US FDA and EMA:

Myocarditis and pericarditis can occur in very rare cases following vaccination and have been added in the product information as new side effects, together with a warning to raise awareness among healthcare professionals and people taking these vaccines.

US FDA Moderna COVID-19 Vaccine

EMA Spikevax: EPAR - Medicine overview (30 Jul 2021)

EMA:

EMA’s human medicines committee (CHMP) has recommended granting an extension of indication for the Moderna COVID-19 vaccine (mRNA 1273) elasomeran to include use in children aged 12 to 17 years. The vaccine is already authorised for use in people aged 18 and above.

CHMP extension of indication variation assessment report (09 Aug 2021)

EMA's human medicines committee (CHMP) has approved a scale-up of the active substance production process at Moderna's COVID-19 vaccine manufacturing sites in the US. This recommendation is expected to have significant impact on the supply of Spikevax, the COVID-19 vaccine developed by Moderna, in the European Union. It is estimated that in the third quarter of 2021, the US supply chain will provide 40 million doses of vaccine for the European market.

EMA's decision reaffirms that the two recently approved US facilities, ModernaTX, Inc. in Norwood, Massachusetts and Lonza Biologics, Inc. in Portsmouth, New Hampshire, are capable of consistently manufacturing high-quality active substance and will enable Moderna to increase

production capacity at these sites.

Increased manufacturing capacity and supply for Spikevax (30 Jul 2021)

Astra-Zeneca COVID-19 vaccine (ChAdOx1-S) [recombinant])

WHO SAGE recommendations:

On 30th July, SAGE recommendations on interchangeability with other COVID-19 vaccines were updated based on new preliminary data using heterologous schedules (i.e. ChAdOx1-S [recombinant] vaccine followed by an mRNA vaccine (tozinameran BNT162b2 or elasomeran mRNA-1273). A section on considerations for deferring the second dose in settings with limited vaccine supply has been added to provide guidance to Member States facing vaccine supply shortages which result in an inability to readily administer second doses.

The section on pregnancy and breastfeeding is updated to reflect recent data and insights with regards to the use of COVID-19 vaccines in pregnancy and breastfeeding women.

The section on contraindications and precautions is updated to reflect data related to TTS and GBS related to ChAdOx1-S [recombinant] vaccine.

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

WHO EUL:

AZ site in Japan approved on 09 July 2021

https://extranet.who.int/pqweb/vaccines/who-recommendation-astrazeneca-mhlw-approved-sites-covid-19-vaccine-chadox1-s-recombinant

AZ site in Australia approved on 09 July 2021

https://extranet.who.int/pqweb/vaccines/who-recommendation-astrazenecatga-approved-sites-covid-19-vaccine-chadox1-s-recombinant

EMA:

The EMA has advised that vaccinated persons need to seek immediate medical attention if they develop weakness and paralysis in the extremities, possibly progressing to the chest and face, after vaccination with COVID-19 vaccine (ChAdOx1-S), as these could be signs of Guillain-Barré syndrome. The product information has been updated.

EMA COVID-19 vaccine safety update VAXZEVRIA (14 Jul 2021)

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

US FDA:

The FDA required changes to the Fact sheet to include new information about Guillain-Barre syndrome to suggest an increased risk of Guillain-Barré syndrome during the 42 days following vaccination.

FDA letter to Janssen (12 Jul 2021)

EMA:

The EMA has advised that vaccinated persons need to seek immediate medical attention if they develop weakness and paralysis in the extremities, possibly progressing to the chest and face,

after vaccination with Janssen COVID-19 Vaccine (Ad26.COV2-S), as these could be signs of Guillain-Barré syndrome.

The PRAC recommended updating the product information of COVID-19 Vaccine Janssen to include immune thrombocytopenia as an adverse reaction, as well as a warning to alert healthcare professionals and people taking the vaccine of this possible side effect. In addition, the PRAC recommended an update to the risk management plan of COVID-19 Vaccine Janssen to re-classify 'thrombocytopenia', currently an important potential risk, as an important identified risk.

Immune thrombocytopenia is a condition in which the immune system mistakenly attacks and destroys blood cells called platelets that are needed for normal blood clotting.

The Committee assessed the available evidence, including scientific literature and cases reported to the European database for suspected side effects (EudraVigilance), to the Vaccine Adverse Event Reporting System (VAERS) in the United States and to the marketing authorization holder's global safety database.

The PRAC concluded that cases of dizziness and tinnitus (ringing or other noises in one or both ears) are linked to the administration of COVID-19 vaccine Janssen. In reaching this conclusion, the Committee took into consideration all currently available evidence. This included an analysis of 1,183 cases of dizziness identified as part of spontaneous reports on anxiety-related reactions to immunization. Regarding tinnitus, EMA investigated 6 cases observed in clinical trials and 108 cases identified by the company during monitoring spontaneous reports.

In light of this, the PRAC has recommended amending the product information to add dizziness and tinnitus as adverse reactions to alert healthcare professionals and people taking the vaccine of these potential side effects.

The benefit-risk balance of the vaccine remains unchanged.

EMA will continue to closely monitor this issue and will communicate further when new information becomes available. PRAC continues to closely review reports of Guillain-Barré syndrome with Vaxzevria.

Meeting highlights from the Pharmacovigilance Risk Assessment Committee (06 Aug 2021)

EMA's latest safety assessment also concluded that people who have previously had capillary leak syndrome must not receive Janssen COVID-19 Vaccine (Ad26.COV2-S). Capillary leak syndrome may also occur as a side effect of Janssen COVID-19 Vaccine (Ad26.COV2-S).

EMA COVID-19 vaccine safety update COVID-19 Vaccine JANSSEN (14 Jul 2021)

Status Update: WHO EUL/PQ evaluation

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

Please visit the site regularly for the latest updated version.

Below is version 06 August 2021.

- **Vaccines** — *Guidance document 06 August 2021*

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

		EUL Assessment			Post-EUL activities		
#	Manufacturer / WHO EUL holder	NRA of Record	Status of assessment	Decision date	Other EUL commitments/changes	Support to countries to facilitate authorization	
1.	Pfizer BioNTech	EMA	Core sites	31 Dec 2020	• Clinical and CMC updates • Extension of storage conditions at 2-8°C from 5 days to 31 days. • New indication	• Access to dossier/reports of the assessment/Post EUL: **55 countries**	• Sharing dossiers/reports with **96 countries** > 394 shared dossiers/reports. • Additional reports of the post-EUL changes/updates. • Briefings on the outcome of the review: AFRO, EMRO, EURO PAHO • Bilateral discussions with countries to facilitate national authorizations • Support to countries actual shipments of vaccines
			Baxter Oncology GmbH, DE Novartis, Switzerland Diluent suppliers	02 Jul 2021 08 Jul 2021 18 Jun 2021			
			Mibe (Darmapharm), DE Pharmacia & Upjohn (Kalamazoo, MI) & Hospira (McPherson, KS) USA	16 Jul 2021			
2.	AstraZeneca / Oxford	EMA	Core data finalized	16 Apr 2021	• Clinical and CMC updates	• Access to dossier/reports of the assessment/Post EUL **79 countries**	
			Finalized: SK-Catalent Wuxi (DS) Chemo Spain	16 Apr 2021 30 Apr 2021 04 Jun 2021			
3.		MFDS	Finalized	15 Feb 2021	• Clinical and CMC updates		
4.	Serum Institute of India Pvt. Ltd.	DCGI	Finalized	15 Feb 2021	• Clinical and CMC updates, • Extension of shelf life at 2-8°C 06 to 09 months	• Access to dossier/reports of the assessment/Post EUL: **56 countries** • Support to countries (donations) on cold chain excursions	
5.	Janssen Infectious Diseases & Vaccines	EMA	Core data finalized (US +NL sites)	12 Mar 2021	• 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)	• Access to dossier/reports of the assessment/Post EUL: **61 countries** • Support on programmatic aspects	
			Additional sites: - Aspen RSA (DP) - Catalent Agnani Italy (DP) - Merck, Durham, UK (DS), - West Point/PA, USA (DP)	25 Jun 2021 02 Jul 2021 - As submitted			
6.	moderna	EMA	Finalized	30 Apr 2021	• Clinical and CMC updates	• Access to dossier/reports of the assessment/Post EUL: **44 countries**	
			ModernaTX, Inc (Norwood), USA Additional data - ongoing	06 Aug 2021	• Support for international shipments • Documentation requested by countries: Certificate of Analysis		
7.	Sinopharm / BIBP[1]	NMPA	Sites in China	07 May 2021	• Clinical and CMC updates New sites and presentation	• Access to dossier/reports of the assessment/Post EUL: **57countries**	
8.	sinovac	NMPA	Sites in China	01 Jun 2021	• Clinical and CMC updates • New sites, presentation, indication	• Access to dossier/reports of the assessment/Post EUL: **42 countries**	

#	Manufacturer / WHO EUL holder	NRA of Record	Status	meetings	Rolling data		
9.	The Gamaleya National Center	Russian NRA	Additional information submitted	Several meetings have been and continue to be held.	"Rolling" data of clinical and CMC has started.	Additional data (Non-CLIN, CLIN, CMC) Required. Following up on inspection observations.	Anticipated date will be set once all data is submitted and follow-up of inspection observations completed.
10.	AstraZeneca / Oxford	Japan MHLW / PMDA	Submission received on 15 June. MHLW submiited review & GMP reports on 16 & 22 June 2021.	Several meetings held separately with AZ & MHLW/PMDA	✓	Finalized Ongoing	09 July 2021
11.	AstraZeneca / Oxford	Australia TGA	Submission from AZ received on 11 June	Several meetings held separately with AZ & TGA	✓		Anticipated date: Week of 05 July
12.	康希诺生物 CanSinoBIO	NMPA	✓	✓	Rolling data in Aug 2021, meeting request		
13.	Bharat Biotech, India	DCGI	✓	✓	Rolling data starting 06 Jul 2021		
14.	NOVAVAX	EMA	✓	✓	Rolling data in Sept 2021		
15.	Sinopharm / WI	NMPA	✓		Rolling data in Aug 2021		
16.	Sanofi Pasteur	EMA	✓	✓	Sept-Nov 2021		
17.	Serum Institute of India Pvt. Ltd. Novavax	DCGI	✓	Planned week of 09 Aug			
18.	CureVac	EMA	✓	Q4 2021			
19.	Clover Biopharmaceuticals	EMA NMPA	✓	Being planned			
20.	Vector State Research Centre of Viralogy and Biotechnology	Russian NRA	Letter received not EOI. Reply sent on 15/01/2021	Q4 2021			
21.	Zhifei Longcom, China	NMPA	Response to 2nd EOI sent 29 Jan 2021. Additional info requested.				
22.	IMBCAMS, China	NMPA	Not accepted, still under initial development				
23.	BioCubaFarma - Cuba	CECMED	Awaiting information on strategy and timelines for submission.				

Supporting national authorization after WHO EUL

To support national authorization after EUL, WHO and manufacturers agreed that documentation submitted to PQ may be shared with national regulatory authorities - after signing a confidentiality agreement - to expedite access globally. WHO also convenes a group of focal points from WHO

regional offices to coordinate COVAX/WHO support for countries going through the regulatory process and help address problems as they arise. Interventions such as these enabled 70% of the countries in the first COVAX allocation round to have issued regulatory authorizations within 15 days of the EUL announcement. Future COVAX allocations are expected to trigger national regulatory authorization for other COVID-19 vaccines.

COVAX SWAT workshop: Connecting primary and booster vaccination goals

On 5th August, the COVAX Clinical Development & Operations SWAT Team and the Enabling Sciences SWAT Team co-organized a workshop on "Connecting COVID-19 primary and booster vaccination goals: historical precedents, immunologic considerations and approaches to meeting regulatory and policy requirements".

Workshop objectives were to:

- Review immunological principles and historical precedents for booster vaccination
- Review recent immunological durability data and ongoing / planned booster studies
- Summarize available regulatory guidance for booster vaccine registration, including study design, endpoints and success criteria, and
- Explore alternative approaches for new or existing vaccines with heterologous and/or reduced dose boost vaccination

Presentation materials

Full vaccination: Key to protecting against serious COVID-19

European Centre for Disease Prevention and Control (ECDC) and EMA update on COVID-19 recommends full vaccination as the key to protecting against serious COVID-19, including disease caused by the Delta variant.

With the increasing circulation of the Delta variant of SARS-CoV-2 in EU/EEA countries, the EMA and the ECDC strongly encourage those who are eligible for vaccination but have not yet been vaccinated to start and complete the recommended COVID-19 vaccination schedule in a timely manner.

Full vaccination with any of the EU/EEA-approved vaccines offers a high level of protection against severe disease and death caused by SARS-CoV-2, including variants, such as Delta. The highest level of protection is achieved after enough time (seven to fourteen days) has passed from the day of the last vaccine dose.

Vaccination is also important for protecting those at highest risk of severe disease and hospitalization, reducing the spread of the virus, and preventing the emergence of new variants of concern.

Mike Catchpole, ECDC's Chief Scientist said "While the available vaccines are highly effective in protecting people against severe COVID-19, until higher proportions of the population are immunised, the risk is not beyond us. We are now witnessing an increasing number of COVID-19 cases across the EU/EEA and vaccines remain the best available option to avoid an increase in severe disease and death."

Infections in vaccinated people do not mean that vaccines do not work.

ECDC and EMA update on COVID-19 (04 Aug 2021)

Safety of COVID-19 Vaccines

WHO guidance for clinical case management of thrombosis with TTS

Thrombotic Thrombocytopenia Syndrome (TTS) has emerged as a new adverse event following immunization in individuals vaccinated with COVID-19 non-replicant adenovirus vector-based vaccines (AstraZeneca COVID-19 ChAdOx-1 vaccine and Johnson & Johnson (J&J) Janssen COVID-19 Ad26.COV2-S vaccine). TTS is a serious and life-threatening adverse event.

WHO has issued interim emergency guidance to increase awareness about TTS in the context of COVID-19 vaccination and help healthcare providers in the assessment and management of potential TTS cases. Knowledge about TTS following vaccination with a COVID-19 adenovirus vector-based vaccine is rapidly evolving. WHO will continue to monitor the situation closely for any changes that may affect this interim guidance and will update the guidance as needed.

> Guidance for clinical case management of thrombosis with TTS following vaccination to prevent coronavirus disease (COVID-19) (19 Jul 2021)

WHO statement on reports of GBS following adenovirus vector COVID-19 vaccines

The GACVS subcommittee, working with the US ACIP and EMA PRAC, has issued a statement on Guillain-Barré syndrome (GBS) following adenovirus vector COVID-19 vaccines. Rare cases of GBS have been reported following vaccinations with adenovirus vector COVID-19 vaccines. Though countries should always consider their individual pandemic circumstances and benefit-risk profiles, overall the subcommittee concluded that the potential benefits of both the Janssen and AstraZeneca COVID-19 vaccines continue to outweigh any potential risk of GBS, particularly given the increase in the more transmissible Delta (B.1.617.2) variant.

Healthcare professionals should be aware of the signs and symptoms of GBS to allow for early diagnosis and treatment. Most people fully recover from GBS.

> Statement of the WHO GACVS COVID-19 subcommittee on reports of Guillain-Barré Syndrome following adenovirus vector COVID-19 vaccines (26 Jul 2021)

WHO guidance on cases of mild myocarditis following COVID-19 mRNA vaccines

The COVID-19 subcommittee of the WHO GACVS has reviewed reports of a small number of cases of myocarditis reported in individuals vaccinated with the COVID-19 mRNA vaccines. Myocarditis is an inflammation of the heart muscle and pericarditis is an inflammation of the lining that surrounds the heart. While it can cause serious illness, it is frequently mild and responds well to conservative treatment. The subcommittee noted that in most of the reported cases, the individuals have recovered.

> COVID-19 subcommittee of the WHO GACVS: updated guidance regarding myocarditis and pericarditis reported with COVID-19 mRNA vaccines (09 Jul 2021)

WHO safety surveillance of COVID-19 vaccines in pregnant and breastfeeding women

A new WHO module on safety surveillance provides an overview of factors to consider when monitoring the safety of COVID-19 vaccines administered to pregnant and breastfeeding women. It describes how national routine AEFI surveillance should be adapted to cater for this specific group of population using both passive and active surveillance methods.

Specific considerations and limitations of each method are provided as well as tools for implementation.

> COVID-19 Vaccines: safety surveillance manual. Module on safety surveillance of COVID-19 vaccines in pregnant and breastfeeding women (12 Jul 2021)

Challenges of vaccinating pregnant and lactating women during the COVID-19 pandemic

COVAX Maternal Immunization working group held a webinar on 13 April and its report has been published.

There is a clear need for post-marketing (post-implementation) active surveillance globally. This effort could leverage existing systems such as pregnancy exposure registries for anti-retroviral drugs.

Suggested immediate next steps for collection of safety data in LMICs are to create platforms to exchange information and methodologies for the assessment of vaccine safety in pregnancy; to develop safety surveillance systems that work across programs and integrate these into routine care; and to focus on cross-cutting collaborative projects and communications.

Key priorities for research should include understanding what pregnant women need to know and from whom to make COVID-19 vaccines more acceptable and accessible; collection of specific data in pregnancy; and effective pharmacovigilance and harmonization of data collection.

> COVAX webinar report: Challenges of vaccinating pregnant and lactating women during the COVID-19 pandemic.

WHO Animal Models Working Group

Progress with phenotyping SARS-CoV-2 variants of concern using human organoid systems was described in the 29 July meeting. Extended shedding was found to be a characteristic of the alpha variant in multiple human epithelial organoids, and the alpha variant was also demonstrated to have a higher replicative fitness than ancestral strains in human airway organoids.

Upcoming events

WHO Consultation on COVID-19 vaccine research

13 August 13:00 - 17:00 CET

The objectives of this consultation will be 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 will debate the methodological strength and limitations of existing data and the potential designs to generate additional data leading to evidence-based decisions.

Registration at https://www.who.int/news-room/events/detail/2021/08/13/default-calendar/who-consultation-on-covid-19-vaccines-research-13-august-2021

COVAX Enabling Sciences: Standardization of Immune Response Assays to COVID-19 Vaccines - A Year's Experience Transferring Assays to a Global Laboratory Network

31 August, 15:30 – 19:30 CET

> Brochure
>
> Registration