28th WHO Regulatory Update on COVID-19

05 February 2021

World Health Organization

Key Messages

Vaccines are giving us a window of opportunity to bring the pandemic under control. The number of vaccinations globally has now overtaken the number of reported infections. But more than three quarters of those vaccinations are in just 10 countries while around 130 countries, with 2.5 billion people, are yet to start their first vaccination. WHO encourages COVID vaccine manufacturers to share their dossiers with WHO faster and more fully for assessment of emergency use listing.

Highlights and main issues

- WHO has been tracking virus variants since the beginning of the COVID-19 outbreak. With the emergence of new variants of concern, these efforts have been stepped-up to set up systems to quickly identify and study emerging variants.
- WHO is working with relevant stakeholders on a common naming system for variants. The aim is to name variants that have potential impact on severity, on transmission and any that have any impact on diagnostics, therapeutics and vaccines.
- On 3 February, COVAX has published an interim distribution forecast to provide information on early projected availability of doses of the Pfizer/BioNTech vaccine in Q1 2021 and the AstraZeneca/Oxford vaccine candidate in first half 2021 to COVAX Facility participants.
- On 29 January 201, the EU granted a conditional marketing authorisation, based on a recommendation from the EMA, for the AstraZeneca COVID-19 Vaccine to prevent coronavirus disease 2019 (COVID-19) in people from 18 years of age.
- The WHO Strategic Advisory Group of Experts (SAGE) on Immunization has issued interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19 in people aged 18 years and older.
- Safety and efficacy data from large phase 3 clinical trials of two investigational COVID-19 vaccines, and one vaccine already being used in some countries, have been released.
- WHO has received reports from multiple sources of suspicious offers to sell or supply COVID-19 vaccines to national regulatory authorities or Ministries of Health. These are attempts to defraud national regulatory authorities or Ministries of Health.
- Tracking of batch numbers of vaccines in distribution should be prioritized in all countries from release of products from the manufacturer to all points up to the point of care.

Contents

New virus variants

WHO's work on virus variants

As part of emergency preparedness and response protocol, WHO and its international network of experts monitor changes to the virus, not just COVID-19 but and track the evolving infectious disease situation, sound the alarm when needed, share expertise, and mount the kind of response needed to protect populations from the consequences of epidemics.

WHO Disease Outbreak News (DONs)

WHO has been tracking COVID-19 virus variants since the beginning of the outbreak. With the

emergence of new variants of concern, these efforts have been stepped-up to set up systems to quickly identify and study emerging variants. Variants of interest are tracked through the Virus Evolution Working Group, which was formalized in June 2020.

WHO is currently developing a Risk Monitoring Framework to identify, monitor and assess SARS-CoV-2 mutations, variants of interest and variants of concern. It will involve components including surveillance (through epidemiological studies, molecular diagnostic testing, genomic sequencing), research on variants of concern (protein modelling, laboratory and epidemiological studies) and evaluation of the impact on diagnostics, therapeutics and vaccines.

WHO Weekly epidemiological update (02 Feb 2021)

WHO Webinar on SARS-CoV-2 virus mutations and variants (03 Feb 2021)

Video recording

WHO EPI-WiN SARS-CoV-2 virus mutations & variants (29 Jan 2021)

LIVE Q&A virus variants with Dr M. Ryan and Dr M. Van Kerkhove (27 Jan 2021)

Epidemiological Update: Occurrence of variants of SARS-CoV-2 in the Americas (26 Jan 2021)

To assist laboratories setting up sequencing programmes, WHO published an interim guidance on genomic sequencing and an implementation handbook. In countries where capacity is not yet available, WHO supports national authorities by transporting samples to international WHO reference laboratories.

Interim guidance on SARS-CoV-2 genomic sequencing for public health goals (08 Jan 2021)

Genomic sequencing of SARS-CoV-2: A guide to implementation for maximum impact on public health (08 Jan 2021)

COVID-19 genome sequencing laboratory network launches in Africa (Sept 2020)

Laboratory biosafety guidance related to coronavirus disease

The purpose of this document is to provide interim guidance on laboratory biosafety related to the SARS-CoV-2 virus to laboratories and stakeholders involved in COVID-19 laboratory work. This also includes the packaging and shipment requirements for sending specimens to WHO reference laboratories providing confirmatory and other testing for COVID-19.

The latest update (28 January 2021) includes the following addition and revision:

- biosafety aspects for working with antigen-detecting rapid diagnostic test;
- handling new variants of SARS-CoV-2 in the laboratory;
- updated assay decontamination before disposal;
- personal protective equipment (PPE) for specimen collection;
- addressing chemical hazards and their safe disposal; and
- the fourth edition of the WHO Laboratory Biosafety Manual (LBM4) is now available and the terminology in this guidance was aligned with the LBM4.

For more details on biosafety, it is encouraged to refer to the WHO Laboratory Biosafety Manual (LBM4) suite, including risk assessment, PPE, decontamination and other subject-specific monographs

Laboratory biosafety guidance related to coronavirus disease (COVID-19): Interim guidance (28 Jan 2021)

The variant first identified in the UK

As of 2nd February, VOC 202012/01, lineage B.1.1.7 has been detected in 80 countries across all six

WHO regions. Studies conducted in more than one country are indicating the increased transmissibility of this variant. Preliminary analyses done on a relatively small number of people was published by New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG), suggesting that there may be an increase in the severity of disease associated with this new variant. More data are currently being collected to clarify the situation.

NERVTAG paper on COVID-19 variant of concern lineage B.1.1.7 (22 Jan 2021)

It should be noted, however, that 6 European countries have reported decreasing trends in new cases over the past two weeks, highlighting that the robust implementation of public health and social measures is effective against this variant.

This variant impacted those PCR tests that target the spike (S) gene of the virus. Because most countries use molecular assays targeting several different viral genes, their assays are likely to continue to work. In the UK where this variant is predominant, the S-gene target failure is being used as proxy for identifying the variant. I n countries where this variant is not predominant, S-gene target failure may not directly identify VOC202012/01 and requires confirmation by sequencing.

Preliminary findings, in-vitro studies available as pre-prints, show that the Pfizer and Moderna vaccines have limited or no significant loss in efficacy against VOC202012/01. These findings require further investigation involving much larger sample sizes. On 28 Jan 2021, Novavax announced that its vaccine was slightly less effective but still sufficiently effective against VOC 202012/01.

The variant first identified in South Africa

As of 2nd February, variant 501Y.V2, lineage B.1.351 has been reported in 34 countries across five of the six WHO regions. WHO AFRO reports that the variant 501Y.V2 variant “is predominant and powering record case numbers in South Africa and the sub-region.” Initial modelling estimates indicate the increased transmissibility of this virus compared to the previously circulating variants.

Despite the increasing circulation of this variant, South Africa and its neighboring countries have reported decreasing incident of cases, highlighting the robust implementation of public health and social measures is also effective against this variant.

Seven things to know about COVID-19 variants in Africa (22 Jan 2021)

Preliminary in-vitro studies are showing that there is a slight reduction of effectiveness of vaccines (like the Moderna, Pfizer mRNA vaccines) but that the protection levels remain high. On 28 Jan 2021, Novavax and J&J announced that their vaccines were effective, but less so, against variant 501Y.V2. There is some evidence that one of the mutations in the variant may affect the impact of some monoclonal antibodies, but research is ongoing.

The variant first identified in Brazil

As of 2nd February, variant P.1, lineage B.1.1.28, initially identified in Brazil on 4th December 2020, is now identified in 10 countries in 4 WHO regions. P.1 variant is now becoming the predominant variant in Amazonas areas in addition to Manaus. Further studies are needed to understand high attack rate, sharp increase in COVID-19 hospital admissions and reinfection in Manaus where levels of infections were high in 2020.

Systematic naming of variants

It is important to have a common nomenclature for variants that is easily understood and does not include geographical references to mitigate stigmatization and geopolitical issues. Currently, three main nomenclatures for SARS-CoV2 variants (GISAID, Nextstrain, Pango), developed for different purposes, have been used. Nomenclature groups, Virus Evolution Working Group and international experts held its first meeting on 2nd February to explore a mechanism to develop a standardized nomenclature that will be more easily understood and will not be associated with any country or a region where viruses are initially identified.

Contact tracing in the context of COVID-19

Contact tracing is a key strategy for interrupting chains of transmission of SARS-CoV-2 and reducing COVID-19-associated mortality. This document provides updated guidance on how to establish contact tracing capacity for the control of COVID-19, and how to prioritize contact tracing activities in different settings.

Contact tracing in the context of COVID-19 (01 Feb 2021)

Online global consultation on contact tracing for COVID-19, 9-11 June 2020

COVID-19 has heavily emphasized how contact tracing is crucial for managing outbreaks, and as part of the strategy for adjusting, and eventually lifting, lockdowns and other stringent public health and social measures. As the pandemic develops further, it will be a core measure to manage further waves of infection. In early June 2020, the World Health Organization (WHO) convened an online global consultation on contact tracing in the context of COVID-19, looking at the lessons of the pandemic to date; known and emerging best practices; and the measures necessary for urgent implementation, scale-up, maintenance and enhancement of contact tracing activities. This report captures the meeting deliberations and key recommendations of WHO and GOARNs COVID 19 response stakeholders, addressing ways to strengthen the contact tracing response and review operational experiences together to further improve collaboration and coordination between partners

Online global consultation on contact tracing for COVID-19, June 2020 (21 Jan 2021)

Update on the ACT-Accelerator

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. Candidates to be included in the COVAX Facility portfolio are being selected from the COVAX R&D portfolio and other clinical candidates.

COVAX publishes first interim distribution forecast

In line with initial guidance delivered on 22 January, and building on the publication of the 2021 COVAX global and regional supply forecast, the COVAX Facility published the indicative distribution forecast. This announcement comes less than two weeks after the announcement of the signed advance purchase agreement with Pfizer/BioNTech and a little more than a month after the first COVID-19 vaccine received WHO EUL approval.

COVAX currently anticipates 1.2 million doses of the EUL listed Tozinameran (Pfizer-BioNTech vaccine) will be available to the COVAX Facility in Q1 2021. Additional volumes of doses of the Tozinameran will be available in the second quarter and beyond, per the signed advance purchase agreement between Gavi and Pfizer-BioNTech for up to 40 million doses.

Forecast includes indicative distribution of 240 million doses of the AstraZeneca/Oxford vaccine, licensed to Serum Institute of India (SII) and 96 million doses of the AstraZeneca/Oxford vaccine for Q1 & Q2 2021. It is important to note that WHO EUL has not yet been granted for the AstraZeneca vaccine, although evaluation processes are currently underway.

The purpose of sharing the interim distribution with countries, even in today's highly dynamic global supply environment, is to provide governments and health systems with the information they need to plan for their national vaccination programmes.

Final allocations will be published in due course.

COVAX publishes first interim distribution forecast (03 Feb 2021)

The COVAX Facility: Interim Distribution Forecast (03 Feb 2021)

Latest list of COVAX Facility participants (15 Dec 2020)

On 5th February, Dr Tedros opened the media briefing by stating that "Countries are ready to go, but the vaccines aren't there. We need countries to share doses once they have finished vaccinating health workers and older people." He then encouraged COVID vaccine manufacturers "to share their dossiers with WHO faster and more fully than they have been doing, so we can review them for emergency use listing."

WHO Director-General's opening remarks at the media briefing on COVID-19 (05 Feb 2021)

Alignment of approaches by regulators

EMA Pilot Project 'OPEN'

Since December 2020, the EMA is piloting a new 'OPEN' initiative to increase international collaboration on the evaluation of COVID-19 vaccines and therapeutics. The collaboration allows sharing of scientific expertise during the evaluation of COVID-19 vaccines and therapeutics at a time when regulatory authorities and pharmaceutical industry are all facing common challenges.

It aims promote overall transparency and contribute to public trust in the vaccines and therapeutics and the pilot will foster better understanding of regulatory outcomes, while retaining scientific and regulatory independence of the participating authorities.

Regulators from Australia, Canada, Japan, Switzerland and the World Health Organization (WHO) are participating in the pilot under the terms of existing confidentiality arrangements.

EMA COVID-19 assessments 'OPEN' to non-EU regulators (04 Feb 2021)

Questions and Answers on the Pilot Project 'OPEN' (03 Feb 2021)

Draft WHO Guidance for comments

Guidelines on monoclonal antibodies for infectious diseases: (inputs by 15 Feb 2021)

WHO is drafting a guideline on the quality and manufacture of monoclonal antibodies (mAbs), as well as a separate regulatory guidance document on the safety and efficacy evaluation of mAbs and antibody mimetics (AMs) for use in the pre-exposure prophylaxis and treatment of infectious diseases. Supplements that provide additional guidance for the development and evaluation of products to specific diseases, including Covid-19, are proposed.

WHO would like to identify any regulatory considerations that may be unique to the clinical evaluation of mAbs, AMs, or DNA/RNA-encoded mAbs directed to Covid-19.

Guidelines on monoclonal antibodies for infectious diseases: call for public comment

Please use the WHO Comment Form to provide your comments to Dr Richard Isbrucker, at isbruckerr@who.int, by 15 Feb 2021

Draft proposals for inclusion in The International Pharmacopeia

Remdesivir (Remdesivirum) (Comments by **28 Feb 2021)**

Remdesivir intravenous infusion (Remdesiviri infusio intraveno) (Comments by **28 Feb 2021)**

Oxygen (Oxygenium) (Comments by **28 Feb 2021)**

Gelatin (Comments by **31 Mar 2021)**

Ethanol, Anhydrous (Comments by **31 Mar 2021)**

Ethanol 96% (V/V) (Comments by **31 Mar 2021)**

Draft guidance for comments:

Good manufacturing practices 6 for medical gases (Comments by **30 Mar 2021)**

Guidance on setting remaining shelf life for the supply and procurement of Emergency Health Kits (Comments by **15 Apr 2021)**

In vitro diagnostics

WHO update on Testing strategies

Testing is part of a comprehensive strategy to suppress transmission and should be conducted by making the best use of available resources and linking to clear public health goals.

WHO published an easy-to-understand presentation on testing strategies.

EPI-WiN: How to use testing to achieve public health measure (15 Jan 2021)

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.

So far, 27 products have been listed as eligible for WHO procurement among a total of 113 expressions of interest (59 for NAT assays, 35 for antibody detection assays and 19 for antigen detection RDTs) have been received.

EUL listed IVDs (26 Jan 2021)

The status of each EUL application (02 Feb 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.

The most recent collated IVDs listed by IMDRF NRAs (26 Jan 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

Update on WHO's clinical management guidelines for COVID-19

On 25 January 2021, WHO updated its living guidelines on COVID-19 clinical management, providing trustworthy guidance that is comprehensive and holistic for the optimal care of COVID-19 patients, throughout their entire illness is necessary.

This guideline now includes Best Practice Statement on caring for COVID-19 patients after their acute illness and 5 new conditional recommendations for:

- clinical judgment and management decisions
- use of pulse oximetry monitoring at home as part of a package of care
- the use of awake prone positioning in patients with severe COVID-19
- use of thromboprophylaxis dosing of anticoagulation rather than intermediate or therapeutic dosing in patients hospitalized with COVID-19
- the use of existing care bundles chosen locally by hospital or ICU and adapted as necessary for local circumstances in patients with critical COVID-19

COVID-19 Clinical management: living guidance (25 Jan 2021)

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.

Convalescent plasma and blood

Advisory Group on Blood Regulation, Availability and Safety: Call for Experts:

WHO has announced a call for experts for an Advisory Group on Blood Regulation, Availability and Safety. One of the functions of the Advisory Group being formed is to provide scientific assessment of current and emerging threats to the safety and availability of blood and blood products. The Advisory Group will advise on the recommended measures and actions to be taken by the Member States in preparedness for and in response to the emerging public health threats.

Nomination requested by **28 February 2021**.

Call for Experts - Advisory Group on Blood Regulation, Availability and Safety

Vaccines

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

Conditional marketing authorization granted by the EU

On 29 January, the EU granted a conditional marketing authorization, based on a recommendation

from the EMA, for the AstraZeneca COVID-19 Vaccine to prevent coronavirus disease 2019 (COVID-19) in people from 18 years of age. Combined results from 4 clinical trials, involving around 24,000 people altogether, in the United Kingdom, Brazil and South Africa showed that the AstraZeneca COVID-19 Vaccine was safe and effective at preventing COVID-19 in people from 18 years of age. The safety of the vaccine has been demonstrated across the four studies. However, the Agency based its calculation of how well the vaccine worked on the results from study COV002 (conducted in the UK) and study COV003 (conducted in Brazil). The other two studies had fewer than 6 COVID-19 cases in each, which was not enough to measure the preventive effect of the vaccine. A 59.5% reduction was seen in the number of symptomatic COVID-19 cases in people given the vaccine according to the two-dose schedule (64 of 5,258 got COVID-19 with symptoms) compared with people given control injections (154 of 5,210 got COVID-19 with symptoms).

Most of the participants in the clinical trials were between 18 and 55 years old. There are not yet enough results in older participants (over 55 years old) to provide a figure for how well the vaccine will work in this group. However, protection is expected, given that an immune response is seen in this age group and based on experience with other vaccines; as there is reliable information on safety in this population, EMA's scientific experts considered that the vaccine can be used in older adults. More information is expected from ongoing studies, which include a higher proportion of elderly participants.

The AstraZeneca COVID-19 Vaccine is given as two injections into the arm, the second between 4 to 12 weeks after the first. The most common side effects with AstraZeneca COVID-19 Vaccine were usually mild or moderate and resolved within a few days after vaccination. The most common side effects are pain and tenderness at the injection site, headache, tiredness, muscle pain, general feeling of being unwell, chills, fever, joint pain and nausea.

The product information approved by the CHMP for COVID-19 Vaccine AstraZeneca contains prescribing information for healthcare professionals, a package leaflet for members of the public and details of conditions of the vaccine's authorisation.

An assessment report with details of EMA's evaluation of COVID-19 Vaccine AstraZeneca and the full risk management plan have been published.

EMA opinion and key facts: COVID-19 Vaccine AstraZeneca (ChAdOx1-S [recombinant])

CHMP summary of positive opinion for COVID-19 Vaccine AstraZeneca

COVID-19 Vaccine AstraZeneca - Product information

Risk management plan summary for COVID-19 Vaccine AstraZeneca (29 Jan 2021)

Moderna COVID-19 (mRNA-1273) vaccine

SAGE interim recommendations

The WHO Strategic Advisory Group of Experts (SAGE) on Immunization has issued interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19 in people aged 18 years and older. The vaccine is safe and effective in people with known medical conditions associated with increased risk of severe disease, such as hypertension, diabetes, asthma, pulmonary, liver or kidney disease, as well as chronic infections that are stable and controlled. Although further studies are required for immunocompromised persons, people in this category who are part of a group recommended for vaccination may be vaccinated after receiving information and counselling. Persons living with HIV are at higher risk of severe COVID-19 disease. Known HIV-positive vaccine recipients should be provided with information and counselling. Vaccination can be offered to people who have had COVID-19 in the past. But individuals may wish to defer their own COVID-19 vaccination for up to six months from the time of SARS-CoV-2 infection. The vaccine can be offered to a breastfeeding woman who is part of a group recommended for vaccination (e.g. health workers); discontinuing breastfeeding after vaccination is currently not recommended.

While pregnancy puts women at a higher risk of severe COVID-19, the use of this vaccine in pregnant women is currently not recommended, unless they are at risk of high exposure (e.g. health

workers). Individuals with a history of severe allergic reaction to any component of the vaccine should not take this or any other mRNA vaccine. While vaccination is recommended for older persons due to the high risk of severe COVID-19 and death, very frail older persons with an anticipated life expectancy of less than 3 months should be individually assessed. The vaccine should not be administered to persons younger than 18 years of age pending the results of further studies.

SAGE recommends the use of the Moderna mRNA-1273 vaccine at a schedule of two doses (100 µg, 0.5 ml each) 28 days apart. If necessary, the interval between the doses may be extended to 42 days. Compliance with the full schedule is recommended and the same product should be used for both doses.

Interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19 (25 Jan 2021)

The Moderna COVID-19 (mRNA-1273) vaccine: what you need to know (26 Jan 2021)

European Public Assessment Report

The Moderna COVID-19 (mRNA-1273) vaccine received a conditional marketing authorisation from the EMA on 06 January 2021. This was granted in the interest of public health because the medicine addresses an unmet medical need and the benefit of immediate availability outweighs the risk from less comprehensive data than normally required. The European Public Assessment Report was published on 20 January, and an update issued on 26 January 2021.

EMA Authorisation details, product information: COVID-19 Vaccine Moderna

EMA vaccine safety update

The update presents the assessment of an investigation of reports of suspected severe allergic reaction coming from a single vaccination site in the United States. The assessment of these reports has not identified new aspects regarding the nature of this known side effect. The benefits of Moderna COVID-19 Vaccine in preventing COVID-19 continue to outweigh any risks, and there are no recommended changes regarding the use the vaccine.

EMA COVID-19 vaccine safety update for COVID-19 Vaccine Moderna (05 Feb 2021)

Pfizer/BioNTech COVID-19 mRNA vaccine, Tozinameran

EMA vaccine safety update

The safety update provides the assessment by EMA's safety committee (PRAC) of deaths reported after vaccination with Tozinameran (Comirnaty is a commercial name), including deaths in frail, elderly people. PRAC carried out an analysis of the cases and took into account the presence of other medical conditions and the death rate for corresponding age groups in the general population. PRAC concluded that the data did not show a link to vaccination with Tozinameran and the cases do not raise a safety concern. Further reports will continue to be carefully monitored. This update is consistent with the assessment from the Global Advisory Committee on Vaccine Safety, which was reported in the 27th Regulatory update.

EMA Authorization details, product information, safety updates: Comirnaty

COVID-19 vaccine safety update for Comirnaty (29 Jan 2021)

Novavax on NVX-CoV2373 COVID-19 Vaccine (Novavax press release)

NVX-CoV2373 is an investigational COVID-19 vaccine that contains a full-length, prefusion spike protein made using recombinant nanoparticle technology and a proprietary saponin-based Matrix-M™ adjuvant. The purified protein is encoded by the genetic sequence of the SARS-CoV-2 spike (S) protein and is produced in insect cells. The press release states the investigational vaccine was 90%

effective at preventing symptomatic COVID-19 disease in its Phase III efficacy trial involving more than 15,000 volunteers in the U.K., where the B.1.1.7 variant has become predominant. In South Africa a Phase 2b clinical trial was stated to demonstrate 60% efficacy (95% CI: 19.9 – 80.1) for the prevention of mild, moderate and severe COVID-19 disease in the 94% of the study population that was HIV-negative. During the trial, the 501Y.V2 variant, which contains three critical mutations in the receptor binding domain (RBD) and multiple mutations outside the RBD, was widely circulating in South Africa. Novavax press release

WHO has not reviewed the data. The manufacturer is in discussion with WHO for submission to the WHO EUL/PQ evaluation process.

Johnson and Johnson on recombinant, replication- incompetent adenovirus type 26 (Ad26) vectored vaccine encoding the (SARS-CoV-2) Spike (S) protein (J&J press release)

Topline safety and efficacy data from a single-dose of an investigational COVID-19 vaccine developed by Jansen Biotech and based on a study of 43,783 participants accruing 468 symptomatic cases of COVID-19 are described in a press release from Johnson and Johnson. The investigational vaccine is a recombinant, replication- incompetent adenovirus type 26 (Ad26) vector encoding the (SARS-CoV-2) Spike (S) protein. Overall, the vaccine candidate was 66% effective in preventing moderate to severe COVID-19, 28 days after vaccination. The onset of protection was observed as early as day 14. The level of protection against moderate to severe COVID-19 infection was 72% in the United States, 66% in Latin America and 57% in South Africa, 28 days post-vaccination. During the trial, the 501Y.V2 variant was widely circulated in South Africa. J&J press release

WHO has not reviewed the data described in the press release. The manufacturer has submitted data for review in the WHO EUL/PQ evaluation process.

The US FDA has scheduled a meeting of its Vaccines and Related Biological Products Advisory Committee (VRBPAC) on Feb. 26, 2021, to discuss the request for emergency use authorization (EUA) for a COVID-19 vaccine from Janssen Biotech Inc.

Gamaleya Gam-COVID-Vac

Preliminary results from the interim analysis of a phase III trial on the efficacy and safety of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine (Gam-COVID-Vac) has been published in a peer reviewed journal. The use of two varying serotypes, which are given 21 days apart, is intended to overcome any pre-existing adenovirus immunity in the population. Between 7th September and 24th November 2020, 21,977 adults in the Russian Federation were randomly assigned to the vaccine group (n=16,501) or the placebo group (n=5,476). The interim analysis of the phase 3 trial of Gam-COVID-Vac showed 91·6% efficacy against COVID-19 and was well tolerated.

> Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia, The Lancet (02 Feb 2021)

WHO has not reviewed the data. The manufacturer is expected to submit data during February for review in the WHO EUL/PQ evaluation process.

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

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.

Version 01 Feb 2021

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

	Manufacturer	Name of Vaccine	NRA of Record	Platform	EOI accepted	Pre-submission meeting held	Dossier accepted for review*	Status of assessment**	Anticipated decision date***
1.	Pfizer BIONTECH	BNT162b2/COMIRNATY Tozinameran (INN)	EMA	Nucleoside modified mNRA	✓	✓	✓	Finalized	31/12/20
2.	AstraZeneca Covishield	AZD1222	Core – EMA Non-COVAX	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	✓	Finalized (non-Covax) Core data relevant for Covax. Covax data to be reviewed as EMA post approval change	EMA 29 Jan 2021 (non- Covax) Core data relevant for Covax. Additional nodes in March/ April for Covax
3.	SK BIO AstraZeneca GAVI	AZD1222	MFDS KOREA	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	Additional data expected 01 and 05 Feb 2021 (CMC for SK Bio)	Assessment in progress in conjunction with MFDS	Earliest 2nd half Feb 2021
4.	**Serum Institute of India**	Covishield (ChAdOx1_nCoV-19)	DCGI	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	✓	In progress	Mid Feb 2021
5.	Sinopharm / BIBP[1]	SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV)	NMPA	Inactivated, produced in Vero cells	✓	✓	✓	In progress	Earliest March
6.	sinovac	SARS-CoV-2 Vaccine (Vero Cell), Inactivated	NMPA	Inactivated, produced in Vero cells	✓	✓	Additional data expected 05 Feb and end of Feb 2021		Earliest March
7.	moderna	mRNA-1273	EMA	mNRA-based vaccine encapsulated in lipid nanoparticle (LNP)	✓	✓	Expected in February		Estimated end of Feb 2021
8.	janssen Infectious Diseases & Vaccines	Ad26.COV2.S	EMA	Recombinant, replication-incompetent adenovirus type 26 (Ad26) vectored vaccine encoding the (SARS-CoV-2) Spike (S) protein	✓	✓	Rolling data to EMA – Dec, 29 Jan 2nd half Feb, March and April	Not yet started. Use abridged procedure relying on EMA	Earliest April -May 2021
9.	THE GAMALEYA NATIONAL CENTER	Sputnik V	Russian NRA	Human Adenovirus Vector-based Covid-19 vaccine	Additional information submitted	Several meetings held. Further clarification requested.	Rolling data expected 08 and 15 February. Clarification on timelines for data for Covax supply awaited.		
10.	康希诺生物 CanSinoBIO	Ad5-nCoV	NMPA	Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector)	Additional information requested	✓	Rolling data starting April 2021		
11.	Vector State Research Centre of Viralogy and Biotechnology	EpiVacCorona	Russian NRA	Peptide antigen	Letter received not EOI. Reply sent on 15/01/2021				
12.	Zhifei Longcom, China	Recombinant Novel Coronavirus Vaccine (CHO Cell)	NMPA	Recombinant protein subunit	Response to Second EOI sent 29 Jan 2021.additional information requested.				
13.	IMBCAMS, China	SARS-CoV-2 Vaccine, Inactivated (Vero Cell)	NMPA	Inactivated	Not accepted, still under initial development				
14.	Sinopharm / WIBP[2]	Inactivated SARS-CoV-2 Vaccine (Vero Cell)	NMPA	No pre-submission meeting yet					
15.	NOVAVAX		EMA	No pre-submission meeting yet.	Introductory meeting requested and being planned.				

1. Beijing Bio-Institute of Biological Products Co-Ltd
2. Wuhan Institute of Biological Products Co Ltd

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

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

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

Technical brief from COVAX Regulatory Advisory Group

An updated technical brief from the COVAX Regulatory Advisory Group (RAG), including views on (a) labelling, carton and insert requirements; (b) use of regulatory reliance for CMC post-approval changes to maintain global vaccine supply; and (c) national authority batch release testing of COVID-19 vaccines is provided as an annex to this document.

The RAG is co-led by WHO and CEPI and is part of COVAX, the vaccines pillar of the ACT-Accelerator. The RAG has members from Regulatory Agencies covering all WHO regions, including Argentina, Australia, Brazil, Canada, Europe (EMA & EDQM), Ghana, Japan, Singapore and USA. The RAG was set up to give feedback on regulatory science questions of an agnostic nature raised by the COVAX teams in order to promote regulatory preparedness among COVID-19 vaccine developers. The feedback, in the form of technical briefs, is intended to serve as a means to make the wider community of Regulatory Authorities aware of questions and challenges vaccine developers are facing in development of COVID-19 vaccines.

Technical Brief: Regulation of COVID-19 Vaccines (04 Feb 2021)

Best practices for technology transfers

On 27th January, the COVAX manufacturing SWAT team held a workshop on "Best practices for

technology transfers". The workshop included case studies, an industry position, and regulatory perspectives.

Presentations from the workshop (27 Jan 2021)

Emerging Challenges to the Development of COVID-19 Vaccines

On 28th January, the COVAX clinical development and operations SWAT team held a workshop on "Emerging Challenges to the Development of COVID-19 Vaccines". The workshop discussed firstly the path to approval of additional COVID-19 vaccines and secondly clinical development gaps.

Presentations from the workshop (28 Jan 2021)

Living mapping and living systematic review of COVID-19 studies

Living mapping and living systematic reviews are available based on daily searches of the literature for candidate vaccines against COVID-19. As of 29 January 2021, the Covid-19 - living NMA initiative collected 151 RCTs and 37 non-randomised studies of vaccines from the ICTRP. 92 of these trials are recruiting patients. The tool allows vaccine comparisons where data are available as well as a table with the general characteristics of each trial. For each vaccine comparison, forest plots for all the outcomes of interest are available as well as the Summary of Findings table.

The mapping tool is available at: https://covid-nma.com/vaccines/mapping/

Landscape and tracker of COVID-19 candidate vaccines

The COVID-19 candidate vaccine landscape database compiles detailed information on COVID-19 vaccine candidates in development. The landscape is updated regularly.

Update (26 Jan 2021)

WHO Working Group: Assays and Reference Preparations

Immune memory to SARS CoV-2 was discussed in the 27 January meeting. There are several working models of immune memory. One research group reported that approximately 6 months after infection with SARS CoV-2, approximately 95% of individuals studies remained positive for 3 or more of 5 measures of immune memory. The remaining 5% of individuals had limited immune memory. It was noted that although immune memory responsible for protection against SARS CoV-2 is complex it should be possible to identify one or more immune correlates of protection.

Another research group had investigated whether the neutralizing antibody response evolves after SARS CoV-2 infection. Data were presented to support the hypothesis that it does so, becoming broader with time. Preliminary information was shared that spike substitutions in variants of concern affect individual monoclonal antibodies but the effect on neutralization by vaccinee or convalescent plasma is small.

An investigation of immune evasion by the 501Y.V2 (B.1.351) variant of SARS CoV-2 was presented in the 3 February 2021 meeting. This variant has mutations in both the receptor binding domain and the N-terminal domain of the spike protein. The majority of neutralizing antibodies to SARS CoV-2 recognize the receptor binding domain. The 501Y.V2 escaped neutralization by these monoclonal antibodies in pseudotype neutralization assays. The neutralization of wild-type virus by plasma or sera from 44 individuals was also tested. A five-fold reduction in mean titre was observed compared to viruses circulating in earlier stages of the pandemic. Results from vaccine studies, as reported in the section on "Vaccines", were recapitulated which showed that although neutralizing antibody titres elicited by the vaccines tested were reduced against 501Y.V2, the vaccines had vaccine efficacy in excess of levels recommended by WHO.

WHO COVID-19 vaccination training course for health workers

WHO is working in collaboration with scientists, businesses and global health organizations to speed up the pandemic response and facilitate the equitable access and distribution of COVID-19 vaccines. This Open course, primarily for frontline health workers provides general information on COVID-19 and specific information on storage, handling and administration of the vaccine, recording and monitoring including for adverse events following immunization (AEFI), and communication (acceptance and demand) through a series of short video lectures and quizzes to test your knowledge.

COVID-19 vaccination training for health workers

Recent publications

COVID-19 vaccine myths vs science

WHO's Dr Kate O'Brien busts some vaccine myths related to infertility, DNA and composition of vaccines in this week's Science in 5.

WHO's Science in 5 on COVID-19 - Vaccine myths vs science (05 Feb 2021)

Standard review form for national deployment and vaccination plan for COVID-19 vaccines (NDVP)

The National Deployment and Vaccination Plan for COVID-19 vaccines (NDVP): Standard Review Form (SRF) is an excel-based resource used by Regional Review Committees to assess NDVPs submitted to the Partners Platform. The SRF enables countries to prepare their NDVPs for the review process and supports regions in conducting a consistent and uniform assessment of the submitted NDVPs. This resource should be used in conjunction with the National Deployment and Vaccination Plan for COVID-19 vaccines (NDVP): Submission and Review Process document.

Standard review form for national deployment and vaccination plan for COVID-19 vaccines (29 Jan 2021)

COVID-19 national deployment and vaccination plan: Submission and review process

NDVP Submission and Review Process document outlines the step-by-step process for NDVP development, submission and review. This document is a helpful resource for countries as they prepare and submit their NDVP to the Partners Platform.

This resource should be used in conjunction with the NDVP: Standard Review Form excel.

COVID-19 national deployment and vaccination plan: Submission and review process (29 Jan 2021)

Excel: Standard review form: NDVP

The National Deployment and Vaccination Plan for COVID-19 vaccines (NDVP): Standard Review Form (SRF) is an excel-based resource used by Regional Review Committees to assess NDVPs submitted to the Partners Platform. The SRF enables countries to prepare their NDVPs for the review process and supports regions in conducting a consistent and uniform assessment of the submitted NDVPs. This resource should be used in conjunction with the National Deployment and Vaccination Plan for COVID-19 vaccines (NDVP): Submission and Review Process document.

Excel: Standard review form (29 Jan 2021)

Considerations for forming a regional COVID-19 review committee (RRC): Technical brief

Considerations for forming a regional COVID-19 review committee (RRC) provides insight on how

these committees can be establish and conduct the review process for NDVPs.

> Considerations for forming a regional COVID-19 review committee (RRC): Technical brief (29 Jan 2021)

Substandard and falsified products

Reports of falsified vaccines and medicines related to Covid-19

There are also reports of such products offered for sale on the internet through unregulated or unauthorized websites. The public should be warned against purchasing Covid-19 vaccines or therapeutics online. Websites that conceal their physical address, landline telephone number, or appear to offer large volumes of products which are normally in short supply, are warned against. It should be noted that no country is untouched by SF medical products and work is being done in all WHO Regions.

Suspicious offers to supply Covid-19 vaccines

WHO has received reports from multiple sources of suspicious offers to sell or supply COVID-19 Vaccines to Ministries of Health. These are attempts to defraud national regulatory authorities or Ministries of Health. Available information suggests that these unsolicited offers may include requests for the advance payment for the vaccines into overseas bank accounts (advance fee fraud) and the non-delivery of products. These offers will appear to be from private individuals or companies in third countries.

WHO recommends that the procurement (purchase and distribution) of vaccines should be subject to heighted scrutiny to reduce the risk of corruption and ensure products are obtained from authorized / licensed suppliers. If the authenticity of a product is in doubt, please contact WHO team (rapidalert@who.int).

WHO requests that national regulatory authorities maintain vigilance and market surveillance for substandard and falsified COVID-19 and influenza vaccines.

Supply updates

Shipments from UN partners

Shipments to countries continue from the UN supply chain consortium and the online portal is being used in an increasing number of countries. Please refer to the updates from the Supply Chain Hub for additional information.

Supply chain of ultracold products

International capacity to deliver cold chain products is currently considered sufficient to manage current demand for transportation; however, advance planning is strongly encouraged due to limited commercial flights and especially to African countries. Tracking of batch numbers in distribution should be prioritized in all countries from release of products from the manufacturer to all points up to the point of care. Some countries are reporting limited capacity of refrigerated vehicles to move vaccines to internal destinations.

Shortages

See below for updated lists, including a watch list, newly added products and two important shortages that are not related to COVID, but that are impacted by limited access to health services during the pandemic.

The following medicines are showing signals of imminent shortage and should be watched carefully.

Hording and speculative procurement should be avoided. Care should be used to ensure the best use of available national inventories. These shortages are reported in Western European and South American countries:

- Propofol
- Morphine
- Heparin (porcine based only)

The shortages of propofol, morphine and heparin are presumed to be from spikes in demand related to the increasing number of cases requiring hospitalization. The heparin shortage limited to countries that do not have access to other forms of heparin (bovine-derived) or other new generation anti-coagulants.

Watch list

WHO is still maintaining a watch list on the following products.

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

Medical Devices

Refreshed website: In Vitro Diagnostics

3rd WHO Model List of Essential in vitro diagnostics

To address the lack of access to tests and testing services in multiple countries, WHO since 2018 has published a yearly essential diagnostics list (EDL), a basket of recommended in vitro diagnostics that should be available at point-of-care and in laboratories in all countries to increase timely and life-saving diagnoses.

The latest edition includes WHO-recommended COVID-19 tests (PCR and Antigen). For the first time, the list includes tests that should not be supplied in countries, either because they are not cost-effective, are unreliable or have been surpassed by newer, easier to use technologies.

‘Access to quality tests and laboratory services is like having a good radar system that gets you where you need to go. Without it, you’re flying blind,’ said WHO Director-General, Dr Tedros Adhanom Ghebreyesus. ‘All countries should pay particular attention to the diagnostics space and use the essential list to promote better health, keep their populations safe, and serve the vulnerable.’

> WHO publishes new Essential Diagnostics List and urges countries to prioritize investments in testing (29 Jan 2021)
>
> eEDL beta version