Key Messages

Investing in sustainable secure manufacturing capacity and national regulatory authorities is critical for providing essential immunization programmes and for building strong, resilient health systems against the inevitable health emergencies of the future. To address this challenge, WHO and partners have established a COVAX Manufacturing Task Force to increase supply in the short-term but also to build a platform for sustainable vaccine manufacturing to support regional health security in the long-term.

Highlights and main issues

- The 13th April issue of the WHO Weekly Epidemiological Update includes update on SARS CoV-2 variants, including the geographical distribution, and emerging evidence surrounding impacts of Variants Of Concern (VOCs) on COVID-19 epidemiology, vaccines and diagnostics.

- More than 815 million vaccine doses have been administered globally, but over 87% have gone to high income or upper middle-income countries, while low-income countries have received just 0.2%. Of the 11 COVID-19 vaccines now in use, AstraZeneca and Pfizer products are the most prevalent.

- The COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety has reviewed available information from Europe and other regions and has said that a causal relationship between the Vaxzevria and the occurrence of a very rare new type of adverse event called Thrombosis with Thrombocytopenia Syndrome (TTS) is plausible, but more investigation is required.

- WHO, EMA and the UK MHRA continue to recommend that the benefits of the vaccine outweigh the risk of these very rare side effects. Countries should encourage clinicians to measure platelet levels and conduct appropriate radiological imaging studies as part of the investigation of thrombosis. Clinicians should also be aware that although heparin is used to treat blood clots in general, administration of heparin in TTS may be dangerous, and alternative treatments such as immunoglobulins and non-heparin anticoagulants should be considered.

- All countries are encouraged to conduct safety surveillance on all COVID-19 vaccines and provide data to their local authorities and to the WHO global database of individual case safety reports. This is urgently needed to support evidence-based recommendations on these life-saving vaccines.

- The updated version of Technical Brief, issued on 14 April, includes deliberations from the COVAX Regulatory Advisory Group on advice on placebo-controlled vaccine efficacy trials and also evaluation of vaccines addressing SARS CoV-2 variants.

- The Global Fund published application materials and technical information notes to support eligible applicants of the COVID-19 Response Mechanism prepare funding requests. Countries are requested to submit proposals for PPE, in vitro diagnostics, medical equipment, and oxygen related needs.
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<td>Upcoming events</td>
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</table>
**Virus variants**

**Epidemiological Update**

The 13th April issue of the WHO Weekly Epidemiological Update includes a special focus on SARS CoV-2 variants. Update are provided on the geographical distribution, and emerging evidence surrounding impacts of Variants Of Concern (VOCs) on COVID-19 epidemiology, vaccines and diagnostics. There is also update on a recent global consultation, and emerging Variants Of Interest (VOIs).

<table>
<thead>
<tr>
<th>Alternate name</th>
<th>First detected by</th>
<th>Earliest sample(s)</th>
<th>Countries reporting cases</th>
<th>Increased transmissibility</th>
<th>Increased severity</th>
<th>Increased reinfection risk</th>
<th>Potential impacts on diagnostics</th>
<th>Potential impacts on vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>VOC 20I/501Y.V1 (B.1.1.7)</td>
<td>United Kingdom</td>
<td>Sep 2020</td>
<td>132</td>
<td>Yes</td>
<td>Inconsistent findings</td>
<td>No/limited</td>
<td>Limited</td>
<td>See the report</td>
</tr>
<tr>
<td>VOC 20H/501Y.V2 (B.1.351)</td>
<td>South Africa</td>
<td>Aug 2020</td>
<td>82</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>See the report</td>
</tr>
<tr>
<td>VOC 20J/501Y.V3 (B.1.1.28.1, alias P.1)</td>
<td>Brazil / Japan</td>
<td>Dec 2020</td>
<td>52</td>
<td>Yes</td>
<td>Limited</td>
<td>Yes</td>
<td>No</td>
<td>See the report</td>
</tr>
</tbody>
</table>

Table showing the simplified information from the WHO Weekly Epidemiological Update.

The number of countries reporting VOCs continue to increase. This information should be interpreted with due consideration of limitations of ongoing surveillance, including but not limited to differences between countries in sequencing capacity and which samples are prioritized for sequencing. WHO continues to advocate for strengthening surveillance and sequencing capacity, and a systematic approach to provide a representative indication of the extent of transmission of SARS-CoV-2 variants; based on the local epidemiological situation and capacity, and the detection of unusual events.

**Weekly epidemiological update on COVID-19** (13 Apr 2021)

**Multivalent COVID-19 vaccines to help address emergence of variants**

On 14th April, the COVAX Workshop was held on “multivalent COVID-19 vaccines: Chemistry, manufacturing and control (CMC) and clinical implications” multivalent” focused on multivalent vaccines (containing for example an antigen against the prototype strain as well as an antigen directed against a variant) and the lessons learned when developing such multivalent vaccines.

Three major CMC themes for vaccine candidates were:

- Impact on potency assays and setting release specifications
- Impact on formulation and stability
- Difference between multiple drug substances (DS) that are blended together versus multiple antigens in a single DS

Three major clinical themes were:

- Risk of immunological interference: Demonstrate the immunological response to the first antigen is undeterred by the addition of the additional type(s).
- How to benchmark the response to the new antigen against the response of the prototype
vaccine antigen.

- Safety: the impact of potentially increased antigen amount versus the risk of reduced-dosing failing non-inferiority.

COVAX Workshop presentations (14 Apr 2021)

Global and local approaches to detect and interpret SARS-CoV-2 variants

Rapid assessment of the biological impacts of new variants of SARS-CoV-2 requires the collaboration of epidemiologists, virologists and immunologists at the local and global level. However, these efforts are often disconnected from one another, resulting in delays and an incomplete picture of the implications for vaccines and diagnostics.

The objective of the COVAX workshop held on 16th April was to share information on how to efficiently connect local pathogen genomic sequencing, epidemiology, virology and immunology to rapidly generate actionable information on the immunological consequences of emerging SARS-CoV-2 variants. There was discussion of how knowledge gained in one country or region can feed into, and benefit from, large international efforts and inform global and local decision making. Ideas were discussed for best practices for assessing virus neutralization activity, and approaches to standardizing assays and protocols to improve interpretation of results generated in different laboratories and geographies.

Workshop presentations will be made available shortly.

Update on the ACT-Accelerator

The ACT-Accelerator partnership:

The Access to COVID-19 Tools (ACT) Accelerator is a time-limited global collaboration designed to rapidly leverage existing global public health infrastructure and expertise to accelerate the development, production, and equitable access to COVID-19 tests, treatments, and vaccines in order to expedite the end of the acute phase of the COVID-19 pandemic.

The ACT-Accelerator is organized into four pillars of work: diagnostics, treatment, vaccines and health system strengthening. Each pillar is vital to the overall effort and involves innovation and collaboration. Cross-cutting all of the work, and fundamental to the goals of the ACT-Accelerator, is the Access and Allocation workstream that is led by WHO and is developing the principles, framework and mechanisms needed to ensure the fair and equitable allocation of these tools.

A newly published “How it works” document outlines the coordination mechanisms and technical workstream structure and schedule of regular meetings for collaboration. Workstreams and leads within each of the pillars are noted. The document also runs through the mechanisms for cross-pillar strategic alignment: Principals Coordination Group, WHO Special Envoys for the ACT-Accelerator and ACT-Accelerator Executive Hub. Information is also provided on the ACT-Accelerator Facilitation Council and how donors can contribute to the agencies that make up the ACT-Accelerator.

What is the Access to COVID-19 Tools (ACT) Accelerator, how is it structured and how does it work? (06 Apr 2021)

COVAX

COVAX, the vaccines pillar of the ACT-Accelerator, is convened by CEPI, GAVI and WHO, with the ambition of contracting enough volumes to equitably deliver 2 billion doses of safe, effective and quality vaccines by the end of 2021. Vaccines included in the COVAX Facility portfolio have been selected from the COVAX R&D portfolio and other clinical candidates.
COVAX achievements: over 100 economies 42 days after first international delivery

More than one hundred economies have received life-saving COVID-19 vaccines from COVAX, the global mechanism for equitable access to COVID-19 vaccines. The milestone comes 42 days after the first COVAX doses were shipped and delivered internationally, to Ghana on 24 February 2021. COVAX has now delivered more than 38 million doses across six continents, supplied by three manufacturers, AstraZeneca, Pfizer-BioNTech and the Serum Institute of India (SII).

Of the over 100 economies reached, 61 are among the 92 lower-income economies receiving vaccines funded through the Gavi COVAX Advance Market Commitment (AMC). Despite reduced supply availability in March and April, COVAX expects to deliver doses to all participating economies that have requested vaccines in the first half of the year.

COVAX reaches over 100 economies, 42 days after first international delivery (08 Apr 2021)

Pfizer-BioNTech vaccine: Allocation from April to June 2021

Based on current knowledge of COVID-19 vaccine supply availability, the third round of COVAX Facility allocations provides information on the provision of 14.1 million doses of Tozinameran to 47 COVAX Facility participants from April to June 2021.

Third round of allocation Pfizer-BioNTech vaccine (12 Apr 2021)

COVAX Regulatory Advisory Group

The COVAX Regulatory Advisory Group (RAG), which is co-led by WHO and CEPI, 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 SWAT teams in order to promote regulatory preparedness among COVID-19 vaccine developers. Feedback from the RAG is communicated back to the COVAX SWAT teams. It is also posted, in the form of a Technical Brief, for the benefit of all COVID-19 vaccine developers and for the wider community of regulatory authorities. The deliberations of the February 2021 RAG provides advice on placebo-controlled efficacy trials and also evaluation of vaccines addressing SARS CoV-2 variants.

The updated Technical Brief (14 Apr 2021)

COVAX Manufacturing Task Force

The COVAX Manufacturing task force aims to increase COVID-19 vaccine supplies by expanding fill/finish mechanisms in a short-term, to expand COVID-19 vaccine manufacturing capacities, then to expand the basic vaccine manufacturing capacity in selected LMICs.

WHO will facilitate the establishment of one (or more, as appropriate) technology transfer hub(s) that will use a hub and spoke model (REF) to transfer a comprehensive technology package and provide appropriate training to interested manufacturers in LMICs. This initiative will initially prioritize the mRNA-vaccine technology but could expand to other technologies in the future.

Expression of Interest: Establishment of a COVID-19 mRNA vaccine technology transfer hub to scale up global manufacturing (16 Apr 2021)

For questions, contact Martin Friede (friedem@who.int) and Raj Long (rlong@who.int)
WHO’s other COVID-19-related work

EPI-Win Update: Safe Ramadan practices
In 2020, an increase of COVID-19 cases associated with Ramada-related activities. EPI-WIN has prepared advice on safely conducting religious gatherings.

EPI-WIN: Safe Ramadan practices during COVID-19 (13 Apr 2021)

Training Materials for Health Care Workers
Based on the most up-to-date clinical guidance, WHO develops training materials via the WHO Academy and OpenWHO platforms. Training is open to anyone interested.

WHO Academy COVID-19 app on Apple store
WHO Academy COVID-19 app on Google Play
OpenWHO Clinical management of COVID-19 course series
The Public Health Emergency Operations Centre (PHEOC)

Alignment of approaches by regulators

Draft WHO Guidance for Comments
WHO guidelines on the transfer of technology in pharmaceutical manufacturing
The current WHO guidelines on the transfer of technology in pharmaceutical manufacturing was published in 2011. Numerous regulatory changes have been made since then. Transfer of technology is considered an integral part of the product life cycle management and is subject to regulatory expectations. This includes a risk-based and science-based process and method design (such as a quality by design approach), achieving a “state of control” and data governance. The original document thus requires updating, not least to support the consistent supply of therapies for critical needs, including public health emergencies.

WHO guidelines on the transfer of technology 6 in pharmaceutical manufacturing (Comments by 01 Jun 2021)

In vitro diagnostics

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

- 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 15 April, 28 products have been listed as eligible for WHO procurement among a total of 136 expressions of interest (61 for NAT assays, 41 for antibody detection assays and 34 for antigen detection RDTs) have been received.

EUL listed IVDs (18 Mar 2021)
Status of each EUL application (13 Apr 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 (08 Apr 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**

**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.


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**

In March 2021, the WHO Coronavirus (COVID-19) Dashboard started publishing data on the global vaccine rollout that are useful to tracking the global rollout of COVID-19 vaccines, including total doses administered, persons vaccinated with at least one dose, and start date of vaccinations, by country, territory and area.

Although large progress has been made with, as of 14 April, 199 countries and economies starting vaccination out of 220, there remains a striking imbalance in the global distribution of vaccines. More than 815 million vaccine doses have been administered globally, but over 87% have gone to high income or upper middle-income countries, while low-income countries have received just 0.2%. Of the 11 COVID-19 vaccines now in use, AstraZeneca and Pfizer products are the most prevalent.

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

WHO Coronavirus (COVID-19) Dashboard
AstraZeneca COVID-19 Vaccine

WHO GACVS:

A very rare new type of adverse event called Thrombosis with Thrombocytopenia Syndrome (TTS), involving unusual and severe blood clotting events associated with low platelet counts, has been reported after vaccination with COVID-19 Vaccines Vaxzevria and Covishield. A specific case definition for TTS is being developed by the Brighton Collaboration. This will assist in identifying and evaluating reported TTS events and aid in supporting causality assessments.

The biological mechanism for this syndrome of TTS is still being investigated. At this stage, a 'platform specific' mechanism related to the adenovirus-vectored vaccines is not certain but cannot be excluded. Ongoing review of TTS cases and related research should include all vaccines using adenoviral vector platforms. The Global Advisory Committee on Vaccine Safety (GACVS) noted that an investigation has been initiated into the occurrence of TTS following the Johnson & Johnson vaccine administered in the United States.

The TTS syndrome has not been linked to mRNA-based vaccines (such as Comirnaty or the Moderna mRNA-1273 vaccine).

Based on latest available data, the risk of TTS with Vaxzevria and Covishield vaccines appears to be very low. Data from the UK suggest the risk is approximately four cases per million adults (1 case per 250 000) who receive the vaccine, while the rate is estimated to be approximately 1 per 100 000 in the European Union (EU). Countries assessing the risk of TTS following COVID-19 vaccination should perform a benefit-risk analysis that takes into account local epidemiology (including incidence and mortality from COVID-19 disease), age groups targeted for vaccination and the availability of alternative vaccines.

At a minimum, countries should encourage clinicians to measure platelet levels and conduct appropriate radiological imaging studies as part of the investigation of thrombosis. Clinicians should also be aware that although heparin is used to treat blood clots in general, administration of heparin in TTS may be dangerous, and alternative treatments such as immunoglobulins and non-heparin anticoagulants should be considered.

GACVS highly recommends that all countries conduct safety surveillance on all COVID-19 vaccines and provide data to their local authorities and to the WHO global database of individual case safety reports. This is urgently needed to support evidence-based recommendations on these life-saving vaccines.

Global Advisory Committee on Vaccine Safety (GACVS) review of latest evidence of rare adverse blood coagulation events with AstraZeneca COVID-19 Vaccine (Vaxzevria and Covishield) (16 Apr 2021)

EMA:

EMA is undertaking a review of vaccination data and data on disease epidemiology (including infection rates, hospitalisations, morbidity and mortality). The review by EMA’s human medicines committee (CHMP) will enable authorities to put the risks of Vaxzevria into the context of the benefits of ongoing vaccination campaigns.

The Committee will also consider whether to update recommendations for a second dose of Vaxzevria in those who have already received the first dose.

Vaxzevria1 (COVID-19 Vaccine (ChAdOx1-S [recombinant])) An overview of Vaxzevria and why it is authorised in the EU (15 Apr 2021)
Vaxzevria Procedural steps taken and scientific information after the authorization (16 Apr 2021)
COVID-19 vaccine safety update, Vaxzevria (14 Apr 2021)
AstraZeneca’s COVID-19 vaccine: EMA to provide further context on risk of very rare blood clots with low blood platelets (14 Apr 2021)
UK MHRA:
The UK MHRA issued an updated regulatory decision on 15 April, adding patients with a history of heparin-induced thrombocytopenia and thrombosis (HITT or HIT type 2) as a contraindication. In addition, patients who have experienced major venous and/or arterial thrombosis occurring with thrombocytopenia following vaccination with any COVID-19 vaccine should not receive a second dose of COVID-19 Vaccine AstraZeneca.

REG 174: Information for UK Healthcare Professionals (14 Apr 2021)

Johnson & Johnson (Janssen) vaccine
As of 12th April, more than 6.8 million doses of the Johnson & Johnson (Janssen) vaccine have been administered in the United States. The US CDC and US FDA are reviewing data involving six reported U.S. cases. Until ongoing reviews are completed, the FDA are recommending a pause in the use of this vaccine in the US out of an abundance of caution.

In these cases, a type of blood clot called cerebral venous sinus thrombosis (CVST) was seen in combination with low levels of blood platelets (thrombocytopenia). All six cases occurred among women between the ages of 18 and 48, and symptoms occurred 6 to 13 days after vaccination. Treatment of this specific type of blood clot is different from the treatment that might typically be administered. Usually, an anticoagulant drug called heparin is used to treat blood clots. In this setting, administration of heparin may be dangerous, and alternative treatments need to be given, however, 4 of the cases were treated with heparin.

Until ongoing reviews are completed, the US FDA are recommending a pause in the use of this vaccine out of an abundance of caution. The rationale is, in part, to ensure that the health care provider community is aware of the potential for these adverse events and can plan for proper recognition and management due to the unique treatment required with this type of blood clot.

Advisory Committee on Immunization Practices (ACIP) held a publication consultation on 14th April.

ACIP presentations: (14 Apr 2021)

Introduction by Dr B Bell
Update on thromboembolic events, COVID-19 vaccines safety surveillance by Dr T Shimabukuro
VaST assessment by Dr G Lee
Work Group interpretation by Dr S Oliver

Joint CDC and FDA Statement on Johnson & Johnson COVID-19 Vaccine (13 Apr 2021)

Safety of COVID-19 Vaccines
Case Definition of Thrombosis with Thrombocytopenia Syndrome (TTS)
To further understanding of a possible association of cases observed with thrombocytopenia and thrombosis following receipt of COVID-19 vaccines, the Brighton Collaboration has drafted a case finding definition for thrombosis with thrombocytopenia syndrome (TTS). The purpose of this case finding definition is to identify individuals that could then be studied using a common study protocol and assessment.

Proposed Brighton Collaboration process for developing a standard case definition for study of new clinical syndrome X, as applied to Thrombosis with Thrombocytopenia Syndrome (TTS) (16 Apr 2021)

For questions, contact Robert Chen at rtchen1135@gmail.com
For comments on TTS case definition, contact Steve Black at stevblack@gmail.com
The Brighton Collaboration is also compiling a draft master list of questions for the follow-up study of TTS patients.

**TTS variable list** (15 Apr 2021)

### Support Materials for Safety of COVID-19 Vaccines

Countries around the world are rolling out COVID-19 vaccines, and a key topic of interest is their safety. Vaccine safety is one of WHO’s highest priorities, and WHO is working closely with national authorities to develop and implement standards to ensure that COVID-19 vaccines are safe and effective.

**Safety of COVID-19 Vaccines** (31 Mar 2021)

**Side Effects of COVID-19 Vaccines** (31 Mar 2021)

**How to monitor and report COVID-19 vaccine side effects** (15 Mar 2021)

**Causality assessment of an adverse event following immunization (AEFI): user manual for the revised WHO classification, 2nd ed., 2019 update**

### 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 14 April 2021.

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

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Name of Vaccine</th>
<th>Mid of March</th>
<th>Position</th>
<th>File accepted</th>
<th>Pre-submission meeting held</th>
<th>Decision accepted for review</th>
<th>Status of assessment</th>
<th>Anticipated decision date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. SINOPHARM</td>
<td>Vero Cell (COVID-19)</td>
<td>mRNA</td>
<td>Vero</td>
<td>mRNA</td>
<td>mRNA</td>
<td>mRNA</td>
<td>Vaccine candidate</td>
<td>In progress</td>
</tr>
<tr>
<td>2. AstraZeneca</td>
<td>ChAdOx1 nCoV-19 (COVID-19)</td>
<td>DNA</td>
<td>DNA</td>
<td>DNA</td>
<td>mRNA</td>
<td>mRNA</td>
<td>Vaccine candidate</td>
<td>In progress</td>
</tr>
<tr>
<td>3. Moderna</td>
<td>mRNA-1273</td>
<td>mRNA</td>
<td>mRNA</td>
<td>mRNA</td>
<td>mRNA</td>
<td>mRNA</td>
<td>Vaccine candidate</td>
<td>In progress</td>
</tr>
<tr>
<td>4. Sinovac Biotech</td>
<td>CoronaVac</td>
<td>mRNA</td>
<td>mRNA</td>
<td>mRNA</td>
<td>mRNA</td>
<td>mRNA</td>
<td>Vaccine candidate</td>
<td>In progress</td>
</tr>
<tr>
<td>5. Pfizer/BioNTech</td>
<td>Comirnaty (COVID-19)</td>
<td>mRNA</td>
<td>mRNA</td>
<td>mRNA</td>
<td>mRNA</td>
<td>mRNA</td>
<td>Vaccine candidate</td>
<td>In progress</td>
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<tr>
<td>6. Janssen</td>
<td>Janssen-Codon Covid-19 Vaccine (Johnson &amp; Johnson)</td>
<td>DNA</td>
<td>DNA</td>
<td>DNA</td>
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<td>11. Biontech/Pfizer</td>
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Support materials:

WHO Vaccine explainer

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<td>SAGE Interim recommendations</td>
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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 08 April 2021, the Covid-19 - living NMA initiative collected 208 RCTs and 70 non-randomized studies of vaccines from the ICTRP. 129 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

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 (16 Apr 2021)

**WHO Assays Working Group**

Sequence analysis of SARS-CoV-2 in nasopharyngeal samples from patients with COVID-19 was presented in the 14th April meeting. SARS-CoV-2 was found to exist as a population, not a single genotype, in patients. This genetic diversity can be influenced by the cell lines to culture samples used as well as the sequencing platforms used.

**WHO Animal Models Working Group**

A preliminary report of characterization of SARS-CoV-2 variants B.1.427/1.429 in hamsters was presented in the 15th April meeting. These two variants have L452R mutations in the spike protein and have rapidly become the dominant circulating strains in California, USA. A recent preprint reported that human serum neutralizing antibody elicited by immunization with the mRNA-1273 vaccine is reduced by 2- to 3-fold for these variants compared to the D614G strain. The spike mutation in these variants renders the monoclonal antibody bamlanivimab ineffective in vitro.

Experiments in hamsters showed that the relative fitness, tropism and virulence of B.1.427 and 614G in lungs is similar. Initial results found however that replication of B.1.427 in the nose may be higher than D614G. Prior infection of hamsters with D614G was found to protect the animals...
from B.1.427 replication. Transmission experiments found that B.1.427 may transmit moderately more rapidly and/or efficiently than D614G or the WA-1 strain.

Note: WHO considers data on COVID-19 vaccines and SARS CoV-2 variants to be limited, early and incomplete. Evidence on protection against severe disease, hospitalization and deaths are especially limited.

Substandard and falsified products

WHO urges all countries and individuals to pay careful attention to the issue of substandard and falsified (SF) products. Any suspicious sale of vaccines should be reported to national authorities, who will report it to WHO. Information flow is essential to map global threats and protect confidence in vaccines.

If you have any information concerning the manufacture, distribution, or supply of SF products, please contact rapidalert@who.int.

Supply Chain

Transportation backlogs

A rapid review is showing backlogs in 40% of existing ocean ports. The key problems are insufficient staff and equipment to clear the backlogs. An additional problem is the return of empty containers.

Progress on traceability

Products should be traced to the batch number level from the manufacturer to all points up to the point of care.

Work is ongoing to develop a repository of master data and serial numbers which is intended to support countries in validation of serial numbers. The system will support real time logistic information management as well as validation of serial numbers. Partners including USAID, World Bank, UNICEF and WHO are working together on a rapid solution.

At present, only 50% of vaccine manufacturers have capacity to include the required bar codes on vaccine packaging. The bar codes are on secondary packaging and are in the form of a 2 dimensional data matrix label with serialization. A deadline for scaling up will be established for aligning progress as the above repository, national and manufacturing capacity scales up to meet this important area of implementation support.

Newly added shortages:

No new shortages have been reported

Shortage watch list

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:

- Antibiotics: azithromycin, levofloxacin, metronidazole, amoxiclav, piperacillin, tazobactam
- Atracurium Injection
- epinephrine and norepinephrine
- Benzodiazepine sedatives: midazolam and lorazepam
- Nonbenzodiazepine sedatives: propofol
- Antipsychotics: haloperidol
- Neuromuscular relaxants: succinylicholine, atracurium, or vecuronium.
- Opioids: morphine and fentanyl
WHO Regulatory Update on COVID-19

- Malaria treatments: hydroxychloroquine, chloroquine, artemether-lumefantrine, artemisinin-based combination therapies, sulfadoxine-pyrimethamine + amodiaquine
- NCD: Metformin and insulin
- Anticoagulants: heparin, porcine based in countries with limited access to new generation anticoagulants
- Antipyretics: paracetamol (aka acetaminophen)
- PPE
- Oxygen and related equipment
- Ventilators

**Medical Devices**

**Global Fund COVID-19 Response Mechanism (C19RM) 2021**

The Global Fund published application materials and technical information notes to support eligible applicants of the COVID-19 Response Mechanism, C19RM, prepare funding requests. Countries are requested to submit proposals for PPE, in vitro diagnostics, medical equipment, and oxygen related needs. Applications must be endorsed by all CCM members, and for COVID-19 control and containment interventions, the national COVID-19 response coordinating body’s endorsement is required.

- [The Global Funds Response Mechanism](#)
- [COVID-19 Response Mechanism (C19RM) 2021: Application Materials](#)

WHO Guidance documents supporting preparation of GF applications

- [Priority medical devices list for the COVID-19 response and associated technical specifications](#)
- [Medical use of Oxygen](#)
- [Personal protective equipment for COVID-19](#)

For request for support, contact [medicaldevices@who.int](mailto:medicaldevices@who.int)

**Emergency Global Supply Chain System (COVID-19) catalogue**

The following catalogue lists all medical devices, including personal protective equipment, medical equipment, medical consumables, single use devices, laboratory and test-related devices that may be requested through the COVID-19 Supply Portal.

- [Emergency Global Supply Chain System (COVID-19) catalogue](#) (12 Apr 2021)

**COVID-19 Essential Supplies Forecasting overview and tool**

This document provides technical details and methodological explanations on the structure of the COVID-19 Essential Supplies Forecasting Tool (ESFT). It is intended to provide information that will allow users to a) trace and understand the calculations, assumptions, and limitations of ESFT; and b) modify these assumptions for different contexts or use cases. It is updated with each iteration of the tool.

- [COVID-19 Essential Supplies Forecasting Tool](#) (07 Apr 2021)

The WHO COVID-19 Essential Supplies Forecasting Tool (ESFT) assists governments, partners, and other stakeholders to forecast the necessary volume of personal protective equipment, diagnostic equipment, consumable medical supplies, biomedical equipment for case management,
and essential drugs for supportive care and treatment of COVID-19. The tool provides the user with a choice among several epidemiological methods for forecasting COVID-19 cases, including an integration with Imperial College’s Susceptible-Exposed-Infectious-Removed (SEIR) model.

WHO COVID-19 essential supplies forecasting tool (COVID-ESFT) (14 Apr 2021)

Upcoming events

WHO Webinar on Global Benchmarking Tool plus Blood
19 April 09:00 – 11:00 CET & 16:00 – 18:00 CET
WHO will hold a Webinar to introduce the Global Benchmarking Tool Plus Blood with interpretation to all WHO languages. The essential audiences of this Webinar will be representatives from MoH, NRAs and National Blood Establishments.

Please register

COVID-19 vaccine safety monitoring
19 April 13:00 – 14:00 CET
WHO webinar to learn about the safety monitoring process of COVID-19 vaccines. Dr Madhava Ram Balakrishnan will discuss vaccine safety and the latest developments on the AstraZeneca and other COVID-19 vaccines.

Please register

Infection prevention and control and public health and social measures in light of the variants of concern:
21 April 2021 14:00 – 15:30 CET
As part of the infection prevention and control (IPC) Webinar Series of 2021, WHO invites you to the global webinar on IPC and the public health and social measures in light of the variants of concern.
Speakers from WHO HQ, Europe regional office and South Africa will present on the global state of the variants of concern identified, as well as which countries have updated their public health and social measures in light of the variants.

Please register

AVAREF facilitated options for vaccine access and clinical trials in Africa
03 June 16:00 – 17:30 CET
Since 2006, the African Vaccines Regulatory Forum (AVAREF) has been working with the countries in Africa to facilitate joint reviews of multi country clinical trials, in a harmonized procedure. Recently, in response to the ongoing pandemic and need for accelerated access to quality vaccines, AVAREF is facilitating the emergency use authorization of vaccines by countries in the continent. Using a procedure developed and approved by the 40 sub-Saharan countries in the WHO AFRO region and the 14 countries in the African continent which are under the WHO EMRO region, AVAREF has to date, facilitated approval of several multi country clinical trials and regulatory authorization of products including COVID-19 vaccines.

More information will be made available shortly.