

# Regulation of in vitro diagnostics, therapeutics, and vaccines

## WHO Update – 14

### Coronavirus disease 2019 (COVID-19)

#### 17 July 2020



World Health  
Organization

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## Key Messages

The potential need for simultaneous regulatory approval of one or more COVID-19 vaccines in a high number of countries with different regulatory contexts is a unique challenge from a regulatory and safety monitoring perspective. There is a critical and urgent need for collaborative regulatory preparedness to be accelerated.

## Highlights and main issues

- One hundred and sixty-five countries have submitted expressions of interest to protect their populations and those of other nations through joining the COVAX Facility, a mechanism designed to guarantee rapid, fair and equitable access to COVID-19 vaccines worldwide. Together, this group of countries represents more than 60% of the world's population.
- International regulators have aligned positions on data needed from laboratory, animal and human studies to allow initiation of phase 3 clinical trials for a COVID-19 vaccine, and also on considerations for study design for phase 3 clinical trials.
- Preliminary findings from a phase 1 trial of a mRNA vaccine have been published showing that the candidate vaccine induced anti-SARS-CoV-2 immune responses in all participants, and no trial-limiting safety concerns were identified.
- The recommendations and conclusions of the Global Advisory Committee on Vaccine Safety, addressing pharmacovigilance preparedness for the roll out of the future COVID-19 vaccines, have been published.
- A new WHO scientific brief summarizes what is known on how, when and where transmission of SARS-CoV-2 can occur, as well outlines key areas where more research is needed.
- WHO issues an Expression of Interest (EOI) for prequalification of manufacturers of dexamethasone and remdesivir.
- WHO has accepted the recommendation from the Solidarity Trial's International Steering Committee to discontinue the trial's hydroxychloroquine and lopinavir/ritonavir arms.
- Seventy-three countries have warned that they are at risk of stock-outs of antiretroviral medicines as a result of the COVID-19 pandemic.

## Epidemiology

The total number of cases reported to WHO has surpassed 13 million. In each of the last 4 weeks, over a million cases were reported. While cases have been on the rise overall, new deaths seem to be relatively stable. The Americas are currently the hardest-hit region, contributing to over half of the new cases. The South-East Asian and African regions are seeing rapid growth in the number of cases. The United States of America, Brazil and India remain the three most affected countries in recent days.

## Transmission of COVID-19

WHO issued a [scientific brief on transmission of COVID-19](#) on 9 July, summarizing an overview of the modes of transmission of SARS-CoV-2, what is known about when infected people transmit the virus, and the implications for infection prevention and control precautions within and outside health facilities.

COVID-19 mainly spreads between people through direct, indirect (through contaminated objects or surfaces), or close contact with infected people via mouth and nose secretions. These include saliva, respiratory secretions or secretion droplets. These are released from the mouth or nose when an infected person coughs, sneezes, speaks or sings, for example. People who are in close contact (within 1 metre) with an infected person can catch COVID-19 when those infectious droplets get into their mouth, nose or eyes.

Airborne transmission of the virus can occur in health care settings where specific medical procedures, called aerosol generating procedures, generate very small droplets called aerosols. Some outbreak reports related to indoor crowded spaces have suggested the possibility of aerosol transmission, combined with droplet transmission, for example, during choir practice, in restaurants or in fitness classes. Based on what we currently know, transmission of COVID-19 is primarily occurring from people when they have symptoms, and can also occur just before they develop symptoms, when they are in close proximity to others for prolonged periods of time. While someone who never develops symptoms can also pass the virus to others, it is still not clear to what extent this occurs and more research is needed in this area.

## ACT-Accelerator update

The Access to COVID-19 Tools Accelerator (ACT-Accelerator) is a global collaboration to accelerate the development, production and equitable access to COVID-19 diagnostics, therapeutics and vaccines. It brings together leaders of government, global health organizations civil society groups, businesses and philanthropies to form a plan for an equitable response to the COVID-19 pandemic.

There are four pillars: diagnostics, therapeutics, vaccines and strengthening health systems.

- The **diagnostics pillar** aims to bring to the market high-quality rapid tests, train 10 000 healthcare professionals across 50 countries and establish testing for 500 M people in low- and middle-income countries. WHO is collaborating with FIND and The Global Fund on this pillar.
- The **therapeutics pillar** focuses on the manufacture and distribution of 250 M treatment for people suffering from COVID-19. WHO is collaborating with Unitaid and Wellcome Trust on this pillar.
- The **vaccines pillar** (Also called 'COVAX') works to maximize the development, equitable access and fair allocation across all countries. It aims to deliver 2 billion doses globally for high-risk populations, including 1 billion which will be purchased for low- and middle-income countries. WHO is collaborating with the Coalition for Epidemic Preparedness Innovations (CEPI) and Gavi on this pillar.
- The **health systems strengthening pillar** will support and enhance healthcare systems and local

community networks needed to defeat this pandemic and ensure the world is ready to take on the next one. WHO is collaborating with the World Bank and Global Fund on this pillar.

Seventy-five countries have submitted expressions of interest to protect their populations and those of other nations through joining the COVAX Facility, a mechanism designed to guarantee rapid, fair and equitable access to COVID-19 vaccines worldwide.

The 75 countries, which would finance the vaccines from their own public finance budgets, partner with up to 90 lower-income countries that could be supported through voluntary donations to Gavi's COVAX Advance Market Commitment (AMC). Together, this group of up to 165 countries represents more than 60% of the world's population. Among the group are representatives from every continent and more than half of the world's G20 economies.

The COVAX Facility forms a key part of the COVAX pillar (COVAX) of the Access to COVID-19 Tools (ACT) Accelerator, a ground-breaking global collaboration to accelerate the development, production, and equitable access to COVID-19 tests, treatments, and vaccines. COVAX is co-led by Gavi, the Coalition for Epidemic Preparedness Innovations (CEPI) and WHO, working in partnership with developed and developing country vaccine manufacturers. COVAX aims to accelerate the development and manufacture of COVID-19 vaccines, and to guarantee fair and equitable access for every country in the world.

It will achieve this by sharing the risks associated with vaccine development, investing in manufacturing upfront so vaccines can be deployed at scale as soon as they are proven successful, and pooling procurement and purchasing power to achieve sufficient volumes to end the acute phase of the pandemic by 2021.

The goal of COVAX is by the end of 2021 to deliver two billion doses of safe, effective vaccines that have passed regulatory approval and/or WHO prequalification. These vaccines will be delivered equally to all participating countries, proportional to their populations, initially prioritising healthcare workers then expanding to cover 20% of the population of participating countries. Further doses will then be made available based on country need, vulnerability and COVID-19 threat. The COVAX Facility will also maintain a buffer of doses for emergency and humanitarian use, including dealing with severe outbreaks before they spiral out of control.

The success of these efforts will ultimately depend on securing enough funding from governments and commitments from vaccine manufacturers to participate at a scale large enough to deliver a global solution. The formal expressions of interest submitted are non-binding; the COVAX pillar will now begin a process of consultation with all 165 countries, with countries funding vaccines through their own domestic budgets being required to provide an upfront payment and a commitment to purchase doses by the end of August to secure involvement in the COVAX Facility.

The ACT-Accelerator was launched at the end of April 2020 by the Director-General of the World Health Organization, the President of France, the President of the European Commission, and The Bill & Melinda Gates Foundation.

It presented its investment case on 26 June 2020. The consolidated investment case calls for US\$ 31.3 billion over the next 12 months.

Link: [The Access to COVID-19 Tools \(ATC\) Accelerator](#)

## **Alignment of approaches by regulatory groups**

### **International regulators align positions on phase 3 COVID-19 vaccine trials**

Medicines regulatory authorities from around the world have published a report highlighting the outcomes of the second workshop on COVID-19 vaccine development that was convened under the umbrella of the International Coalition of Medicines Regulatory Authorities ([ICMRA](#)).

The report describes the regulatory positions agreed by the meeting participants on two key topics:

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- Data needed from laboratory, animal and human studies to allow initiation of phase 3 clinical trials for a COVID-19 vaccine; and
- Considerations for study design for phase 3 clinical trials.

The meeting participants stressed the need for large phase 3 clinical trials that enrol many thousands of people, including those with underlying medical conditions, to generate relevant data for the key target populations.

There was also broad agreement that clinical studies should be designed with stringent success criteria that would allow a convincing demonstration of the efficacy of COVID-19 vaccines. However, whether a vaccine would be considered as acceptable for approval is assessed case-by-case on the basis of all available data on its safety and efficacy.

[ICMRA SARS-CoV-2 Vaccines Workshop #2 - Summary](#)

## *In vitro* diagnostics

### **WHO EUL for SARS-CoV-2 virus IVDs: scope expanded to antibody detection enzyme immunoassays**

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

On 3 July 2020 the EUL scope will be expanded to antibody detection enzyme immunoassays. The following IVDs are therefore eligible for EUL submission:

- Assays for the detection of SARS-CoV-2 nucleic acid;
- Rapid diagnostic tests for the detection of IgM/IgG to SARS-CoV-2; and
- Rapid diagnostic tests for the detection of SARS-CoV-2 antigens.

Manufacturers interested in the EUL submission are invited to contact WHO at [diagnostics@who.int](mailto:diagnostics@who.int) and schedule a pre-submission call.

### **WHO EUL submissions and listing update**

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.

40 expressions of interest for NAT assays, 15 for antibody detection RDTs have been received so far.

The status of each application: [update](#) (14 July 2020)

15 products have been listed as eligible for WHO procurement based on their compliance with WHO EUL requirements:

Date Listed	Product name	Product code(s)	Manufacturer
9 July 2020	COVID-19 Coronavirus Real Time PCR Kit	JC10223-1NW-50T	Jiangsu Bioperfectus Technologies Co.,Ltd
6 July 2020	Simplexa COVID-19 Direct and Simplexa COVID-19 Positive control Pack	MOL4150, MOL4160	DiaSorin
23 June 2020	Xpert® Xpress SARS-CoV-2	XPRSARS-COV2-10	Cepheid AB
15 June 2020	COVID-19 Real-Time PCR Kit	HBRT-COVID-19	Chaozhaou HybriBio Biochemistry Ltd.
11 June 2020	Novel Coronavirus 2019-nCoV Nucleic Acid Detection Kit (Real Time PCR)	GZ-D2RM25	Shanghai GeneDx Biotechnology Co., Ltd

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5 June 2020	SARS-CoV-2 Nucleic Acid Test (Real-time PCR)	KH-G-M-574-48	Shanghai Kehua Bio-engineering Co., Ltd
22 May 2020	Novel Coronavirus (SARS-CoV-2) Real Time Multiplex RT-PCR Kit	RR-0485-02	Shanghai ZJ Bio-Tech Co., Ltd
21 May 2020	FTD SARS-CoV-2	11416300	Fast Track Diagnostics Luxembourg S.à.r.l.
19 May 2020	Multiple Real-Time PCR Kit for Detection of 2019-CoV	CT8233-48T	Beijing Applied Biological Technologies Co., Ltd.
14 May 2020	Detection Kit for 2019 Novel Coronavirus (2019-nCoV) RNA, (PCR- Fluorescence Probing)	DA0930, DA0931 and DA0932	Da An Gene Co., Ltd. Of Sun Yat-sen University
07 May 2020	Real-time fluorescent RT-PCR kit for detecting 2019-nCoV	MFG030010	BGI Europe A/S
24 April 2020	PerkinElmer® SARS-CoV-2 Real-time RT-PCR Assay	SY580	SYM-BIO LiveScience Co., Ltd
09 April 2020	Abbott Realtime SARS-CoV-2	09N77-090 and 09N77-080	Abbott Molecular Inc.
07 April 2020	Primerdesign Ltd COVID-19 genesig Real-Time PCR assay	Z-Path-COVID-19-CE	Primerdesign Ltd.
03 April 2020	cobas SARS-CoV-2 Qualitative assay for use on the cobas 6800/8800 Systems	09175431190 and 09175440190	Roche Molecular Systems, Inc.

On 6 July and 9 July 2020 respectively, WHO listed the following NAT assays under the emergency use listing procedure:

- The **Simplexa COVID-19 Direct and Simplexa COVID-19 Positive control Pack** manufactured by **DiaSorin** is a real-time RT-PCR system that enables the direct amplification of Coronavirus SARS-CoV-2 RNA from nasopharyngeal swabs (NPS), nasal swabs (NS), nasal wash/aspirate (NW) or bronchoalveolar lavage (BAL) specimens. The system consists of the Simplexa™ COVID-19 Direct assay, the LIAISON® MDX (with LIAISON® MDX Studio Software), the Direct Amplification Disc and associated accessories.
- The **COVID-19 Coronavirus Real Time PCR Kit** manufactured by **Jiangsu Biopertectus Technologies Co.,Ltd** is a real-time RT-PCR In Vitro Diagnostic (IVD) reagent using a fluorescent PCR technology to qualitatively detect SARS-CoV-2 from throat swab, nasopharyngeal swab specimens and sputum. The assay is intended to be used in combination with the Qiagen QIAamp Viral RNA Mini Kit or the Biopertectus Technologies Viral nucleic acid isolation kit and a Real-time PCR thermal cycler among the Applied Biosystems 7500 (software version V2.3 and V2.4), QuantStudio™ 5 (software version V1.4.3 and V1.5.1), Roche LightCycler®480 (software version V1.5.1.62), Bio-Rad CFX96™ (software version V3.1), and the Shanghai Hongshi SLAN-96P/S (software version V8.2.2).

## **COVID-19 in vitro diagnostics 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 lists: [update](#) (06 July 2020)

**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

### **WHO issues an Expression of Interest for manufacturers of dexamethasone and remdesivir**

Recognizing the worldwide need for quality-assured products for treatment of Covid-19, WHO issued an Expression of Interest (EOI) for manufacturers of dexamethasone and remdesivir products on 10 July. These drugs have been shown in scientific studies to provide clinical benefit for patients.

The aim of the EOI invitation is to increase the range of selected products and sources available. Dossiers for these products may be submitted by manufacturers for assessment by the WHO Prequalification Team. Specifications for characteristics and formulations of the two invited products are outlined in detail in the EOI.

Once the Prequalification Team is satisfied that WHO recommended standards for quality and safety / efficacy are met, the product (as produced at the specified manufacturing site) is added to the WHO List of Prequalified Medicinal Products. This will allow procurement agencies and others to confidently obtain and recommend use of specific dexamethasone and remdesivir products in patient care.

[Invitation to Manufacturers to submit EOI](#) for product evaluation of **dexamethasone and remdesivir**

### **WHO discontinues hydroxychloroquine and lopinavir/ritonavir treatment arms for COVID-19**

On July 4<sup>th</sup> WHO accepted the recommendation from the Solidarity Trial's International Steering Committee to discontinue the trial's hydroxychloroquine and lopinavir/ritonavir arms. The Solidarity Trial was established by WHO to find an effective COVID-19 treatment for hospitalized patients.

The International Steering Committee formulated the recommendation in light of the evidence for hydroxychloroquine vs standard-of-care and for lopinavir/ritonavir vs standard-of-care from the Solidarity trial interim results, and from a review of the evidence from all trials presented at the 1-2 July WHO Summit on COVID-19 research and innovation.

These interim trial results showed that hydroxychloroquine and lopinavir/ritonavir produced little or no reduction in the mortality of hospitalized COVID-19 patients when compared to standard of care. Solidarity trial investigators interrupted the trials with immediate effect.

For each of the drugs, the interim results did not provide solid evidence of increased mortality. There were, however, some associated safety signals in the clinical laboratory findings of the add-on Discovery trial, a participant in the Solidarity trial. These will also be reported in a peer-reviewed publication.

This decision applies only to the conduct of the Solidarity trial in hospitalized patients and does not affect the possible evaluation in other studies of hydroxychloroquine or lopinavir/ritonavir in non-hospitalized patients or as pre- or post-exposure prophylaxis for COVID-19. The interim Solidarity results are now being readied for peer-reviewed publication.

### **Research mapping of candidate therapeutics for COVID-19**

A living research mapping of candidate COVID-19 therapeutics, displaying studies per country, showing study design, disease severity in study participants, and type of treatment being studied, as well as network maps of these studies, has been made available at: <https://www.covid-nma.com/dataviz/>

### **Living synthesis of Covid-19 study results**

A list of treatment comparisons, a summary of the evidence for that comparison, and a detailed description of primary studies, including a risk of bias assessment is at: [https://covid-nma.com/living\\_data/index.php](https://covid-nma.com/living_data/index.php)

## Vaccines

### **Preliminary findings from mRNA vaccine phase 1 clinical trial**

Preliminary findings from a phase 1 trial to evaluate the safety and immunogenicity of an mRNA SARS-CoV-2 vaccine have been reported. The phase 1 trial involved 45 healthy adults, 18 to 55 years of age, who were assigned to receive the candidate vaccine at one of three dose levels (25 µg, 100 µg, or 250 µg) given as two vaccinations 28 days apart.

The preliminary findings represent the first of three reports of data from a phase 1 study of this candidate vaccine; a second report including similar data from adults older than 55 years of age and a final report summarizing the safety and durability of immunity for both study cohorts are also planned.

The mRNA-1273 vaccine induced anti-SARS-CoV-2 immune responses in all participants, and no trial-limiting safety concerns were identified. The authors concluded that the findings support further development of this vaccine.

[An mRNA Vaccine against SARS-CoV-2 — Preliminary Report](#)

### **WHO Global Advisory Committee on Vaccine Safety**

The 42nd GACVS virtual meeting on 27–28 May 2020 addressed pharmacovigilance preparedness for the launch of the future COVID-19 vaccines. This included identification and assessment of adverse events of special interest (AESI) as a high priority. Designating an event as an AESI has the advantage that countries can then prepare, with case definitions, collect information on background rates, collate relevant scientific literature, set up collaborations with relevant partners, and establish platforms and strategies to assess signals rapidly. Tools to assist stakeholders in assessing the benefit–risk profiles of vaccine platforms were identified. Lessons learnt from the epidemics of H1N1 influenza and Ebola virus disease will be used to efficiently leverage the 3 levels of WHO and its global partners for pharmacovigilance preparedness.

Each country should have a framework plan for introducing COVID-19 vaccination, and the risk management plan recommended by the national regulatory authority must be implemented and communicated, including active and enhanced passive Adverse Events Following Immunization (AEFI) and AESI surveillance nationwide.

A WHO COVID-19 vaccine(s) communication plan was also reviewed. To build and maintain trust and confidence in a situation full of unknowns, it will be important to communicate transparently, early and often, in ways that people trust; to communicate clearly and for various levels of health literacy; acknowledge uncertainty in both qualitative and quantitative terms; communicate honestly and openly; listen and respond to the specific concerns of stakeholders; and prioritize key population groups.

[GACVS summary report](#) WHO Weekly epidemiological record (10 July 2020)

### **WHO Working Group on vaccine prioritization – call for nominations by 22 July**

The candidate vaccine prioritization working group will be set up with the aim of establishing an independent process to advise WHO on the selection of the candidate vaccine(s) against COVID-19 that should be evaluated first in the SOLIDARITY trial.

The program of work for the WG is to:

1. Review the data and information on all candidate vaccines under development against COVID-19 using the *a priori* defined attributes and criteria;
2. Provide an individual score for each candidate vaccine and a recommendation on the pertinence of prioritizing one or more given candidates for support and further evaluation;

3. Provide continuous review (monthly) of the emerging information and evidence on all candidate vaccines;

WHO will consider the recommendations of this Working Group and consult with other pertinent advisory bodies to inform their opinion. Regulatory expertise is one area of expertise being sought for the WG. Nominations should be received no later than **Wednesday 22 July, 23:59 CET**.

[How to submit nominations](#) (submission to be received by 22 July, 23:59 CET)

## **Preparing for real-world monitoring of COVID-19 vaccines**

A European infrastructure will be in place to effectively monitor COVID-19 vaccines in the real world, once these are authorised in the European Union. The ACCESS (vACCine Covid-19 monitoring readinESS) project will be led by the University Medical Center Utrecht (UMCU) and Utrecht University.

They will coordinate a EU Pharmacoepidemiology and Pharmacovigilance Research Network, a public-academic partnership of 22 European research centres, to conduct preparatory research into data sources and methods that can be used to monitor the safety, effectiveness and coverage of COVID-19 vaccines in clinical practice. The infrastructure put in place by Utrecht University will provide additional information from clinical practice to complement data collected pre-authorisation through clinical trials and post-authorisation through spontaneous reporting.

## **Detection of adventitious agents by next generation sequencing methods**

A meeting report has been published on the use of next generation sequencing (NGS) as a rapid method for adventitious virus detection assays which can facilitate SARS-CoV-2 vaccine development. The report reflects the current state of the art and will be an aid to regulators and vaccine developers to NGS methods, including the importance of international virus standards for such work.

[Report : Next generation sequencing for adventitious virus detection in biologics for humans and animals](#)

## **Landscape of candidate vaccines for SARS-CoV-2**

A landscape analysis of candidate SARS-CoV-2 vaccines is regularly published by WHO.

[Landscape of COVID-19 candidate vaccines](#) (15 July 2020)

## **Convalescent plasma**

### **Maintaining a safe and adequate blood supply during the COVID pandemic outbreak**

This document provides interim guidance on the management of the blood supply in response to the pandemic outbreak of coronavirus disease (COVID-19). It emphasizes the importance of being prepared and responding quickly and outlines key actions and measures that the blood services should take to mitigate the potential risk to the safety and sufficiency of the blood supplies during the pandemic.

It should be read in conjunction with [WHO Guidance for National Blood Services on Protecting the Blood Supply During Infectious Disease Outbreaks](#), which provides general guidance on the development of national plans to respond to any emerging infectious threats to the sufficiency or safety of the blood supply.

New interim Guidance: [Maintaining a safe and adequate blood supply during the pandemic outbreak of coronavirus disease](#) (10 July 2020)

## **Enabling research: Animal models, clinical trial protocols, assay development, standards**

### **WHO Working Group on Assays and Reference Preparations**

The 8 July meeting discussed optimization of ELISAs, including multiplex assays, by laboratories developing methods that will be used to assess samples from vaccine clinical trials.

One laboratory has developed and validated a multiplex assay that simultaneously analyses antibody responses the SARS-CoV-2 spike, N and receptor-binding domain protein. The final format of the assay is under discussion with regulators and, once agreed, will be used by high-throughput contract research organizations to test CT samples. In addition, a multiplex assay is under development to simultaneously detect the antibody response to the SARS-CoV-2 antigens above plus antibodies to the 4 human coronaviruses that were circulating prior to the pandemic.

A second laboratory illustrated the benefits of having common reference materials available to optimize assays that will be used to assay samples from vaccine clinical trials. The reference materials allowed a comparison of commercially available antigens, and selection of the most suitable antigen, to use in an ELISA format to detect IgG antibodies to SARS-CoV-2.

In the 15 July meeting, the [US DARPA](#) presented data on a new diagnostic methodology, epigenetic characterization and observation (ECHO). The development of a COVID-19 epigenetic signature was reported, based on expression patterns of selected genes. Further development is needed to verify that the system can distinguish between SARS-CoV-2 infection and immunization with SARS-CoV-2 vaccines. A request has been made to the US FDA for an Emergency Use Authorization (EUA) for diagnostic tests based on the COVID-19 epigenetic signature.

The Institute for Biological Products, Thailand provided an update on progress with vaccine development in Thailand. An issue of concern raised by Thai investigators is that there is no globally agreed gold standard method for serological testing of vaccines, and a variety of assays are being used by developers worldwide. The availability of a WHO International Standard to help calibrate serological assays would be very beneficial. Preparation and evaluation of such a material is currently underway.

WHO also reported an initiative to develop a guidance document on propagation of SARS-CoV-2 viruses for either use as challenge inocula in animal experiments or as reagents in assays. The scientific community were invited to share data on experience with propagation of SARS-CoV-2 to inform development of the document.

### **WHO Working Group on Animal Models**

#### ***Mapping of animal model capacity to accelerate COVID-19 vaccines and therapeutics development***

WHO has published an updated table that lists laboratories that have established one or several COVID-19 animal models and have expressed interests in collaborating with COVID-19 vaccine and therapeutic developers to accelerate candidate product evaluation using the animal models they have developed. Information on each participant laboratory was obtained through a survey that was disseminated through the WHO ad-hoc group of experts on COVID-19 animal models and additional networks.

[Global animal laboratories capacities to support vaccine and therapeutic evaluation](#)

#### ***Working Group meetings***

In the 9 July meeting, US FDA presented their work to identify an animal model to study SARS-CoV-2 treatments and vaccines. The Syrian hamster was selected and SARS-CoV-2 infection in the model was

characterized. Key findings were that assay of subgenomic mRNA is the best indicator of virus replication; that a 100 TCID<sub>50</sub> challenge dose was the minimum inoculum to reliably induce virus pneumonia; that aged hamsters (animals > 1 year old) had higher clinical scores than younger animals; previously infected animals were protected on re-challenge and did not transmit the virus to contact animals.

Another group showed that induction of transient immunosuppression of Syrian hamster with cyclophosphamide increased the clinical scores in this model, suggesting the model may be useful for vaccine studies.

Results of testing candidate therapeutics in cynomolgus macaques was also reported. Lopinavir/ritonavir prophylaxis was shown to have no effect when the animals were subsequently challenged with SARS-CoV-2. Favipiravir prophylaxis was shown to have no antiviral effect when the animals were subsequently challenged with SARS-CoV-2. Moreover, animals that received favipiravir prophylaxis had a worse clinical outcome than controls, including more severe lung pathology. Plasma levels of favipiravir were elevated in SARS-CoV-2 infected animals, suggesting a lack of metabolism of the drug.

A call was made by BMGF for a consortium of imaging groups to work together to define the imaging measures that would be most useful as quantitative readouts of disease severity. The goal is to determine how data from CT and PET/CT scans of non-human primates might be used to assess whether enhanced disease occurs after vaccination.

In the 16 July meeting, results of an immunogenicity study in cynomolgus macaques of mRNA-based COVID-19 vaccines (Chula-Cov19) under development in Thailand were presented. Also, a mouse adapted SARS-CoV-2 MA10 model was described. The mouse adapted virus replicates to high titers in wild type mice, leads to high morbidity and mortality in mice dependent on age and genetic background, reproduces disease symptoms observed in human population and is considered by the researchers to highly valuable to evaluate therapeutics and vaccines against SARS-CoV-2 in the future.

## **Supply chain updates from WHO HQ and Regional Offices**

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

WHO has published a catalogue that 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. The catalogue is available at:

[Emergency Global Supply Chain System \(COVID-19\) catalogue](#) (09 July 2020)

### **Access to HIV medicines severely impacted by COVID-19**

Seventy-three countries have warned that they are at risk of stock-outs of antiretroviral (ARV) medicines as a result of the COVID-19 pandemic, according to a new WHO survey. Twenty-four countries reported having either a critically low stock of ARVs or disruptions in the supply of these life-saving medicines.

In 2019, an estimated 8.3 million people were benefiting from ARVs in the 24 countries now experiencing supply shortages. This represents about one third (33%) of all people taking HIV treatment globally. While there is no cure for HIV, ARVs can control the virus and prevent onward sexual transmission to other people.

A failure of suppliers to deliver ARVs on time and a shut-down of land and air transport services, coupled with limited access to health services within countries as a result of the pandemic, were among the causes cited for the disruptions in the survey.

WHO recently [developed guidance](#) for countries on how to safely maintain access to essential health services during the pandemic, including for all people living with or affected by HIV. The guidance encourages countries to limit disruptions in access to HIV treatment through “multi-month dispensing,” a policy

whereby medicines are prescribed for longer periods of time – up to six months. To date, 129 countries have adopted this policy. Countries are also mitigating the impact of the disruptions by working to maintain flights and supply chains, engaging communities in the delivery of HIV medicines, and working with manufacturers to overcome logistics challenges.

## **Substandard and falsified (SF) products**

An update of Alert n5/2020 (defibrotide) has been issued noting that defibrotide is used in COVID-19 clinical trials in some places. Currently there is no concrete evidence to suggest these specific reports were in relation to covid19

Alert n5/2020: [Falsified and contaminated Defibrotide identified in WHO regions of Western Pacific, Europe and Eastern Mediterranean](#) (01 July 2020)

United Nations Office on Drugs and Crime (UNODU) has issued a research brief on COVID-19 related crime and SF medical products

[Increased trafficking in falsified medical products due to COVID-19, says UNODC research](#) (July 2020)

## **Medical Devices**

Final draft of COVID-19 technical specifications for the following medical devices for clinical management of COVID-19 patients were published on 10 July 2020, describing the minimum requirements that the medical devices must comply with to ensure quality, safety and effectiveness when used for the management of COVID-19.

[Technical specifications for procurement of oxygen therapy and monitoring devices](#) (10 July 2020)

[Technical specifications for infusion devices](#) (10 July 2020)

[Technical specifications for portable ultrasound](#) (10 July 2020)

The 3 draft specifications above will be integrated in a single publication along with other sets that are being updated including PPE.

[updated information on the PPE](#)

[Medical devices for COVID-19 patient management](#)

## **Access to regulatory updates by WHO staff**

All WHO staff have access to the Regulatory Updates at the following location:

P:\PubPersons\RPQ\COVID\_Regulatory\_Updates