WHO Regulatory Update on COVID-19

World Health Organization

Regulation and Prequalification, Geneva

07 May 2020

Context

World Health Organization

WHO is coordinating a global research effort* to develop diagnostic tests, therapeutics and vaccines for SARS-CoV-2, and has published ethical guidelines** for conducting research on COVID-19

The Regulation and Prequalification (RPQ) Department is closely involved with the WHO R&D effort, ensuring that regulators are involved in all activities

RPQ is also collaborating with regulators worldwide to provide a platform for the rapid exchange of information on COVID-19 developments

The aim is to promote regulatory alignment to facilitate access to quality, safe and effective products as quickly as possible – feeding in to ACT accelerator

* www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus/en/

** www.who.int/blueprint/priority-diseases/key-action/liverecovery-save-of-ethical-standards-for-research-during-public-health-emergencies.pdf?ua=1

Director General at G20: “Fight, unite, ignite“

“This is a global crisis that requires a global response.”

www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-g20-extraordinary-leaders-summit-on-covid-19---26-march-2020

Fight: Fight hard. Fight like hell.

- immediately build, expand, train and deploy health workers to find, test, isolate and treat every case and trace every contact. This is not an option; it’s an obligation.

Unite: No country can solve this crisis alone

- a paradigm shift in global solidarity – in sharing experiences, expertise and resources, and in working together to keep supply lines open, and supporting nations who need our support
- increase production, remove export bans and ensure equity of distribution

Ignite:

- repurpose the industrial
- ignite global production for the tools we need to save lives
- ignite innovation for vaccines and therapeutics
- and ignite a global movement to ensure this never happens again

The actions we take now will have consequences for decades to come.

the opportunity to come together as one against a common threat, and to build a common future

ACT Accelerator launched on 24 April

WHO, together with global health actors, private sector partners and other stakeholders, to accelerate the development, production and equitable access to new COVID-19 diagnostics, therapeutics and vaccines

Mission:

- Accelerate development and availability of new COVID-19 tools
- Accelerate equitable global access to safe, quality, effective, and affordable COVID-19 diagnostics, therapeutics and vaccines
- Ensure that in the fight against COVID-19, no one is left behind

LEAVE NO ONE BEHIND

www.who.int/news-room/detail/24-04-2020-global-leaders-unite-to-ensure-everyone-everywhere-can-access-new-vaccines-tests-and-treatments-for-covid-19

A European rolling pledging campaign started on 4 May 2020 to accelerate achievement of the objectives of this global collaboration.

Other activities to ensure access

- Medicines Patent Pool extends remit to COVID-19

  https://medicinespatentpool.org/what-we-do/our-work/covid-19/

- WHO supports Costa Rica proposal to create a pool of rights to tests, medicines and vaccines, with free access or licensing on reasonable and affordable terms for all countries and is working with Costa Rica to finalize the details

  www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30137-6/fulltext

- WHO calls on all countries, companies and research institutions to support open data, open science and open collaboration

IVDs for SARS-CoV-2: as of 27 April 2020

- 9 IMDRF* countries (Australia, Brazil, Canada, China, Japan, Russia, Singapore, South Korea, USA) have listed IVDs for diagnosis of COVID-19 on the basis of expedited regulatory assessments. To help other countries, WHO published links to these emergency lists, together with contact details

  Link to the most recent IMDRF update (27 April)

- Assays for the detection of SARS-CoV-2 nucleic acid (NAT) and SARS-CoV-2 antibodies (Ab RDT) are eligible for Emergency Use Listing (EUL) assessment

EUL Listed	Product name	Product code(s)	Manufacturer
24 April	PerkinElmer® SARS-CoV-2 Real-time RT-PCR Assay	SY580	SYM-BIO LiveScience Co., Ltd
09 April	Abbott Realtime SARS-CoV-2	09N77-090 and 09N77-080	Abbott Molecular Inc.
07 April	Primerdesign Ltd COVID-19 genesig Real-Time PCR assay	Z-Path-COVID-19-CE	Primerdesign Ltd.
03 April	cobas SARS-CoV-2 Qualitative assay for use on the cobas 6800/8800 Systems	09175431190 and 09175440190	Roche Molecular Systems, Inc.

Link to: Instruction for Use of above-mentioned products and Public Reports

IMDRF*: International Medical Device Regulators Forum

Testing strategies for COVID-19

WHO advice on use of RDTs for Antigen and Antibody for SARS-CoV-2 (08 April):

- Based on current evidence, WHO recommends the use of these new point-of-care immunodiagnostic tests **only in research settings**.
- **They should not be used in any other setting, including for clinical decision making**, until evidence supporting use for specific indications is available.

WHO advice on “immunity passports” (24 April):

- No study has determined that the presence of antibodies to SARS-CoV-2 confers immunity to subsequent infection by this virus in humans.
- In vitro diagnostics for detection of antibodies to SARS-CoV-2 in people, including RDTs, may identify people who have previously infected with SARS-CoV-2 but this does not indicated they have immunity to COVID-19.

Substandard and Falsified (SF) products

- WHO has published a global alert on falsified medical products related to COVID-1D and a specific alert on Chloroquine products circulating in Africa

  www.who.int/medicines/publications/drugalerts/en/

- WHO continues to receive numerous notifications of SF medical products related to Covid19, in particular chloroquine and hydroxychloroquine and scam/fraud websites that cover a wide range of products, including ventilators
- Any suspected or confirmed falsified/substandard medical products should be reported to rapidalert@who.int
- WHO Information Notice for Users, version 3 issued on 22 April, provides advice to end-users of IVDs:

  www.who.int/diagnostics_laboratory/procurement/200422_who_info_covid_falsified_ivds_en.pdf?ua=1

SF Products: Medical Product Alert No 4/2020

Ref. RPQ/REG/ISF/Alert N°4.2020 09 April 2020

Falsified chloroquine products circulating in the WHO region of Africa

Identified in	Product name	Stated manufacturer	Batch #	Expiry date	Date of manufacture
Cameroon	Chloroquine Phosphate (100mg)	Jiangsu Pharmaceutical Inc.	660	May 2021	05/2017
	Chloroquine Phosphate (250mg)	Jiangsu Pharmaceutical Inc.	660	Sept 2022	09/2018
	Chloroquine Phosphate (250mg)	Astral pharmaceuticals	EBT 2542	Oct 2022	01/2019
DRC	CLOROQUINE (250mg)	Dawa Limited	1605059	Apr 2023	05/2019
	Chloroquine Phosphate (250mg)	Brown & Burk Pharmaceutical Ltd	065622	Nov 2022	11/2018
Niger	Samquine 100 (100mg)	None indicated	NBJT01	Oct 022	11/2019
	Chloroquine phosphate tablets B.P (100mg)	None indicated	HV1116	May 2023	06/2019
	Chloroquine phosphate tablets B.P (100mg)	None indicated	NBJT02	Oct 2022	11/2019
	Niruquine (100mg)	None indicated	Unknown	Aug 2022	09/2019

Solidarity Clinical Trials for COVID-19 treatments

As of 8th April, more than 90 countries are engaging or have expressed an interest in the Solidarity Trials announced by the WHO DG on the 18th of March.

www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments

Aim of the solidarity trial is to:

- use the same or similar protocols,
- allow data to be reviewed / compared from the same view point and rapidly discover whether any of the drugs slow disease progression or improve survival,
- provide simplified procedures to enable overloaded hospitals to participate without additional required paperwork

A landscape analysis of candidate COVID-19 therapeutics is regularly published by WHO to analyse clinical trials to evaluate therapeutics for COVID-19

Therapeutics for COVID-19 (1)

- Adaptive trial design of local standard of care alone, OR local standard of care plus one of;
  - Remdesivir;
  - Chloroquine or hydroxychloroquine;
  - Lopinavir with Ritonavir;
  - Lopinavir with Ritonavir plus Interferon beta-1a

currently inclusion of Favipiravir is under consideration

Informal consultation on the potential inclusion of favipiravir in the solidarity trial

- An unintended consequence of the identification by WHO of candidate therapeutics for clinical evaluation has been stock-outs of these drugs. To assist decision makers, WHO have issued a statement on off-label and compassionate use* of pharmaceutical products for COVID-19
- Importance of adverse drug reporting and monitoring stressed

*www.who.int/news-room/commentaries/detail/off-label-use-of-medicines-for-covid-19

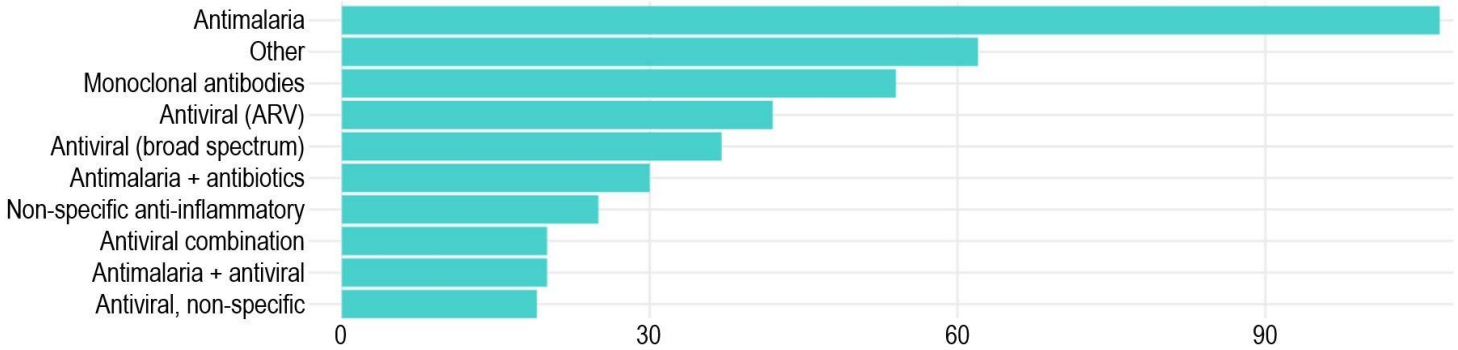
Therapeutics for COVID-19 (2): as of 29 April

World Health Organization

As of 29 April, **626** randomized controlled trials have been registered

- 526 trials evaluating treatments intervention
  - 408 trials (78%) assessing pharmacological treatments
  - 98 trials (19%) assessing non-pharmacological treatments

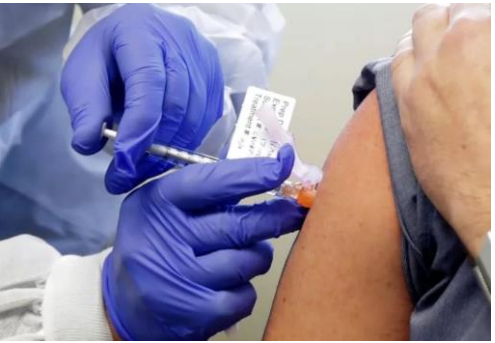
https://covid-nma.com/networks/



- Living synthesis of Covid-19 study results is made available by a group of researchers to monitor and to identify gaps and deficiencies of existing evidence with an aim to help prioritizing and optimizing future research
- A team of the LIRIS/CNRS laboratory is performing a Data Visualization
- Screening electronic databases is available to identify results of RCTs and other studies

Link: Living mapping and living systematic review of COVID-19 studies

Vaccines for SARS-CoV-2



- ICMRA* developed generally agreed positions on Preclinical data required to support proceeding to First in Human (FiH) clinical trials

*ICMRA: International Coalition of Medicines Regulatory Authorities

- There is a need to address the theoretical risk for SARS-CoV-2 vaccine-induced disease enhancement prior to proceeding to FIH clinical trials

- 8 vaccines are in clinical trial (67 candidates in pre-clinical evaluation)
  - a mRNA construct in the USA & Germany
  - a DNA construct in the USA
  - an adeno5 construct in China
  - a chimp adeno construct in the UK (partnership with Serum Institute of India)
  - 2 inactivated alum adjuvanted whole virion vaccines in China

Draft landscape of COVID 19 candidate vaccines (05 May)
https://www.who.int/who-documents-detail/draft-landscape-of-covid-19-candidate-vaccines

- 29th April SEARO Vaccines meeting: extensive pipeline of vaccines under development in India, Indonesia and Thailand
- Standards for calibration of serological assays for SARS-CoV-2 under development (NIBSC)

See Weekly Regulatory Update 7 for details

R&D Blueprint* and COVID-19

World Health Organization

WHO Working Group	(Terms of Reference and members – see each webpage)
Vaccine Core Protocol	provide a phase 2b/3 protocol that will enable the concurrent evaluation of the benefits and risks of each promising candidate vaccines
Vaccine Target Product Profile	develop a global target product profile for long term protection and for reactive use in outbreak settings
Vaccine prioritization	review pipeline, discuss their value in protecting against the nCoV and make preliminary recommendations on prioritization of candidate vaccines
Vaccine R&D	discuss approaches to demonstrate the effectiveness, resource utilization in vaccine development and considerations for vaccine deployment

* www.who.int/teams/blueprint/covid-19

Blood supply and use of convalescent plasma (CP)

- The epidemic has the real potential however to reduce the supply of blood and blood components and adversely affect blood system activities
- WHO has published guidance to assist blood services to take steps to assess, plan, and respond appropriately and proportionately on blood supplies through reduced blood donation
- Countries conducting clinical trials for CP include USA, Canada, Germany. Protocols have been developed by Saudi Arabia and Philippines
- Both Clinical Trials and compassionate use interventions are being explored
- WHO has collected a listing and links (see Weekly Regulatory Update for details)

Medical Devices

Technical guidance and tools for essential resource planning:

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/covid-19-critical-items

- Priority medical devices for COVID prevention, diagnostics and management:
- Personal protective equipment
- Medical equipment and consumables to manage the patient
- For innovative technologies for COVID
- Global collaboration for medical devices for COVID

Recently launched the COVID-19 essential Supplies forecasting tool (1st May 2020)

In vitro diagnostics:

- Laboratory testing guidance

Clinical Management of patients:

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/patient-management

(see Weekly Regulatory Update for details)

Regulatory flexibility:

To mitigate the risks of shortages and stockouts, a number of regulators have produced temporary guidance on regulatory flexibility (See Regulatory Update 7 for updated list)
WHO will work with international regulators to develop best practices.

EU	Regulatory flexibility guidance
MHRA	Exceptional Good Distribution Practice (GDP) flexibilities for medicines during the coronavirus (COVID-19) outbreak
MHRA	Exceptional Good Manufacturing Practice (GMP) flexibilities for medicines imported from third countries during the coronavirus (COVID-19) outbreak
US FDA	Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency
US FDA	Postmarketing Adverse Event Reporting for Medical Products and Dietary Supplements During a Pandemic
US FDA	Permanent Discontinuance or Interruption in Manufacturing Under Section 506C of the FD&C Act
ID BADAN POM	Establishment of Drug Guidelines in the Handling of Corona Virus Disease 2019 (COVID-19)
IN CDSCO	Regulatory Pathway for fast track review or approval of Vaccines: a) Accelerated Approval Process Quick or b) Expeditious review process

RPQ work on Local Production:

- On 21 April, Interagency committee on Local Production was held with 12 UN agencies and partners to identify synergies and explore collective ways to promote local production to combat COVID-19. Regular meetings will be organized.
- On 24 April, a Webinar was co-organized with UNCTAD to exchange views and identify areas to scale up investment in quality local production in LMIC for production and supply chain of health products.

  Roundtable discussion focused on domestic capacities of candidate therapeutics and vaccines, required provisions to ensure production with quality and sustainability and the role of development partners.

Regulatory activities: Unite, Collaborate, Cooperate

- WHO is encouraging regulatory networks to consider joint reviews, fast track approvals of Clinical trials and when appropriate marketing authorisations
- African Vaccines Regulatory Forum (AVAREF): building on the Ebola experience, agreed to expedite clinical trial reviews and approvals for new multinational preventive, diagnostic and therapeutic interventions for COVID-19
- African Medical Devices Forum (ADMF) provide weekly updates
- Bi-weekly meetings with PAHO and Pan American Network for Drug Regulatory Harmonization
- WHO calls for international approach to “regulatory flexibility” and will develop best practice principles
- WHO is preparing weekly regulatory updates for wide circulation and regional meetings of regulators, welcoming suggestions for further improvement

World Health Organization

WORKING TOGETHER

Department of Regulation and Prequalification, WHO