


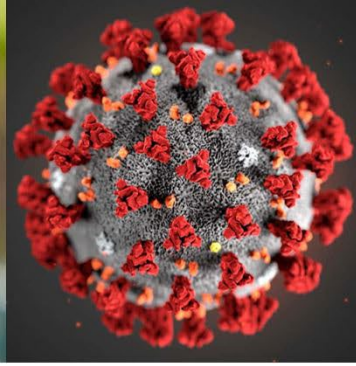

WHO EUL- principles, process and lessons learnt

21 September 2021

EXTRAORDINARY INTERNATIONAL CONFERENCE OF DRUG REGULATORY AUTHORITIES

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Department of Regulation and Prequalification (RPQ)

World Health Organization




Role of regulation:
Promoting and protecting public health

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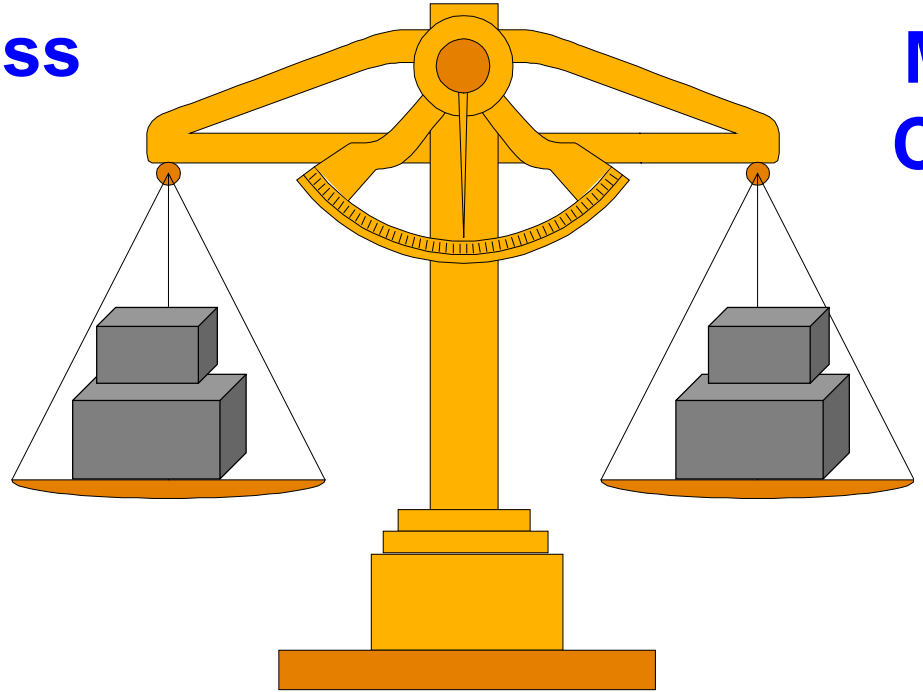
Access

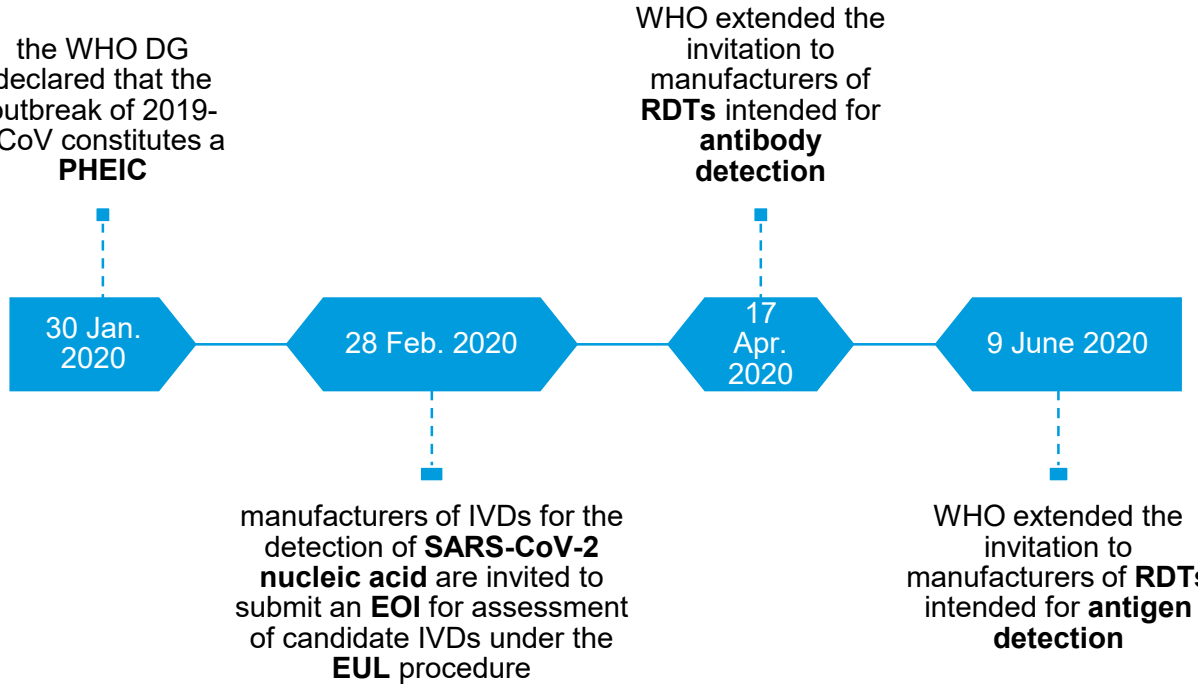
Market Control

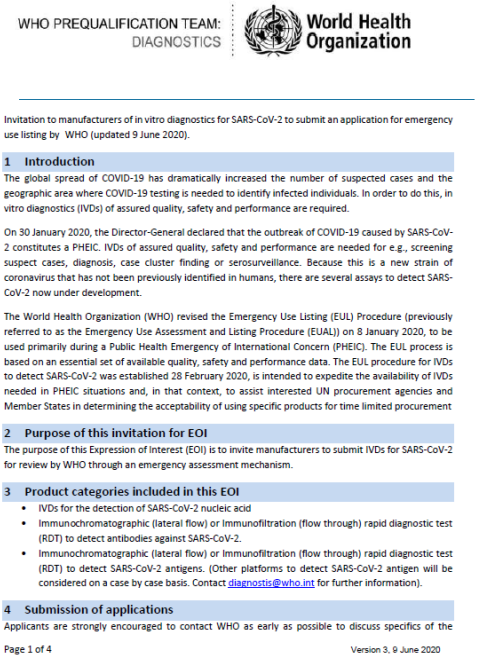


WHO EUAL/EUL background

- WHO Emergency Use Assessment and Listing (EUAL) mechanism developed in response to the 2014 - 2016 Ebola outbreak
- Risk-based approach to expedite the availability of health products needed in public health emergency situations
- It is intended to assist interested procurement agencies and Member States on the suitability for use of a specific health products, based on a minimum set of available **quality, safety,** and **performance** data
- EUL status is time-limited

EUL of IVDs in context of the COVID pandemic





WHO PREQUALIFICATION TEAM: DIAGNOSTICS

World Health Organization

Invitation to manufacturers of in vitro diagnostics for SARS-CoV-2 to submit an application for emergency use listing by WHO (updated 9 June 2020).

1 Introduction

The global spread of COVID-19 has dramatically increased the number of suspected cases and the geographic area where COVID-19 testing is needed to identify infected individuals. In order to do this, in vitro diagnostics (IVDs) of assured quality, safety and performance are required.

On 30 January 2020, the Director-General declared that the outbreak of COVID-19 caused by SARS-CoV-2 constitutes a PHEIC. IVDs of assured quality, safety and performance are needed for e.g., screening suspect cases, diagnosis, case cluster finding or serosurveillance. Because this is a new strain of coronavirus that has not been previously identified in humans, there are several assays to detect SARS-CoV-2 now under development.

The World Health Organization (WHO) revised the Emergency Use Listing (EUL) Procedure (previously referred to as the Emergency Use Assessment and Listing Procedure (EUAL)) on 8 January 2020, to be used primarily during a Public Health Emergency of International Concern (PHEIC). The EUL process is based on an essential set of available quality, safety and performance data. The EUL procedure for IVDs to detect SARS-CoV-2 was established 28 February 2020, is intended to expedite the availability of IVDs needed in PHEIC situations and, in that context, to assist interested UN procurement agencies and Member States in determining the acceptability of using specific products for time limited procurement

2 Purpose of this invitation for EOI

The purpose of this Expression of Interest (EOI) is to invite manufacturers to submit IVDs for SARS-CoV-2 for review by WHO through an emergency assessment mechanism.

3 Product categories included in this EOI

- IVDs for the detection of SARS-CoV-2 nucleic acid
- Immunochromatographic (lateral flow) or Immunofiltration (flow through) rapid diagnostic test (RDT) to detect antibodies against SARS-CoV-2.
- Immunochromatographic (lateral flow) or Immunofiltration (flow through) rapid diagnostic test (RDT) to detect SARS-CoV-2 antigens. (Other platforms to detect SARS-CoV-2 antigen will be considered on a case by case basis. Contact diagnostis@who.int for further information).

4 Submission of applications

Applicants are strongly encouraged to contact WHO as early as possible to discuss specifics of the

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How does PQT/EUL-IVD focus on the needs of member states especially LMICs

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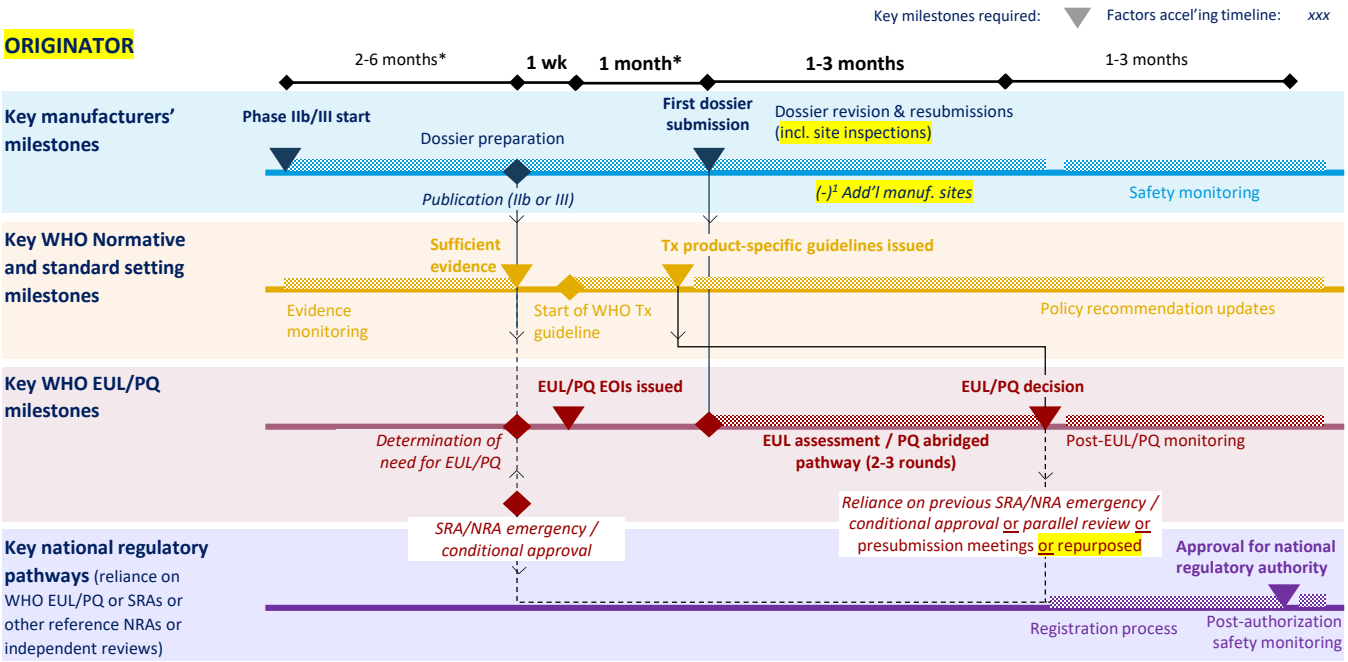
- PQ is designed based on best international practice combined with assessing aspects of particular relevance for LMIC
  - Risk management: has the manufacturer taken into account risks related to the user (non-medical education, multi-tasking health worker with limited training), the environment (temperature, humidity, dust, light etc.)
  - Are products sufficiently robust (flex studies stretching the product by adding too much reagent, reading after official reading time)
  - Has the product been validated with the target population in place, including interfering substances and cross-reactivity in different regions
  - Are the instructions for use clear for a typical user in a LMIC

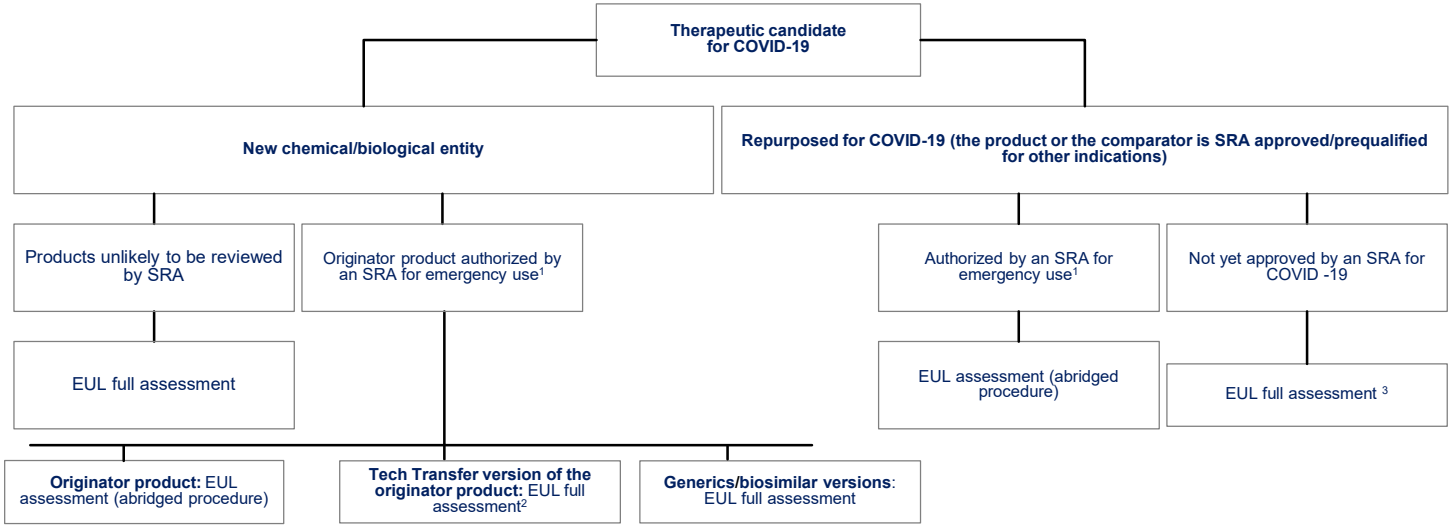
Total lead time of ~2-4 months from evidence of data – publication – to EUL/PQ decision for **originators**



* Timelines not WHO PQ / EUL or national regulatory activity -dependent

1 Decelerating factor; need for comparability data (e.g., contract manufacturing)

EUL pathways for COVID-19 medicines



1. The emergency use authorization should have been granted based on review of available quality, safety and efficacy data
2. The EUL assessment for Tech transfer products may be facilitated by access to the SRA assessment reports of the original emergency use authorization
3. Depending on whether the EOI issued by WHO is for EUL or PQ, which in turn depends on the extent of the available clinical data

Note: For mABs and other biologics, the same procedure and requirements for EUL will be followed but specific guidelines and requirements may be developed depending on the particular type of product.

Note: WHO will promote the use of the collaborative procedure to facilitate national emergency use authorization.

WHO alignment activities for COVID-19 vaccines ongoing since Feb 2020

✓Completed • Ongoing ☐ Details on following slides

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Development criteria	Submission requirements	Assessment process	In-country approval for use & post approval monitoring
✓ **Target Product Profiles** ✓ **Expert Committee on Biological Standards** guidance ✓ **Regulatory guidelines**	✓ **EUL and PQ guidance** and **Questions & Answers** ✓ **EUL/PQ Expressions of Interest** (conditions & evaluation criteria) • Labelling & packaging requirements	• **Evaluation of candidates** for EUL/PQ (incl. inspection, lot release process & post-listing commitment) • **Interactions & agreements** with NRAs/SRAs* • **Global assessment process*** with region-designated national authority reps	• **Country regulatory reliance** on EUL/PQ* • Support for **safety monitoring** (based on safety preparedness manual) • Tools for **risk communication** and strengthening **response capabilities**

- **Roadmap*** to enable product specific regulatory alignment (assessment process, in-country approval & post-listing monitoring)
- **Alignment ongoing** (Regulatory Advisory Group, ICMRA, regional regulatory networks, Vaccine cluster etc.)
- Regulatory **updates and webinars**
- Best practice principles for **regulatory "agility"**

* Elements of the *Roadmap for WHO Assessment of* vaccine x *during the COVID-19 Public Health Emergency (model roadmap published on 30 Oct 2020)*

Eligibility of candidate products

- The disease for which the product is intended is serious or immediately life threatening, has the potential of causing an **outbreak, epidemic or pandemic** and it is reasonable to consider the product for an EUL assessment, e.g., there are **no licensed products** for the indication or for a critical subpopulation (e.g., children);
- Existing products have not been successful in eradicating the disease or preventing outbreaks (in the case of vaccines and medicines);
- The product is manufactured in **compliance with current Good Manufacturing Practices (GMP)** in the case of medicines and vaccines and under **a functional Quality Management System (QMS)** in the case of IVDs; and
- The applicant **undertakes to complete the development of the product** (validation and verification of the product in the case of IVDs) and **apply for WHO prequalification** once the product is licensed

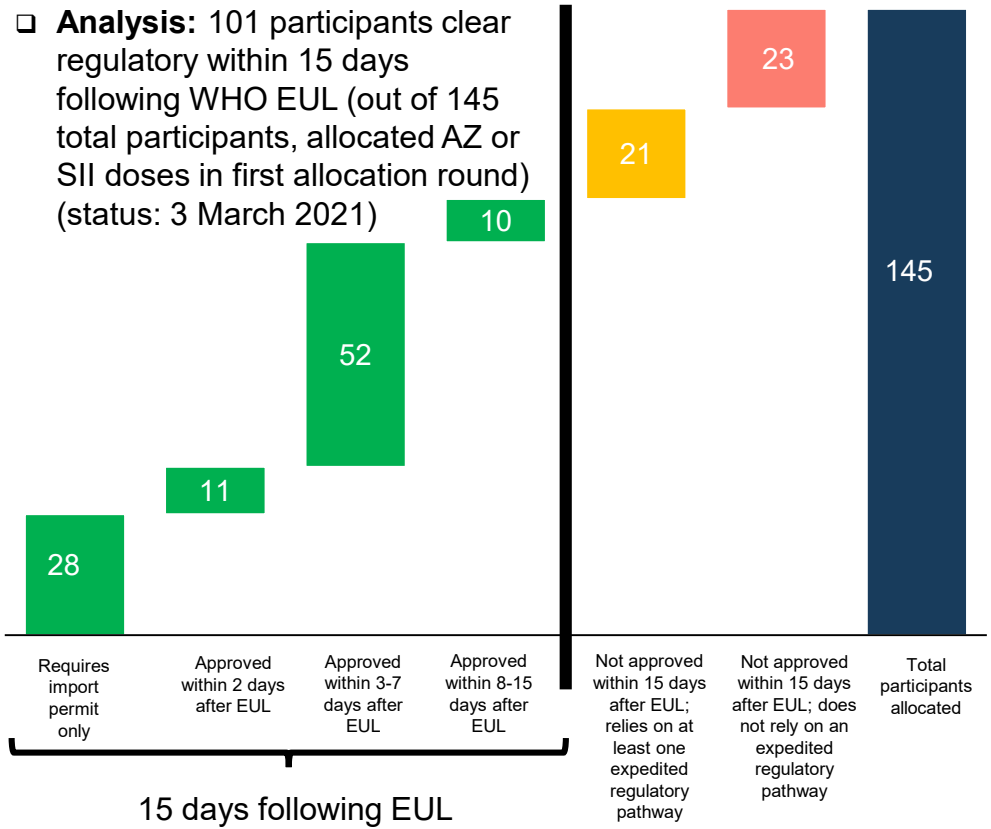
Some results

- EUL: 12 vaccines, 28 IVDs, Dexamethasone, Seven (0.3 ml AD) Injection devices
- Regulatory flexibilities: desk and remote inspections.
- Document on triggers for WHO clinical guidelines and PQ EOIs for Tx (Parallel process)
- Facilitation of authorization and access at national level
  - EUL workshops held for regulators in the 6 WHO regions
  - Development of global mechanisms for facilitating access of COVID-19 vaccines.
  - Regulators from WHO regions involved in the assessment of COVID-19 vaccines (47)
  - Under OPEN, participated in EMA evaluation process.
  - Dossiers and reports (408) shared with 97 countries, briefing workshops on the outcome of the EUL review in different regions.

Regulatory approaches adopted by countries under COVAX

- **Country granting Emergency-use authorization (EUA) using reliance**
  - Regulatory approach based on reliance to WHO PQ EUL (or Stringent Regulatory Authority EUA)
  - Some countries requested access by NRAs to documentation submitted by manufacturers to WHO PQ when applying for EUL, as well as respective assessment reports (issued by PQ).
  - Few countries insisted on the submission of an application by a manufacturer.
- **"Import authorization" or other authorization for use under exceptional circumstances**
  - Requirement for regulatory authorization is "waived", relying on referring to the WHO EUL.
  - Supply is based on an import authorization, without issuance of a national EUA.

- **Analysis:** 101 participants clear regulatory within 15 days following WHO EUL (out of 145 total participants, allocated AZ or SII doses in first allocation round) (status: 3 March 2021)



Flexibilities to allow for continuation of mandate of PQT by performing:

- Remote real time inspections of BE sites, Vx sites, QCL, NCL, FPP
- Desk Reviews and reliance on work done by Mature NRA
- Joint inspections conducted with EMA Inspectors
- Extension of the WHOPIR validity from 3 years to 4 years
- EUL applications - Evaluation of QMS of manufacturing sites

Take home messages

- ✓ PQ has proven to be a valuable WHO tool for international response against COVID-19 pandemic – facilitating robust evaluation of health products and facilitating their access and approval at national level.

- ✓ Success depends on mutual collaboration with manufacturers, other UN agencies, development partners, procurers, national and regional regulators.

Acknowledgements:

NRAs of WHO Member States

World Health Organization

WHO/Otto B.

WORKING TOGETHER

Department of Regulation and Prequalification, WHO