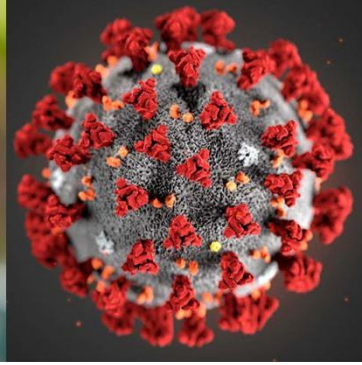


WHO Regulatory alignment on COVID-19 vaccines

16 December 2020

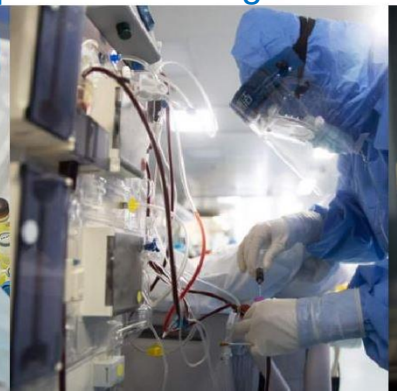
World Health Organization

2020 eVPPEF

Engaging with countries planning to procure the COVID-19 vaccines

Carmen Rodriguez Team lead vaccines PQ

Department of Regulation and Prequalification (RPQ)

Goal & objectives

Goal of this WHO work: to optimize access & availability to safe, efficacious, quality-assured COVID-19 products by further aligning regulatory processes

Objectives of today's presentation:

- Explain and update on **WHO's roadmap** for aligning regulatory processes impacting access to COVID-19 vaccines

https://www.who.int/publications/m/item/roadmap-for-evaluation-of-astrazeneca-azd1222-vaccine-against-covid-19

- Collaboration with National regulatory authorities.
- Packaging and labelling updates.

Features of PQ and EUL

Prequalification (PQ) 1987

- Review of extensive quality, safety and efficacy and PSPQ for international supply
- Assessment performed by WHO independent experts
- Reliance on WHO Listed Authority (WLA) - abbreviated process under oversight of mature regulators (evaluation and oversight of programmatic aspects by WHO)
- Pre-submission meetings encouraged
- Post-PQ monitoring
- Reassessment/requalification

Emergency Use Listing (EUL) 2015

- **Risk benefit assessment of essential set of quality, safety and efficacy data for use during PHEs**
- **Rolling review of data**
- Assessment performed by WHO independent experts in collaboration with National Regulatory Authorities (WLA)
- Reliance on WLA - abbreviated process under oversight of mature regulators (evaluation and oversight of programmatic aspects by WHO)
- Pre-submission meetings encouraged
- **Post- deployment monitoring**
- **Time limited recommendation**
- **Development should continue for MA/PQ**

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

✓Completed • Ongoing

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)*

WHO regulatory alignment roadmap for COVID-19 vaccines: overview of recognized pathways, and summary of related alignment activities

World Health Organization

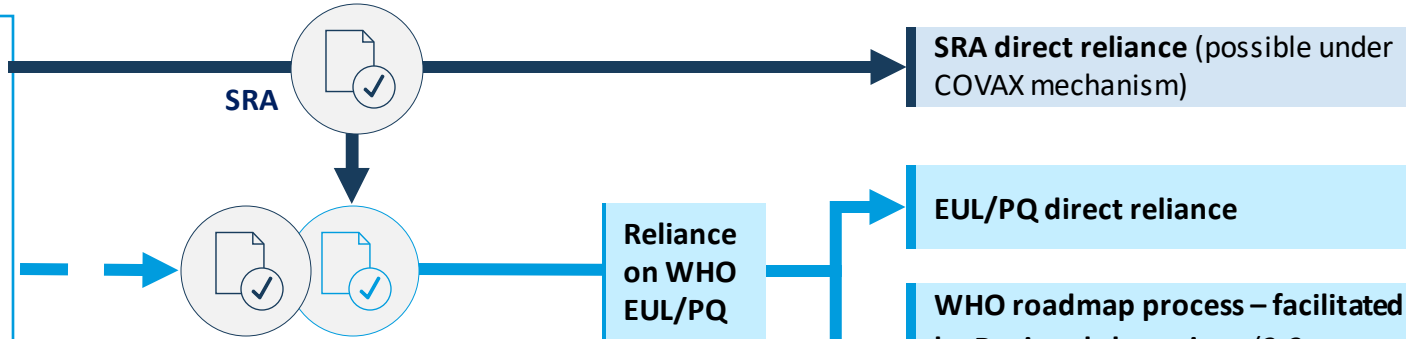
Submission requirements	Assessment process	In-country approval for use & post-listing monitoring

Data in dossier:
- Efficacy
- Safety
- Quality

Inspection data (GMP, GCP, GLP, GVP)

Lot release data

Etc…



- **Aligned requirements** with NRA / SRA in charge of oversight
- **Participant NRA requirements** captured
- **Single format for application** submitted by manufacturers

- **Interactions & agreements with NRAs/ SRAs in charge of oversight** early in process (incl. report sharing, aligned requirements)
- **Global assessment** with region-designated national authority representatives

- **Transparent sharing of reports** with all regulatory authorities for decision making process
- **Promotion of reliance principles** in countries based on facilitated pathways (direct, through regional networks, via regional champions/NRAs of reference)

In-country expedited approval for use & post-listing monitoring: the WHO regulatory alignment roadmap*

World Health Organization

1. Preliminary activities	2. Launching of EOIs	3. Submissions & assessment	4. Recommendation for listing	5. Post-listing monitoring
• **Global regulatory cooperation** • Establishment of **strategies for expedited approval** in participants & post-listing monitoring	• **Manufacturers EOIs** (Phase IIb/III & approval by NRA/SRA in charge of oversight within 6 months & compliance with criteria for assessment) • Discussions on **rolling submission** procedure	• Establishment of **assessment pathway** according to NRA/SRA in charge of oversight • Establishment of **Review team** (NRA/SRA in charge of oversight & regulators /reviewers from potential user participants)	• **Approval** granted by NRA/SRA in charge of oversight • **Advisory group** convened (post-listing commitment) • **WHO EUL/ PQ recommendation** with conditions	• Implementation of **strategies for safety, quality & effectiveness monitoring** • **Validity of listing** based on new data generated • Possible **conversion of EUL to PQ**

COVAX | EUL/PQ | NRA reliance on EUL/PQ

Facilitated access to countries

- **Sharing of assessment/ inspection reports / lot release** with regional-designated country reps
- WHO-facilitated **national approval process**

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

updates on regulatory

Ongoing Global Assessment Programme:

- WHO continues to engage countries to participate in this programme. 20+ letters have been sent to regional regulators
  - AFRO: Ethiopia, Ghana, Tanzania, South Africa
  - EMRO: Iran, Saudi Arabia, Egypt.
  - AMRO: Argentina, Cuba, Mexico, Brazil
  - SEARO: Bhutan, India, Indonesia, Thailand.
  - EURO: Serbia
  - WPRO: South Korea
  - Specific NRAs: Australia (TGA) / Belgium / Swiss Medic / France / Health Canada / Germany / Japan, others etc.
- Countries are expected to nominate representatives
- Briefings with other countries are planned

DG wrote to FDA and EMA for collaboration

- Meetings with FDA have taken place since March 2020; Latest meeting on Nov. 24
- Meetings with EMA since March as well

Setting expectations…

WHO's regulatory alignment roadmap* is based on **collaborative principles** & **to be successful…**

- **Regional networks** must identify regional experts to take part in global assessment
- **Agreements** must be established with NRAs/SRAs in charge of oversight
- The **WHO reliance mechanism** must be adopted by participating countries
- **National regulatory agencies** must commit to sharing information & fast decision making

Estimated best case scenarios:

- First full EUL/PQ application submission –December 2020/ **Jan 2021**
- Timely EUL/PQ recommendation (contingent on parallel review) – **within days of approval by NRA / SRA in charge of oversight**
- Translation to in-country decisions or approval – **1 month post EUL/PQ**

* *Roadmap for WHO Assessment of* vaccine AstraZeneca ADZ1222 *during the COVID-19 Public Health Emergency*

Next steps on WHO regulatory alignment activities for COVID-19 vaccines

- Continue **implementation discussions with regional networks & reference NRAs**
  - Two round tables of discussion with Regional offices for establishment of a mechanism for expedited approval in countries and monitoring performance of vaccines deployed to countries August 2020.
  - Nominations of regulatory authorities received from several regions.
  - Official communication with regulatory authorities.
  - Briefing on WHO led mechanisms to regulatory authorities and networks planned.
- Continue support for planning of **post-marketing / safety monitoring** in countries
- Continue engagement & alignment with **regulatory bodies** (e.g. ICMRA, regional regulatory networks, Reference NRAs)

Submission requirements: Labelling, Barcoding, QR codes
Current working position

Labelling • Goes beyond regulatory processes; national exemptions from legal requirements will be needed	**Progress on regulatory agreement on single label (model)** –
Bar codes on **secondary packaging** (i.e. carton) to support traceability	**Preferred characteristic** by UNICEF[1]
Bar codes on **primary packaging** (i.e. vials) to support traceability and monitoring	**Optional** but not as a replacement for other printed label information
QR codes *in lieu* of statutory labelling information printed on the **vial and/or inserts**	**Not acceptable**
QR codes *in addition* to statutory labelling information printed on the **vial and/or inserts**	**Acceptable**
Translated inserts	**Expected**

1. UNICEF has not officially released their tender document, but it will be a "preferred product characteristic"

WHO working position on labelling and package inserts

- **Labelling models** being developed: generic vial label and carton label for all vaccine platforms & platform-specific package inserts
- **Single** language for vials & carton labels
- Exploring mechanisms (e.g. QR code) to allow **extension of expiry date** as more data becomes available (for shipment of initial batches)
- Exploring possibility for using **manufacturing date in lieu of expiry** (only for initial batches)
- Recommending possible **country actions** (e.g. take over printing of translated local language inserts)
- **Mechanisms to make insert information available** as early as possible to support development of training materials
- Country actions on **cold chain maintenance** when data available does not match any existing Vaccine Vial Monitor (VVM) category

Summary of WHO position

Including bar codes, QR codes on primary packaging has costs that may not bring sufficient benefit.

The different uses or environments of these technologies for current discussions are for traceability and for sharing information.

Many AMC countries do not have capacity to use traceability technology in their supply chains at present; however, some scale up efforts are underway.

Packaging level	Traceability	"eLeaflet" or information sharing
Primary packaging	Currently, benefits may not be sufficient to outweigh the costs, especially for AMC countries	
Secondary packaging	Standard for many markets	Limited use cases, but may be a short term solution for leaflet translations and expiration date updates.

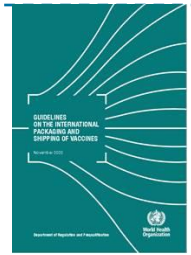
WHO considerations for evaluation of Covid 19 vaccines*.

Main outcome	Submission requirements	Assessment process	Programmatic suitability & post approval monitoring
Storage conditions and shelf-life, (in-use storage conditions and shelf-life).	**Stability data for the vaccine produced at the scale intended for distribution**	• **scientific risk-based approach** to determine the proposed vaccine shelf life in the absence of real time stability data on the commercial batches • **Consideration of** platform stability data, prior knowledge from early clinical batches or statistical modelling may also be applied to forecast expiry of product.	• **storage at less than -20°C:** • **if storage below +2°C, period, a minimum period of storage between +2°C and +8°C is required** **Assistance with regards to infrastructure for vaccine storage and distribution at required temperatures.**

- **The summary should include results, from forced degradation studies and stress conditions, as well as conclusions with respect to storage conditions and retest date or shelf-life, as appropriate.**
- **Information on the analytical procedures used to generate the data and validation of these procedures should be included**

* Evaluation criteria https://www.who.int/medicines/regulation/prequalification/prequal-vaccines/resources/1_EOI-Covid-19_Vaccines.pdf?ua=1

Path forward

Challenge	Requirements	Solution
International Transportation		• ultra-low shipment supplement to the WHO shipping guidelines will be developed published in Q1 2021) • Shipping validation to show evidence that the amount of dry ice used is able to maintain the temperature inside the shipping container at between - 80 degrees to – 60 degrees for 48 hrs.
Containers		• Passive Insulated polystyrene boxes can be used with dry ice as the coolant. • Dry ice sublimates at about 3-5 kg per 24 hrs. so the weight of dry ice needs to be factored-in • For a 48 hr. trip for example it would be safe to have about 6-10 kg of dry ice

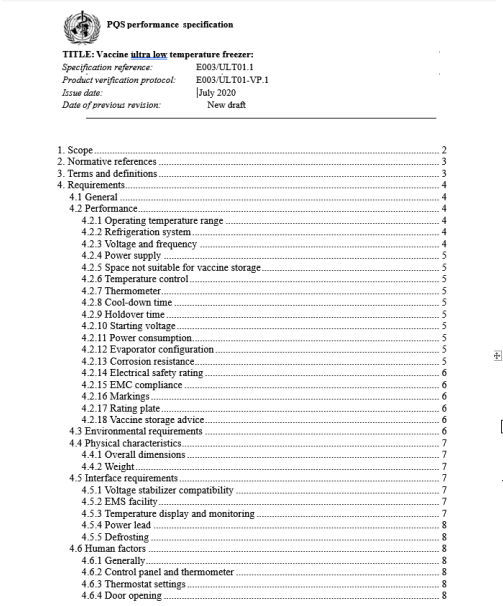
Path forward

Challenge	Requirements	Solution
Dataloggers		• Current WHO prequalified data loggers cannot perform at temperatures below -30 degrees. • WHO has been in touch with manufacturers of devices which can perform down to -80 degrees. • Specifications for ultralow data loggers available in Q1 2021
Vaccine vial monitor		• WHO has been in touch the VVM manufacturer and they are ready to develop VVMs of appropriate categories to suit the stability of ultralow temperature vaccines as needed • There are currently specifications for VVM1 and there is they have the capability to develop VVM0.5 and 0.25 as well

Path forward: Country preparedness

- **Ultra-low temperature freezers:**
- WHO specifications for ULT freezers and associated power requirements, and transport cold boxes will be published in December 2020

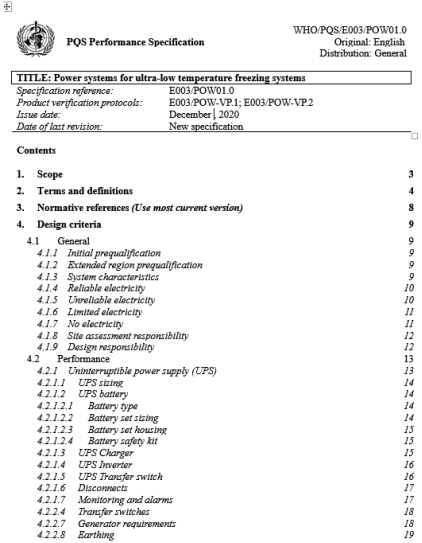
- **Training**
- Appropriate cold chain and vaccine management training package tailored to ultralow temperature vaccines for health workers will be needed, including training on safety and the provision of safety equipment such as gloves



PQS performance specification

TITLE: Vaccine ultra low temperature freezer:

Specification reference:	E003/ULT01.1
Product verification protocol:	E003/ULT01-VP.1
Issue date:	July 2020
Date of previous revision:	New draft



PQS Performance Specification

WHO/PQS/E003/POW01.0
Original: English
Distribution: General

TITLE: Power systems for ultra-low temperature freezing systems

Specification reference:	E003/POW01.0
Product verification protocols:	E003/POW-VP.1; E003/POW-VP.2
Issue date:	December 2020
Date of last revision:	New specification

Contents

Additional information EUL:

Procedure and Questions and Answers

https://www.who.int/medicines/regulation/prequalification/prequal-vaccines/EUL_PQ_Vaccines/en/

Target product profile

https://www.who.int/docs/default-source/blue-print/who-target-product-profiles-for-covid-19-vaccines.pdf?sfvrsn=1d5da7ca_5&download=true

Evaluation criteria and EOI. https://www.who.int/medicines/regulation/prequalification/prequal-vaccines/resources/1_EOI-Covid-19_Vaccines.pdf?ua=1

Roadmap https://www.who.int/publications/m/item/roadmap-for-evaluation-of-astrazeneca-azd1222-vaccine-against-covid-19

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WORKING TOGETHER

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