JOINT UNICEF – UNFPA – WHO meeting

PROGRAMMATIC SUITABILITY

Prequalification of Vaccines

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Programmatic Suitability for PQ (PSPQ)

Ensure that vaccines used in low- and middle-income countries can be used safely and effectively, given the constraints and conditions of their immunization systems

Nicaragua, rotavirus delivery, Photo: Gates Foundation

Mali, polio campaign, Photos: WHO/Olivier Ronveaux

PSPQ: https://apps.who.int/iris/bitstream/handle/10665/148168/WHO_IVB_14.10_eng.pdf

RATIONALE FOR ESTABLISHMENT OF PSPQ

- Vaccines produced in higher income countries made available to emerging countries

- Such vaccines show characteristics that while being acceptable for industrialized countries are not always suitable for emerging markets.

  Examples:

  - A pneumococcal vaccine filled in non-autodisable pre-filled syringes
  - A rotavirus vaccine with poor stability used in situations prone to cold chain break

Objective of PSPQ

- Judge the programmatic suitability against defined mandatory, critical and preferred characteristics

Benefits of PSPQ

- Give clear directions to vaccine industry before submission
- Reduce decision-making time

PROCESS OF REVIEWING THE CHARACTERISTICS OF CANDIDATE VACCINES

PQ dossiers are screened for:

- completeness and compliance with the required format and contents
- compliance with programmatic suitability criteria
  - Rejection of dossier if mandatory characteristics are not met
  - Identified deviation from the critical characteristics or a unique characteristic detected: the product will be referred to the PSPQ Standing Committee (PSPQ SC) for independent review

The PSPQ Standing Committee

- Is an independent advisory group to the WHO PQ - experts on immunization programmes, regulatory and policy experience.
- Aligned with Immunization Practices Advisory Committee (IPAC).
- Review, discussion and recommendation-making
- The maximum allowed time for review by the PSPQ Standing Committee is 90 days.

Types of vaccine characteristics

Mandatory	• Compliance is compulsory
Critical	• Compliance is compulsory • Deviations in vaccine characteristics will be reviewed by the PSPQ SC
Preferred	• Not compulsory • Reflect programmatic preferences
Unique & innovative	• There is no guidance document developed • Will be referred to the PSPQ SC

Mandatory characteristics

- **Anti-microbial preservative** required in ready to use vaccines containing more that two-doses
- **Thermo-stability.** The vaccine or any component presented for PQ should not required storage at less than -20°C
- **Dose volume** should not be more that 1 ml/per dose for children > 5 years.
- Vaccine presented should not require an intravenous **route of administration**

Critical characteristics (1)

- The vaccine should fit into currently commonly used schedules of **vaccination visits**.
- Oral vaccines should be ready to use
- **Thermo-stability/ storage**: Vaccines submitted for prequalification requiring storage below +2°C during its shelf-life period should have a minimum of storage above 2°C of 6 months
- **Vaccine Vial Monitor (VVM)**: vaccine submitted should present data confirming that it has a thermostability profile to apply VVM.

Critical characteristics (2)

- Packaging material that can be disposed of appropriately in the field using standard procedures
- Vaccines in pre-filled injection devices should have an auto-disable feature
- Vaccine dosed in standardized volumes (e.g. 1, 0.5, 0.25 ml)

Preferred characteristics

- Antigenic stability after reconstitution
- Small packed volume
- Small and standardized dose volumes for oral vaccines
- Minimize number of doses that cannot be reused in subsequent sessions once the container is open
- Doses per primary container:
  ≤10 doses per vial in routine setting
  ≥10 doses per vial in campaign setting

Unique or innovative characteristics

Examples:

- Nano-patches
- Nasal aerosols
- Micro-needle application

“Assessing the programmatic suitability of vaccine candidates for WHO prequalification”

https://www.who.int/publications/i/item/WHO-IVB-14.10

THANK YOU

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WHO PQ: Risk benefit assessment procedures

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Outline of presentation

- Goal and objectives
- WHO regulatory alignment roadmap
- Transition EUL to PQ

Goal and objectives

Goal

- to optimize access & availability to safe, efficacious, quality-assured COVID-19 products by further aligning regulatory processes

Objectives :

- Explain and update on **WHO's roadmap** for aligning regulatory processes impacting access to vaccines during public health emergencies (nOPV2, Covid-19, Mpox)

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

- Explain the activities of the evaluation of vaccines under the EUL

WHO PQ assessment

Prequalification (PQ) 1987	Emergency Use Listing (EUL) 2015
• Review of extensive quality, safety and efficacy and PSPQ for international supply	• **Risk benefit assessment of essential set of quality, safety and efficacy data for use during PHEs**
• Assessment performed by WHO independent experts	• **Rolling review of data**
• Reliance on WHO Listed Authority (WLA) - abbreviated process under oversight of mature regulators (evaluation and oversight of programmatic aspects by WHO)	• 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	• Pre-submission meetings
• Post-PQ monitoring	• **Post- deployment monitoring**
• Reassessment/requalification	• **Time limited recommendation**
	• **Development should continue for MA/PQ**

Risk benefit i.e Monkeypox → **Stockpiles** → **Risk benefit snake antivenoms**

WHO regulatory preparedness for COVID-19 vaccines

WHO released “Considerations for the assessment of COVID-19 vaccines” (2020, 2022)


World Health Organization

CONSIDERATIONS FOR EVALUATION OF COVID19 VACCINES

Points to consider for manufacturers of COVID19 vaccines

Version 24 September 2020

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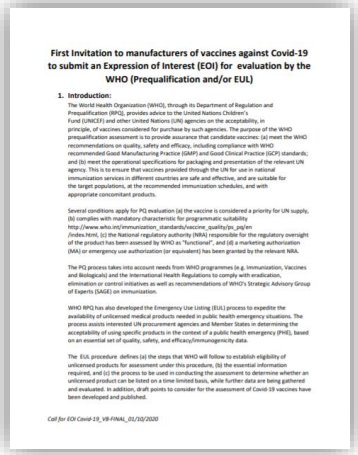
WHO issued a call for Expressions of Interest for Emergency Use Listing of COVID-19 Vaccines (2020)


First Invitation to manufacturers of vaccines against Covid-19 to submit an Expression of Interest (EOI) for evaluation by the WHO (Prequalification and/or EUL)

1. Introduction:

The World Health Organization (WHO), through its Department of Regulation and Prequalification (RPQ), provides advice to the United Nations Children's Fund (UNICEF) and other United Nations (UN) agencies on the acceptability, in principle, of vaccines considered for purchase by such agencies. The purpose of the WHO prequalification assessment is to provide assurance that candidate vaccines: (a) meet the WHO recommendations on quality, safety and efficacy, including compliance with WHO recommended Good Manufacturing Practice (GMP) and Good Clinical Practice (GCP) standards; and (b) meet the operational specifications for packaging and presentation of the relevant UN agency. This is to ensure that vaccines provided through the UN for use in national immunization services in different countries are safe and effective, and are suitable for the target populations, at the recommended immunization schedules, and with appropriate concomitant products.

Several conditions apply for PQ evaluation (a) the vaccine is considered a priority for UN supply, (b) complies with mandatory characteristic for programmatic suitability http://www.who.int/immunization_standards/vaccine_quality/pv_pq/en /index.html, (c) the National regulatory authority (NRA) responsible for the regulatory oversight of the product has been assessed by WHO as "functional", and (d) a marketing authorization (MA) or emergency use authorization (or equivalent) has been granted by the relevant NRA.

The PQ process takes into account needs from WHO programmes (e.g. Immunization, Vaccines and Biologicals) and the International Health Regulations to comply with eradication, elimination or control initiatives as well as recommendations of WHO's Strategic Advisory Group of Experts (SAGE) on immunization.

WHO RPQ has also developed the Emergency Use Listing (EUL) process to expedite the availability of unlicensed medical products needed in public health emergency situations. The process assists interested UN procurement agencies and Member States in determining the acceptability of using specific products in the context of a public health emergency (PHE), based on an essential set of quality, safety, and efficacy/immunogenicity data.

The EUL procedure defines (a) the steps that WHO will follow to establish eligibility of unlicensed products for assessment under this procedure, (b) the essential information required, and (c) the process to be used in conducting the assessment to determine whether an unlicensed product can be listed on a time limited basis, while further data are being gathered and evaluated. In addition, draft points to consider for the assessment of Covid-19 vaccines have been developed and published.

Call for EOI Covid-19_V8-FINAL_01/10/2020

... aiming for timely regulatory process while maintaining high evaluation stds for EUL/PQ

Source: https://www.who.int/medicines/regulation/prequalification/prequal-vaccines/WHO_Evaluation_Covid_Vaccine.pdf?ua=1

WHO alignment activities for COVID-19 vaccines

Development criteria

- ✓ **Target Product Profiles**
- ✓ **Expert Committee on Biological Standards** guidance
- ✓ **Regulatory guidelines**

Submission requirements

- ✓ **EUL and PQ guidance** and **Questions & Answers**
- ✓ **EUL/PQ Expressions of Interest** (conditions & evaluation criteria)
- **Labelling & packaging**

Assessment process

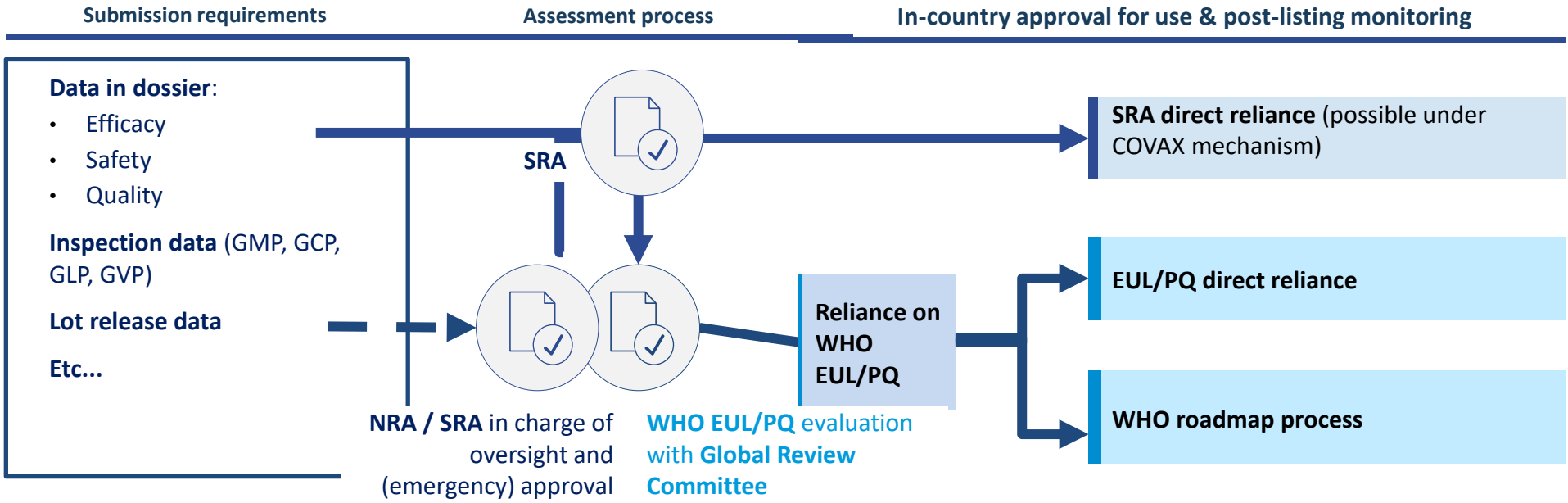
- **Evaluation of candidates** for EUL/PQ (incl. inspection, lot release process & post-listing commitment)
- **Interactions & agreements** with NRAs/SRAs*
- **Global assessment process*** with region-designated national authority reps

In-country approval for use & post approval monitoring

- **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"**

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



- **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)

Support to regions & countries

Designate lead NRAs in the region: WHO EUL assessment

Facilitation expedited national approval

Product Evaluation group PEG: Roster of experts, Regulatory experts all regions.

Technical Advisory group EUL (TAG-EUL): Risk benefit assessment

https://extranet.who.int/pqweb/vaccines/TAG-EUL

Collaboration agreement with NRAs of references and others on regulatory oversight

1. Sharing dossier and EUL reports with 105 countries
2. Discussion on outcome of review
3. Additional guidance for decision making on expedited authorization
   - One on one discussion with countries
   - Support to RO and agencies providing relevant docs
4. Post listing changes: Sharing assessment reports

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

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 Committee** (NRA/SRA in charge of oversight & regulators /reviewers from potential user participants)	• **Approval** granted by NRA/SRA in charge of oversight • **Advisory committee** 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**

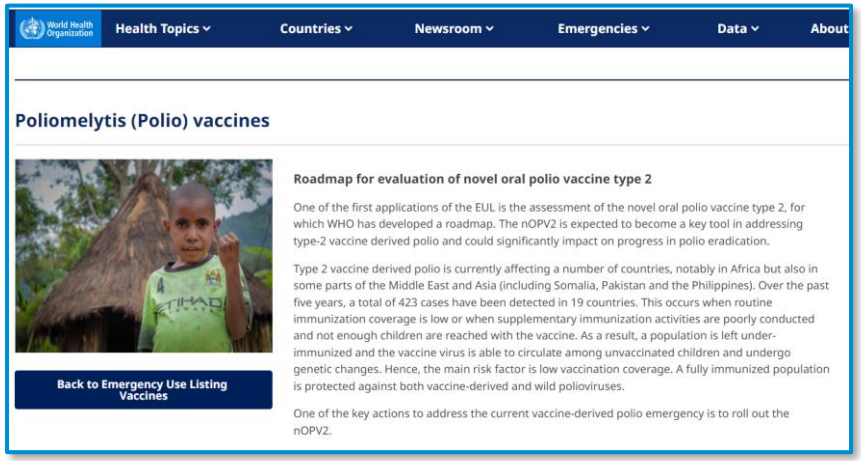
COVAX | EUL/PQ | NRA reliance on EUL/PQ

Facilitated access to countries

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




Novel oral polio vaccine type 2



Highlights of Covid 19 vaccines under EUL

Main features

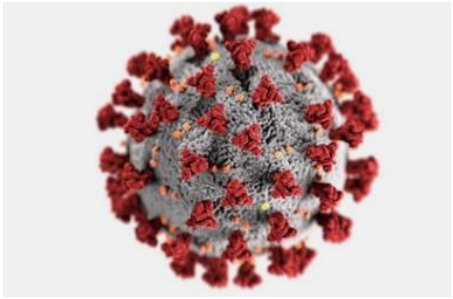
12 vaccines with different manufacturing platforms
- mRNA (2)
- Viral vector (4)
- Inactivated (3)
- Protein subunit (3)

- Expanding regulatory oversight and manufacturing sites
- 19 NRAs of reference (mainly EMA)
- over 70 manufacturing sites

A range of age indications, shelf life and storage conditions

Covid 19 adapted vaccines → Approval by authority of reference → WHO EUL recommendation



The WHO Director-General concurs with the advice offered by the Committee regarding the ongoing COVID-19 pandemic. He determines that COVID-19 is now an established and ongoing health issue which no longer constitutes a public health emergency of international concern (PHEIC).

Implications of the use of EUL/PQ if PHEIC is terminated

	Covid-19 vaccines	In vitro diagnostics	Medicines / Biologicals
EUL listed	EUL status is maintained for a limited period while the product transitions to PQ and if the product continues to be supplied to LMICs	EUL status and procurement eligibility will be maintained until a PQ decision is taken, provided that the product is submitted for PQ assessment*	• All Covid-19 treatments are assessed under PQ procedure • Based on clinical recommendation, PQed products will be maintained in the PQ list • PQ assessment will continue based on clinical recommendations, but with less priority than during the PHEIC
Under EUL assessment	EUL applications to be closed except for those close to EUL listing		
New	Submission and acceptance for PQ assessment is made on a case-by-case basis based on public health bel defined in collaboration with other WHO departments	PQ applications are accepted if products are within PQ eligibility (defined in collaboration with WHE)	

* Ag RDTs and NAT assays to be transitioned into PQ with a 6-month transition period for submission

Implications to regulators in LMICs and procurement agencies

	Covid-19 vaccines	In vitro diagnostics	Medicines / Biologicals
NRAs* in LMICs	• Each NRA in LMICs may decide to switch from emergency authorization to standard market authorization, provided that the NRA receives an application Note: As of 31 Dec 2022, NRAs in >110 countries have issued 5'436 regulatory clearances for 7 EULed vaccines	• Procurement decisions taken by each country and procurement agencies • If a product is maintained in the PQ list, WHO PQ teams assist NRAs' decision making by sharing assessment reports (including variation reports) via Collaborative Registration Procedures	

* NRAs: National Regulatory Authorities

Transition EUL to PQ

Steps for transition Covid-19 vaccines from EUL to PQ

Available data	• Availability of data to fulfill EUL listing commitments and PQ requirements
NRA of Record	• Full authorization by the NRA of reference
Submission to PQ	• Submission to WHO for PQ – consolidated updated dossier
PQ review	• Programmatic suitability • Additional data
PQ listing	• PQ listing
National Authorization	• Facilitation of national authorization.

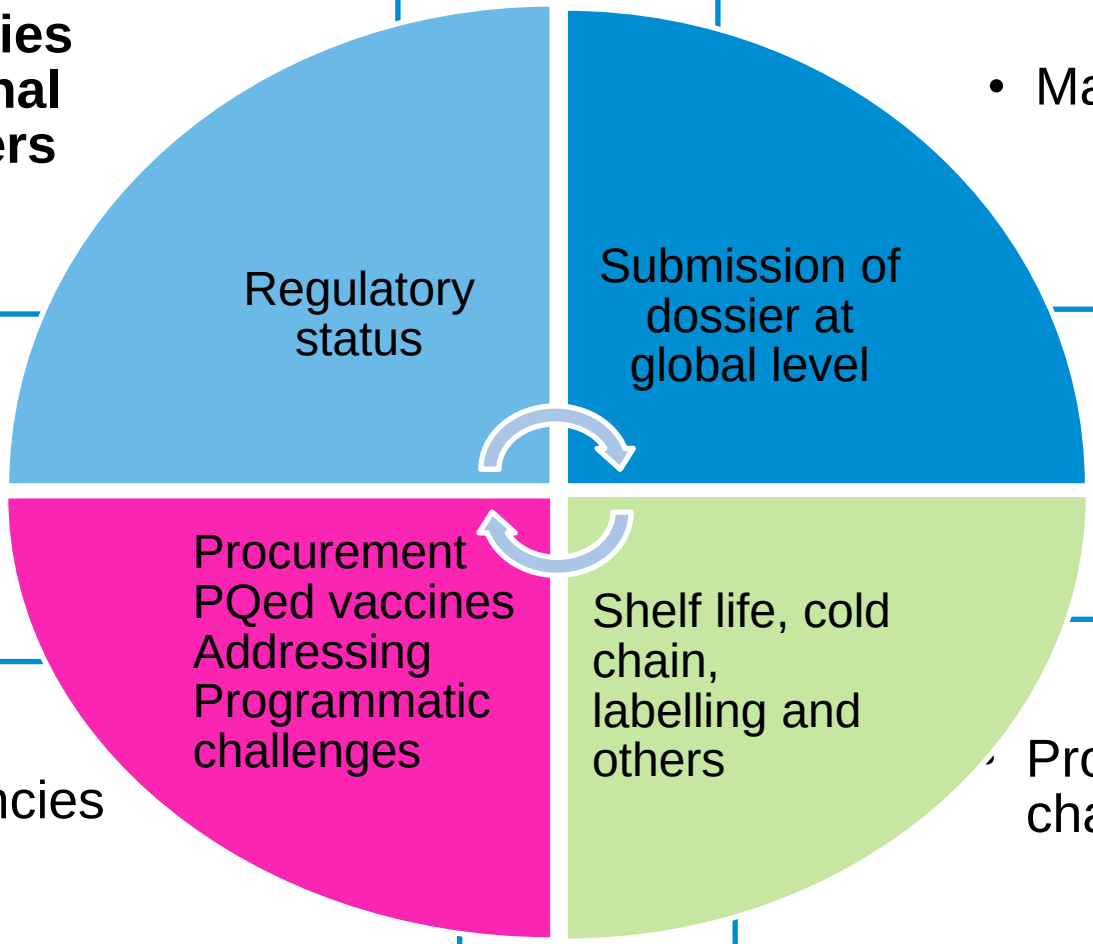
Covid 19 vaccines recommended under EUL
Deviation Programmatic suitability criteria for PQ

Criteria	Applicable to	Solutions & implications
Mandatory: Storage conditions less than – 20 C	mRNA Pfizer vaccine	Ultra Cold chain equipment at central level Training Health care workers **Implications:** Wastages
Mandatory: Antimicrobial preservative more than 2 doses	All Covid 19 vaccines	Training HCW to discard vaccines at the end of the session once vial is opened **Implication:** Wastages
Critical: Storage at 2-8 for more than 6 months	mRNA Moderna	Training HCW **Implication:** Wastages
Critical VVM	All Covid 19 vaccines	Maintenance cold chain **Implication:** Wastages

Support to member states

- **Countries**
- **Regional advisers**

- Manufacturers



- UN agencies COVAX

- Programmatic challenges

WHO COVID-19 advisory groups develop recommendations on boosters, variants and variant vaccines along a comprehensive pathway

Aim: Monitor & assess SARS-CoV-2 variants and evaluate their impact on countermeasures, including vaccines, therapeutics, diagnostics or effectiveness of public health and social measures.

Virus

Monitoring & surveillance

TAG-Virus Evolution (VE)

- determines where variants are circulating
- advises on VOI or VOC determination based on alteration in:
  - transmission or disease characteristics or
  - impact vaccines, therapeutics, diagnostics or
  - effectiveness of public health and social measures

Vaccine

Research, evidence & assessment

TAG-CO-VAC

determines if changes to vaccine composition needed through evidence-based assessment

Vax Research Expert Group

methods for vaccine development & assessment

Vax Effectiveness WG

assesses & supports VE and impact studies

Regulatory TAG

advises on EUL of vaccines through evidence-based assessment

Vaccine impact

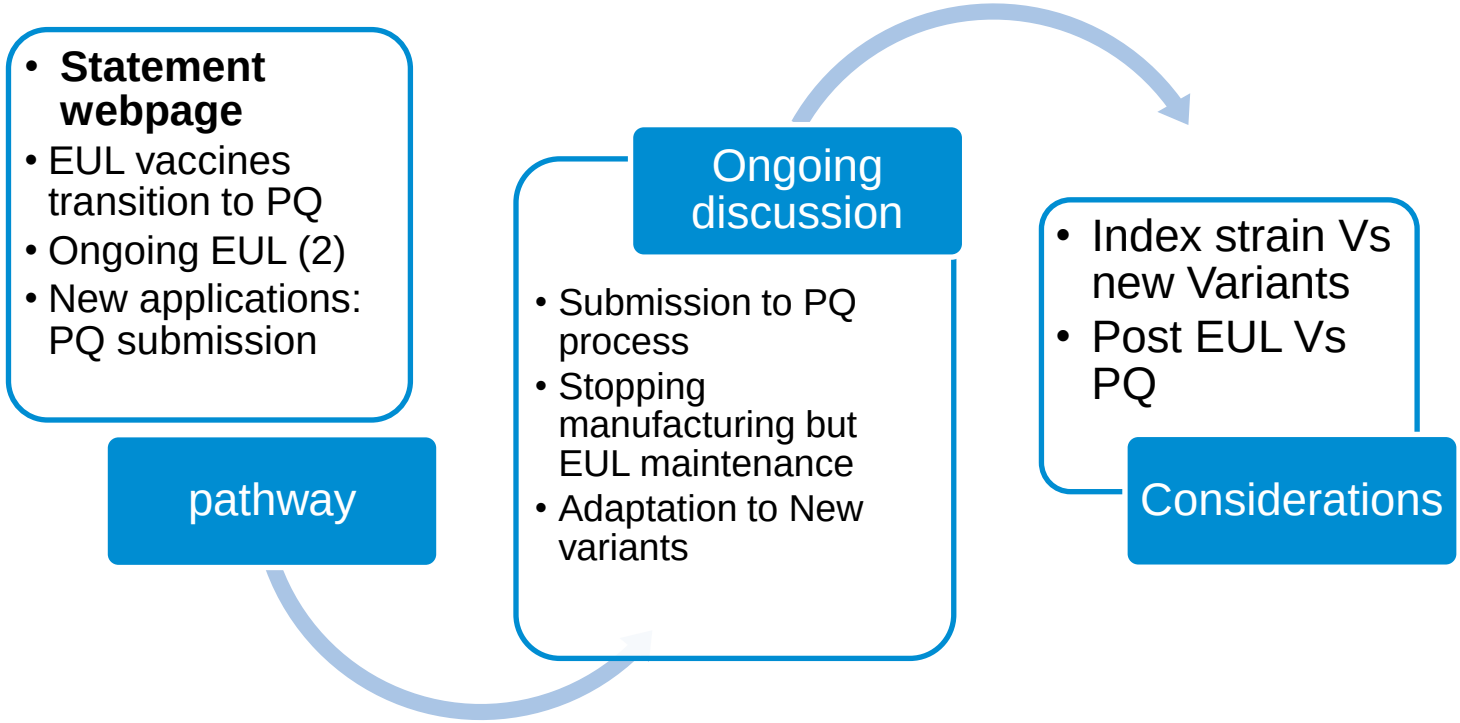
Policy

SAGE

- recommends policies & strategies on vaccine use and immunization programmes through evidence-based assessment




Path forward



PHEIC_web_31May2023.pdf (who.int)

Considerations

PQ related

- Fees
- Dossier submission
- PSPQ

Critical key changes

- Complexities of key changes introduced as post EUL and impact on timelines for transition to EUL
- Clear timelines to be set on potential critical changes that may be submitted post EUL (ie VOC), during the PQ assessment and Post PQ.

SAGE policy recommendations

TAG COVAC

Staff Resources

Additional information PQ&EUL:

PQT/VXA procedure [TRS 978, Annex 6 (2013]
http://www.who.int/entity/immunization_standards/vaccine_quality/TRS_978_61st_report_Annex_6_PQ_vaccine_procedure.pdf

Programmatic Suitability for Prequalification
http://www.who.int/immunization_standards/vaccine_quality/pspq2_v140512.pdf

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

Additional information PQ&EUL:

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

Contact: EUL@who.int

World Health Organization

WORKING TOGETHER

Department of Regulation and Prequalification, WHO