JOINT UNICEF – UNFPA – WHO PREQUALIFICATION UPDATES

Prequalification of Vaccines

Rolando Dominguez

Vaccine Prequalification (PQ VAX)
Prequalification Team (PQT)
Regulation & Prequalification Dept. (RPQ)
Medicines and other Health Technologies (MHP)
World Health Organization
Geneva, Switzerland
E-mail: vaccprequalification@who.int

OUTLINE 1

- ✓ **General on the format and content of a VPQD**
- ✓ **PQ Procedure**
- ✓ **Performance**
- ✓ **Future**

OUTLINE 2

- ✓ **Post PQ Activities**

Quality requirements for prequalification (CMC)

- General understanding of production process and quality control methods
- Production consistency at commercial scale
- Compliance with GMP
- Programmatically suitable
- Cold chain, VVM
- Compliance with WHO recommendations and UN tender specifications including labels, package inserts, shipping

Specifics

Quality requirements for prequalification (CMC)

Vaccine-specific standardization (e.g., WHO TRSs)

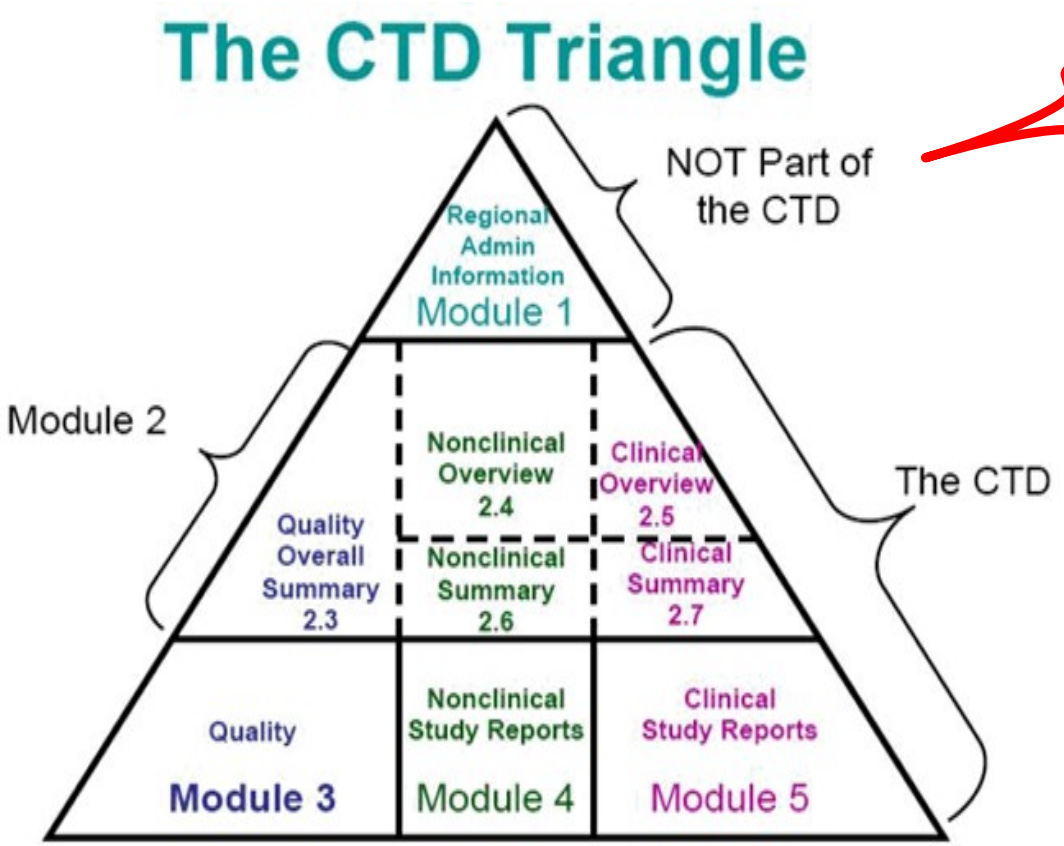
General topics and regulatory guidance (e.g., GMPs; stability; clinical)

Related links (e.g., WHO Vaccine Position Papers)

Procedure for assessing the acceptability in principle, of vaccines for purchase by UN agencies Annex 6 TRS 978 (2013).

Health products policy and standards (who.int)

Quality requirements for prequalification (CMC)



WHO M1

S.1	P.1
S.2	P.2
S.3	P.3
S.4	P.4
S.5	P.5
S.6	P.6
S.7	P.7
	P.8

Quality requirements for prequalification (CMC)

WHO Module 1:

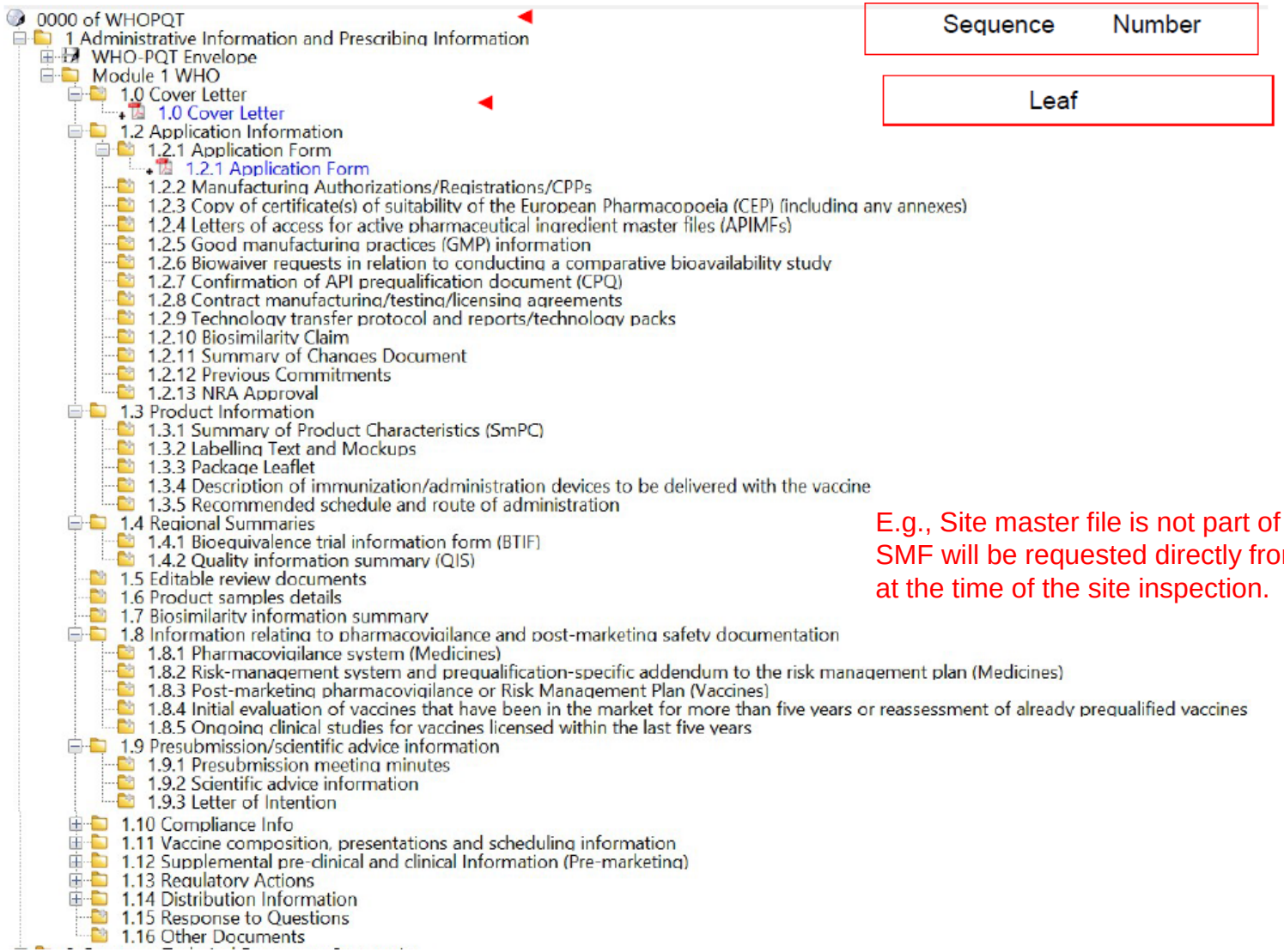
The Module 1 of the VPQD is very specific:

- ***It contains information not included in other modules but required to assess the product for prequalification purposes.***

Quality requirements for prequalification (CMC)

Module 1 Format & Content

1.1 TABLE OF CONTENTS
1.2 CORRESPONDENCE
1.3 SITE MASTER FILE (SMF)
1.4 COMPLIANCE INFORMATION
1.5 VACCINE COMPOSITION, PRESENTATIONS AND SCHEDULING INFORMATION
1.6 SUPPLEMENTAL PRE-CLINICAL & CLINICAL INFORMATION (PRE AND POST MA)
1.7 REGULATORY ACTIONS
1.8 DISTRIBUTION INFORMATION
WHO Guidelines on the international packaging and shipping of vaccines should be followed (6 ed. 2020).



E.g., Site master file is not part of the eCTD.
SMF will be requested directly from the WHO-PQT INS at the time of the site inspection.

Quality requirements for prequalification (CMC)

Module 2 Format & Content

As per ICH guidelines:

2.1 Table of Contents (Modules 2-5)
2.2 VPQD Introduction
2.3 Quality Overall Summary
2.4 Nonclinical Overview
2.5 Clinical Overview
2.6 Nonclinical Written and Tabulated Summaries
2.7 Clinical Summary. Studies Clinical Efficacy, Clinical Safety, Literature References. Synopses of Individual Studies.

Quality requirements for prequalification (CMC)

DRUG SUBSTANCE (DS)

- The DS is the unformulated active (immunogenic) substance which in purified bulk form, that may be subsequently formulated with excipients to become the drug product (DP).

E.g., whole bacterial cells, viruses, purified antigens isolated from killed or living cells; recombinant or synthetic carbohydrate, protein or peptide antigens; polynucleotides (as in plasmid DNA and mRNA vaccines); conjugates; viral vectors.

Quality requirements for prequalification (CMC)

Module 3 Format & Content

3.2.S DRUG SUBSTANCE (NAME, MANUFACTURER)

3.2.S.1 General Information (name, manufacturer)

3.2.S.2 Manufacture (name, manufacturer)

3.2.S.3 Characterization

3.2.S.4 Control of Drug Substance

3.2.S.5 Reference Standards or Materials

3.2.S.6 Container Closure System

3.2.S.7 Stability

Quality requirements for prequalification (CMC)

3.2.P DRUG PRODUCT (NAME, DOSAGE FORM)

3.2.P.1 Description and Composition of the Drug Product (name, dosage form)
3.2.P.2 Pharmaceutical Development
3.2.P.3 Manufacture
3.2.P.4 Control of Excipients
3.2.P.5 Control of Drug Product
3.2.P.6 Reference Standards or Materials
3.2.P.7 Container Closure System
3.2.P.8 Stability

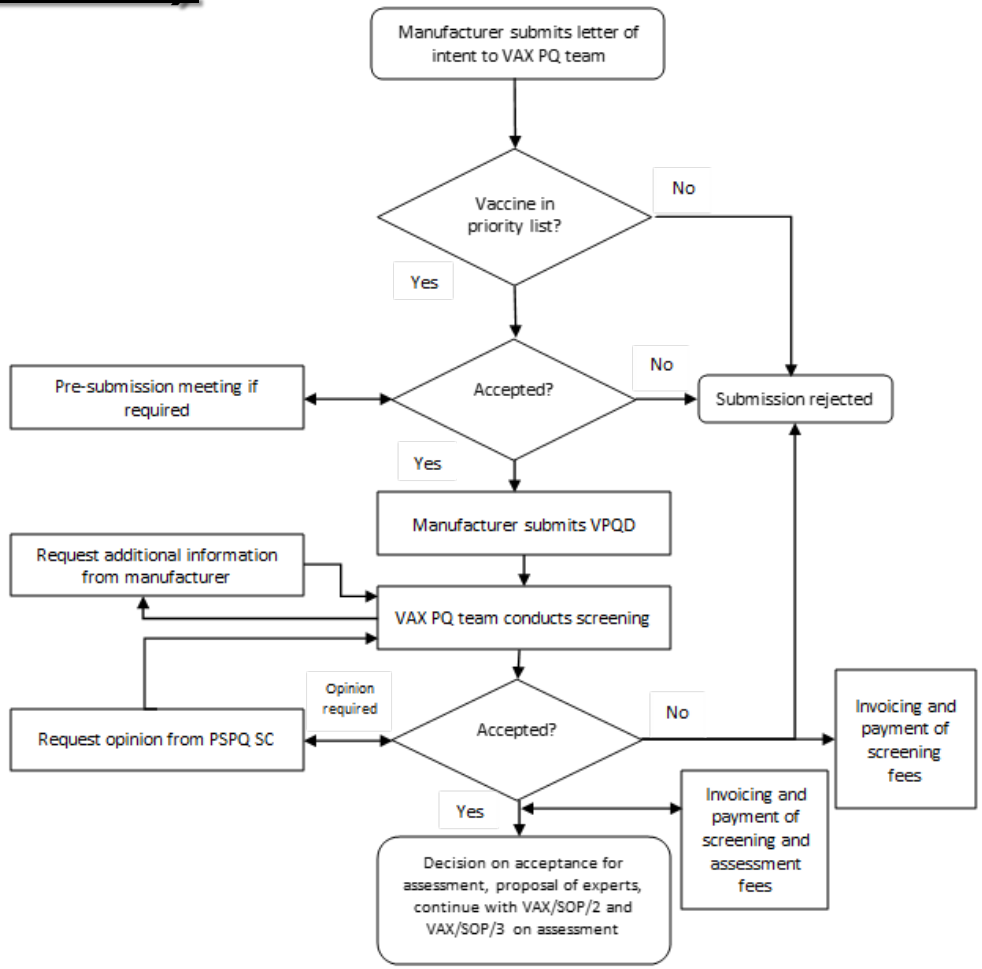
3.2.A APPENDICES: Facilities, equipment; adventitious agents safety evaluation; novel excipients; literature.

Quality requirements for prequalification (CMC)

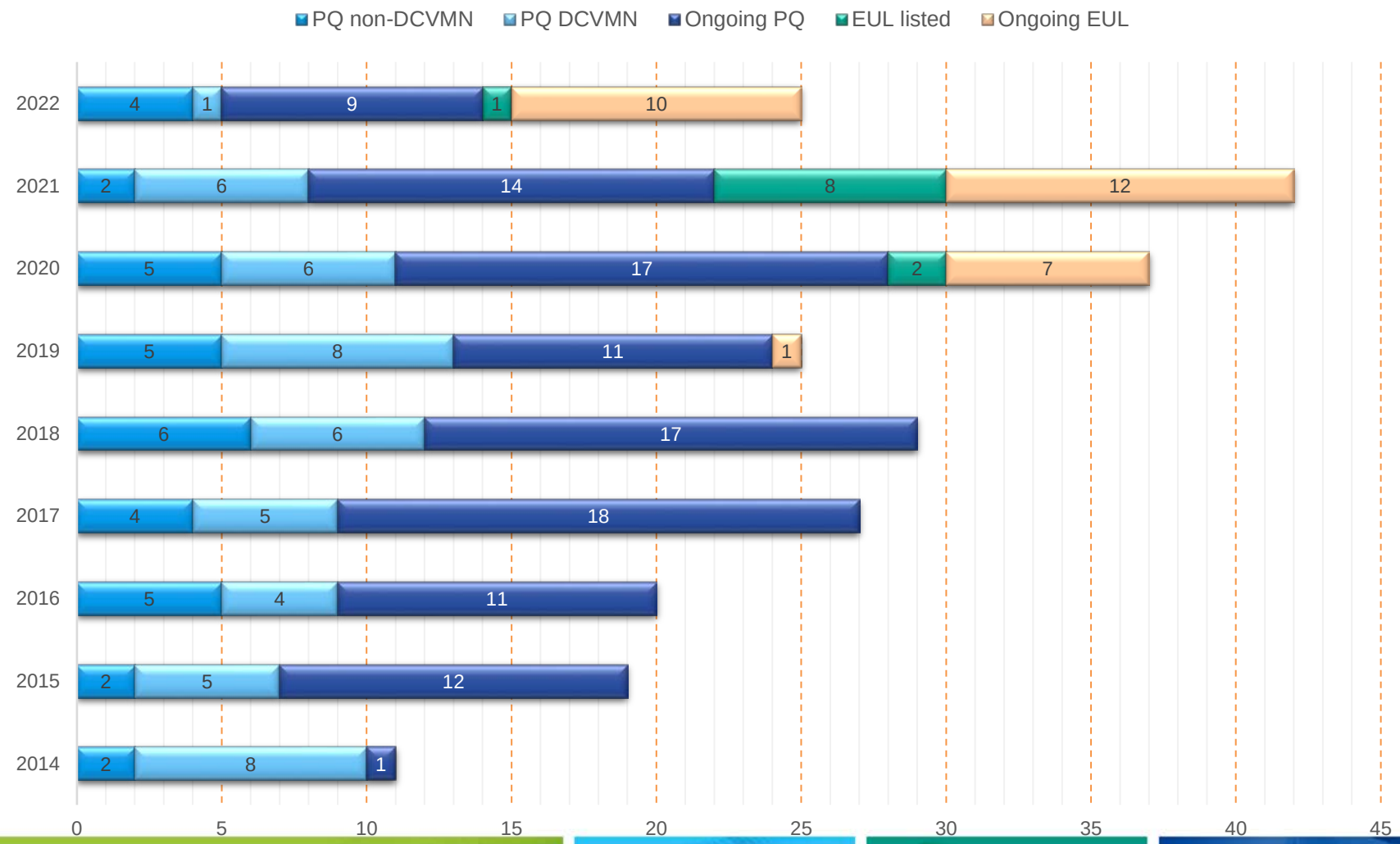
PQ Acceptance Process

Dates: 31 JAN, 31 MAY, 30 SEPT

- VPQD is screened in 30 days
- If PQ application rejected it is communicated within 15 days
- 90 days for VPQD Review
- PQ Applicant 90 days to answer to PQ.
- No answer = PQ process terminated
- PQ 90 days to review complementary information



Number of vaccines PQed and EUL from 2014 to 2022

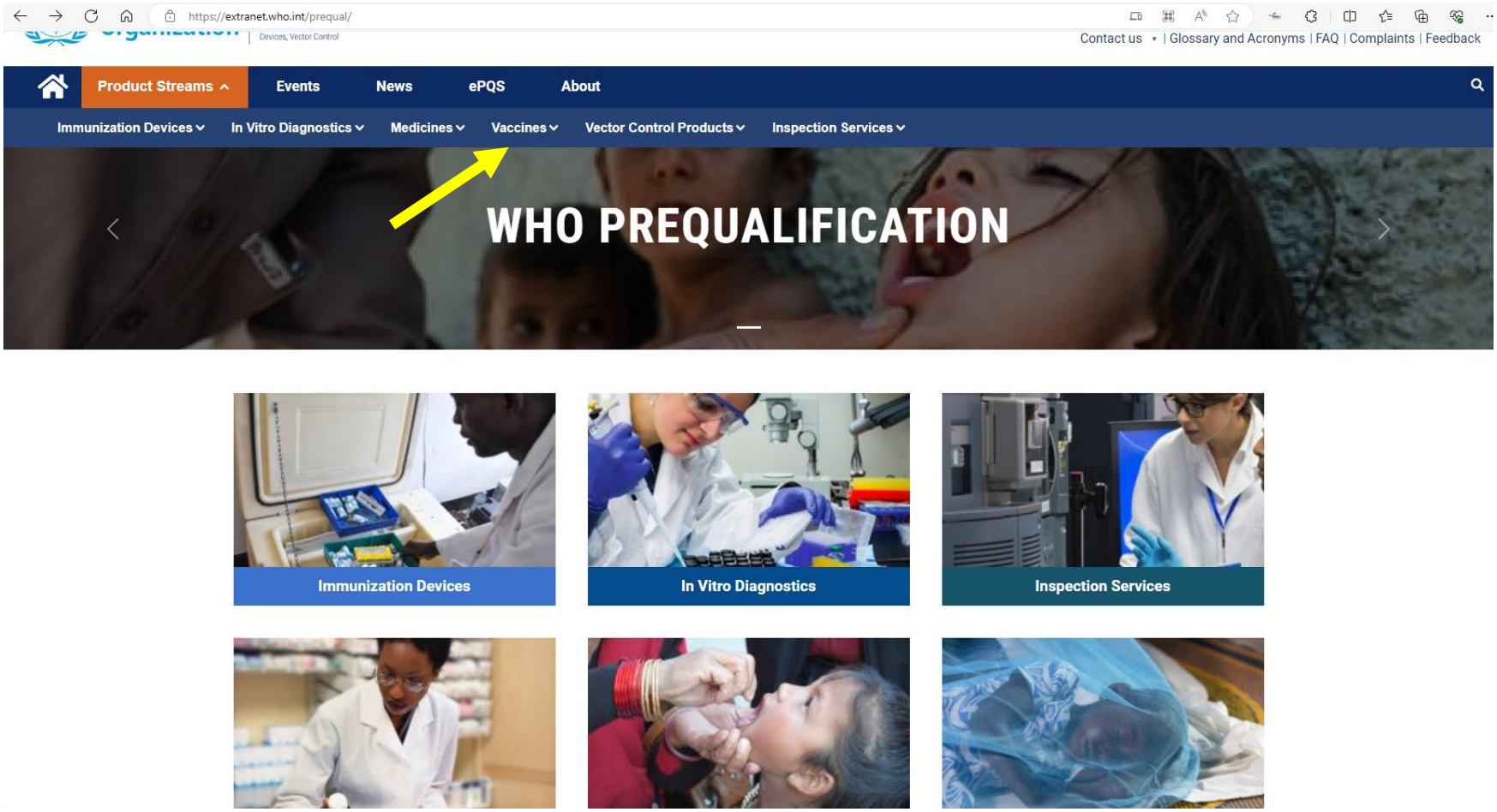


Quality requirements for prequalification (CMC)

Messages to take with you:

- Follow recent guidelines rigorously (e.g., WHO TRSs) or justify.
- Ask questions if anything is not clear to you (e.g., pre sub meetings)
- We are collaborators

WHO PQT Web site (VAX)



Messages to take with you:

Home | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)

List of Prequalified Vaccines | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)

Health products policy and standards (who.int)

eCTD Portal | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)

Module 1 eCTD specification

Interlude

Prequalification of Vaccines Post-PQ Activities

- PQed Vaccine Life Cycle
  - Obligations Post-PQ evaluation
    - Reporting
    - Level of reporting depends on the information that relates directly to the dossier content (e.g., changes, additional information
    - Maintaining a life cycle offers several benefits such as traceability and transparency
    - Continued interaction & collaboration: WHO VXA PQ & MFG & ROs & NRAs

Prequalification of Vaccines
Post-PQ Activities

Obligations after PQ is granted

- ✓ **Reporting variations**
- ✓ **Submitting Prequalified Vaccines Annual Report (PQVARs)**
- ✓ **Report of complaints**

Prequalification of Vaccines
Post-PQ Activities

Obligations after PQ is granted
VARIATIONS

The PQ holder **must** report to PQ VAX of changes/variations regarding the formulation, presentation, methods of manufacture or quality control, specifications, facilities, or any other aspects that might:

(a) result in a change of safety and/or efficacy of the vaccine; or
(b) change the basis of the regulatory approval of the NRA or WHO PQ VAX.

Prequalification of Vaccines
Post-PQ Activities

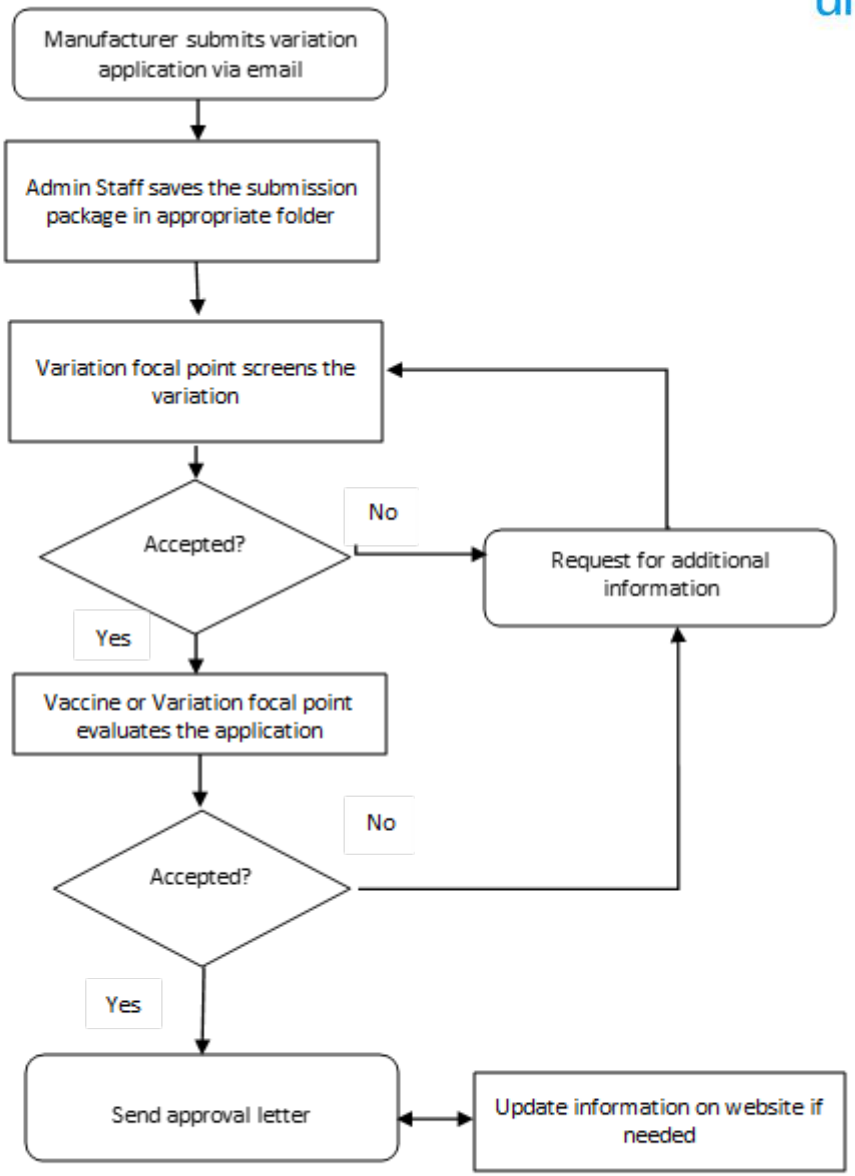
VARIATIONS

To be in compliance with WHO VXA July 2015 Guidance on Variations to a PQed Vaccine, a submission of a type A variation must include:

- A cover letter (see Appendix 4)
- A variation application form (see Appendix 5)
- Documentary evidence, as per
  - ✓ Appendix 2 for manufacturing changes
  - ✓ Appendix 3 for efficacy and safety related changes

VXA ALWAYS RELY ON THE NRA of RECORD!!!!!

VARIATIONS



WHO PQ VXA	
Type	**Time Frame**
N	30 days
A	90 days
PQVAR	120 days

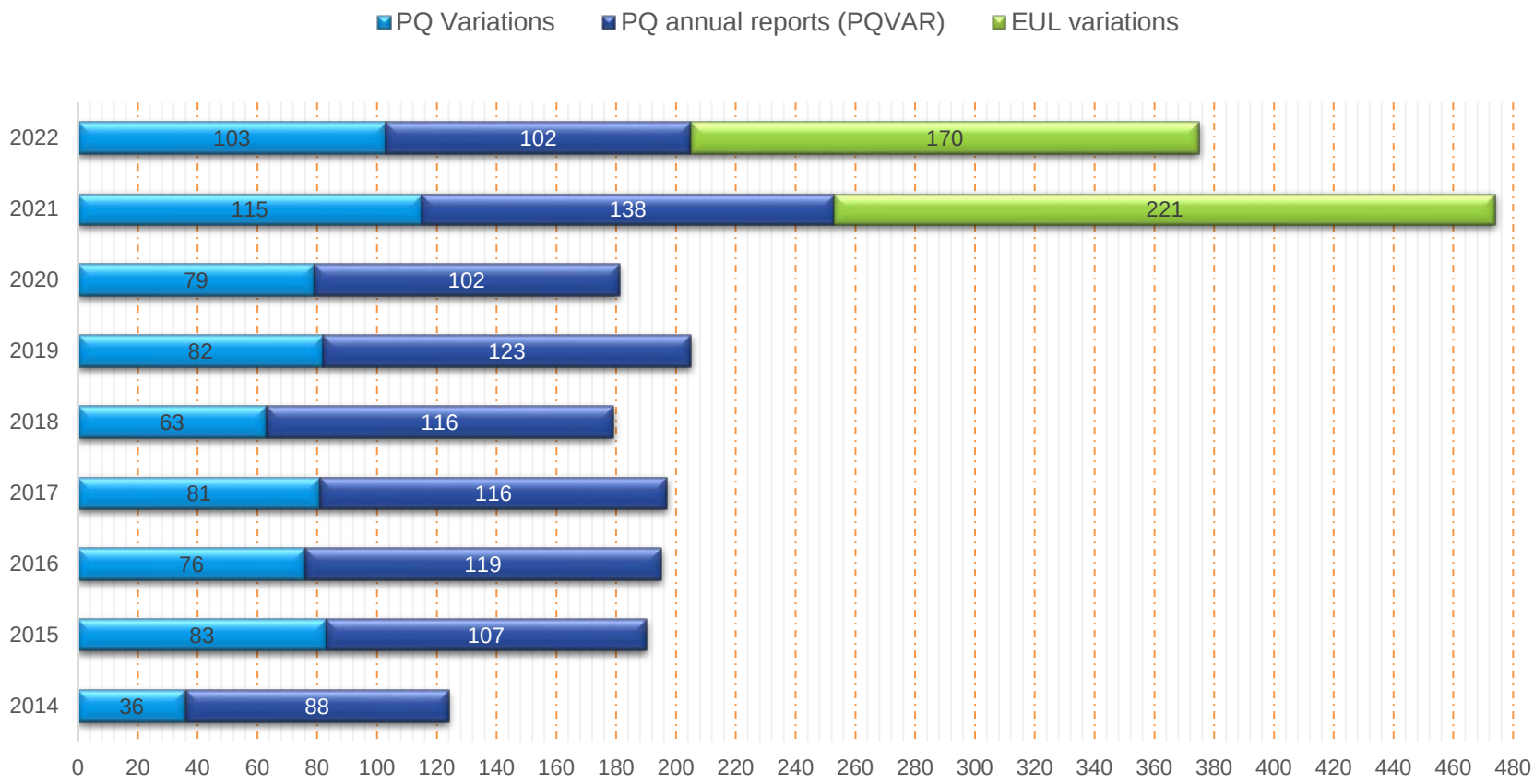
Prequalification of Vaccines
Post-PQ Activities

Obligations after PQ is granted
PQVARs

PQVARs is a comprehensive and summarized information on:

- **Summary on annual changes**
- **Stability results from ongoing stability study as per the stability protocol**
- **Production and Distribution Data**
- **GMP information**
- **PSUR**
- **Post-PQ commitments**

Prequalification of Vaccines
Post-PQ Activities



Prequalification of Vaccines

Complaints

- Vaccine quality (e.g. OOS)
- Vaccine safety (e.g. AEFIs)
- Cold chain complaints (e.g. excursions)

Investigation: MFG + NRA

Complainant is requested to provide critical information depending on the nature of the complaint:

Associated to a vaccine: complaint, when and where; vaccine; batch, expiry date; presentation; manufacturer; distribution data; testing outcome and trend; inspection……

Cold chain issues: VVM; recording monitoring device; setting of the alarms; shipping route; calibration of the fridge; power backup;……..

AEFIs: VXA liaises with WHO Safety & Vigilance Team (SAV).

Prequalification of Vaccines
Post-PQ Activities

Other activities:

- Technical Review of tenders for UNICEF
- Technical support to member states (e.g., workshops)
- Supports Member States in their authorization of high priority vaccines (e.g., pandemic vaccines)

Prequalification of Vaccines
Post-PQ Activities

Thank you

STAY WELL
BE SAFE
PROTECT YOURSELF & THE OTHERS