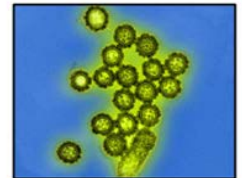


JOINT UNICEF – UNFPA – WHO PREQUALIFICATION UPDATES

Prequalification of Vaccines

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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)

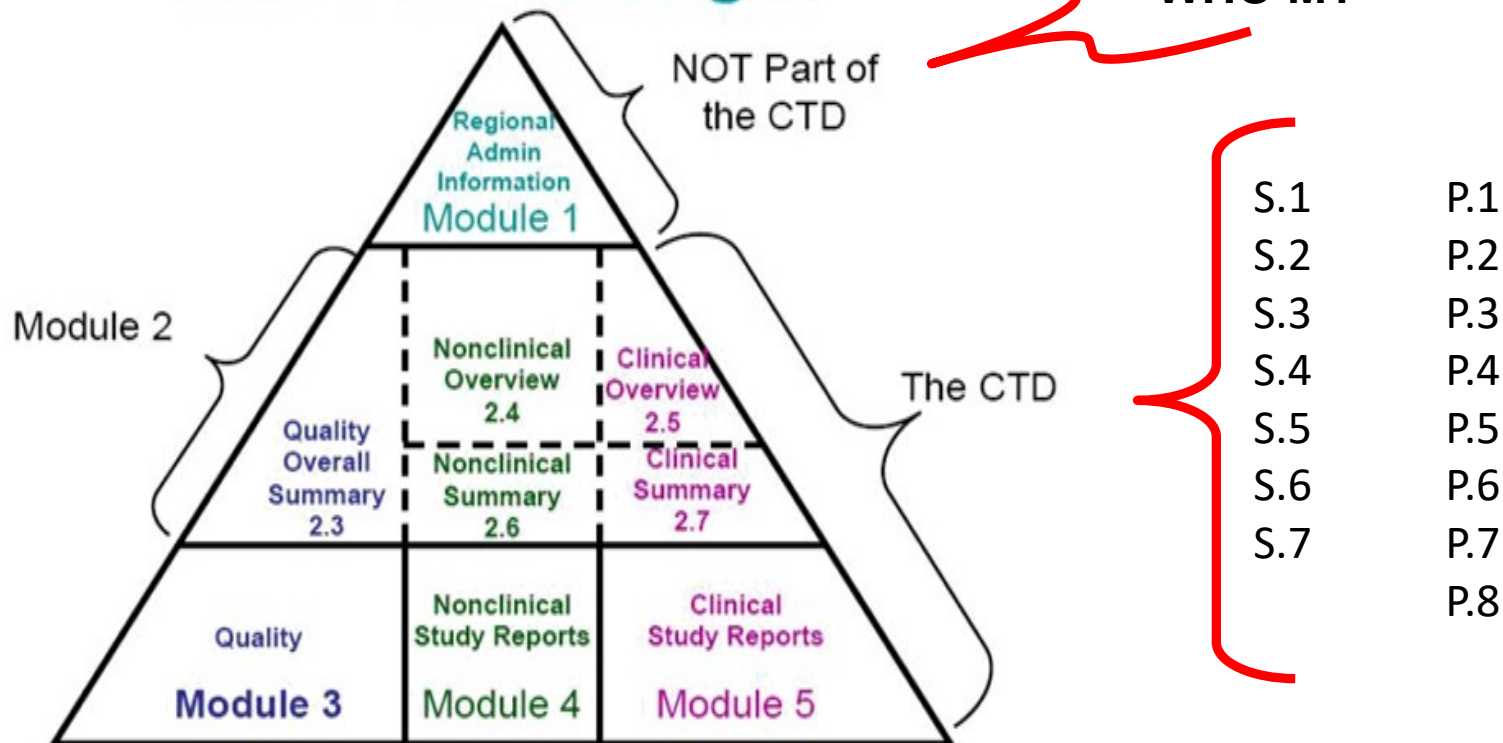
Related links (e.g., WHO Vaccine Position Papers)

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

[Health products policy and standards \(who.int\)](https://www.who.int/po-communication/health-products-policy-and-standards)

Quality requirements for prequalification (CMC)

The CTD Triangle



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
<i>WHO Guidelines on the international packaging and shipping of vaccines should be followed (6 ed. 2020).</i>

0000 of WHOPQT

- 1 Administrative Information and Prescribing Information
 - WHO-PQT Envelope
 - Module 1 WHO
 - 1.0 Cover Letter
 - 1.0 Cover Letter
 - 1.2 Application Information
 - 1.2.1 Application Form
 - 1.2.1 Application Form
 - 1.2.2 Manufacturing Authorizations/Registrations/CPPs
 - 1.2.3 Copy of certificate(s) of suitability of the European Pharmacopoeia (CEP) (including any annexes)
 - 1.2.4 Letters of access for active pharmaceutical ingredient master files (APIMFs)
 - 1.2.5 Good manufacturing practices (GMP) information
 - 1.2.6 Biowaiver requests in relation to conducting a comparative bioavailability study
 - 1.2.7 Confirmation of API prequalification document (CPQ)
 - 1.2.8 Contract manufacturing/testing/licensing agreements
 - 1.2.9 Technology transfer protocol and reports/technology packs
 - 1.2.10 Biosimilarity Claim
 - 1.2.11 Summary of Changes Document
 - 1.2.12 Previous Commitments
 - 1.2.13 NRA Approval
 - 1.3 Product Information
 - 1.3.1 Summary of Product Characteristics (SmPC)
 - 1.3.2 Labelling Text and Mockups
 - 1.3.3 Package Leaflet
 - 1.3.4 Description of immunization/administration devices to be delivered with the vaccine
 - 1.3.5 Recommended schedule and route of administration
 - 1.4 Regional Summaries
 - 1.4.1 Bioequivalence trial information form (BTIF)
 - 1.4.2 Quality information summary (QIS)
 - 1.5 Editable review documents
 - 1.6 Product samples details
 - 1.7 Biosimilarity information summary
 - 1.8 Information relating to pharmacovigilance and post-marketing safety documentation
 - 1.8.1 Pharmacovigilance system (Medicines)
 - 1.8.2 Risk-management system and prequalification-specific addendum to the risk management plan (Medicines)
 - 1.8.3 Post-marketing pharmacovigilance or Risk Management Plan (Vaccines)
 - 1.8.4 Initial evaluation of vaccines that have been in the market for more than five years or reassessment of already prequalified vaccines
 - 1.8.5 Ongoing clinical studies for vaccines licensed within the last five years
 - 1.9 Presubmission/scientific advice information
 - 1.9.1 Presubmission meeting minutes
 - 1.9.2 Scientific advice information
 - 1.9.3 Letter of Intention
 - 1.10 Compliance Info
 - 1.11 Vaccine composition, presentations and scheduling information
 - 1.12 Supplemental pre-clinical and clinical Information (Pre-marketing)
 - 1.13 Regulatory Actions
 - 1.14 Distribution Information
 - 1.15 Response to Questions
 - 1.16 Other Documents

Sequence Number

Leaf

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.
Synopsis 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

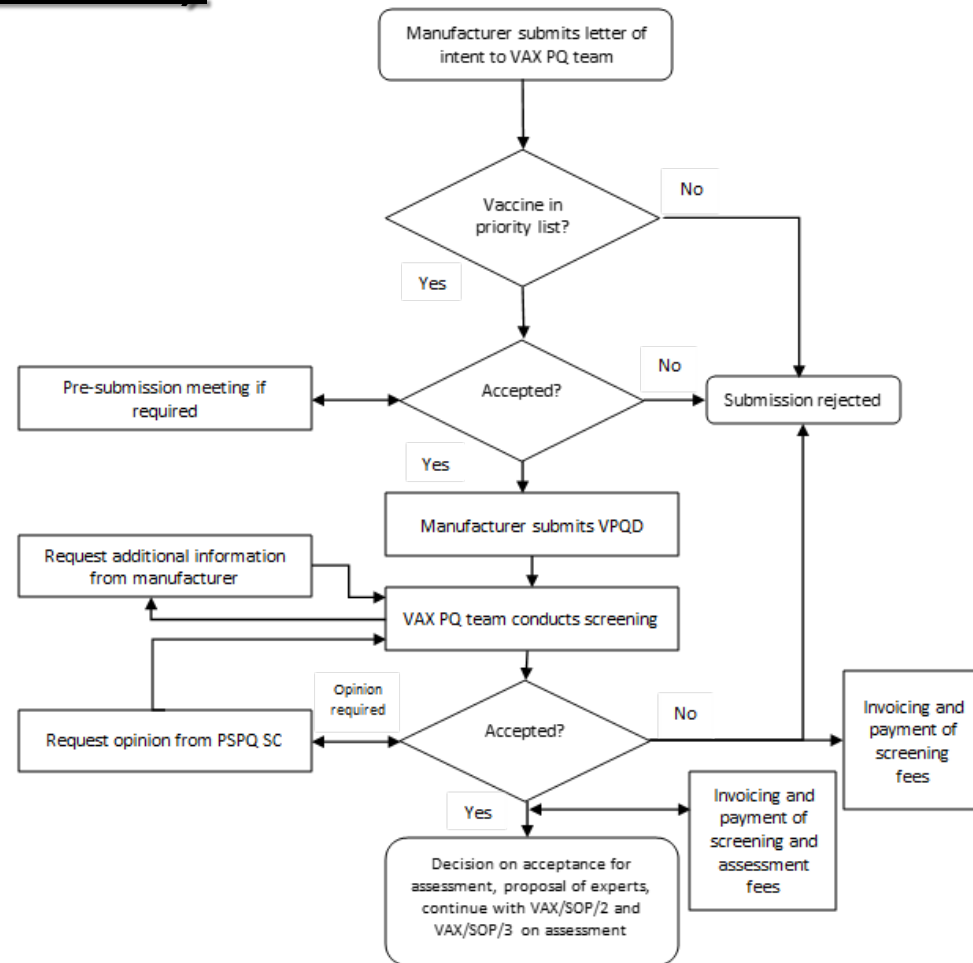
3.2.A APPENDICES: Facilities, equipment; adventitious agents safety evaluation; novel excipients; literature.

Quality requirements for prequalification (CMC)

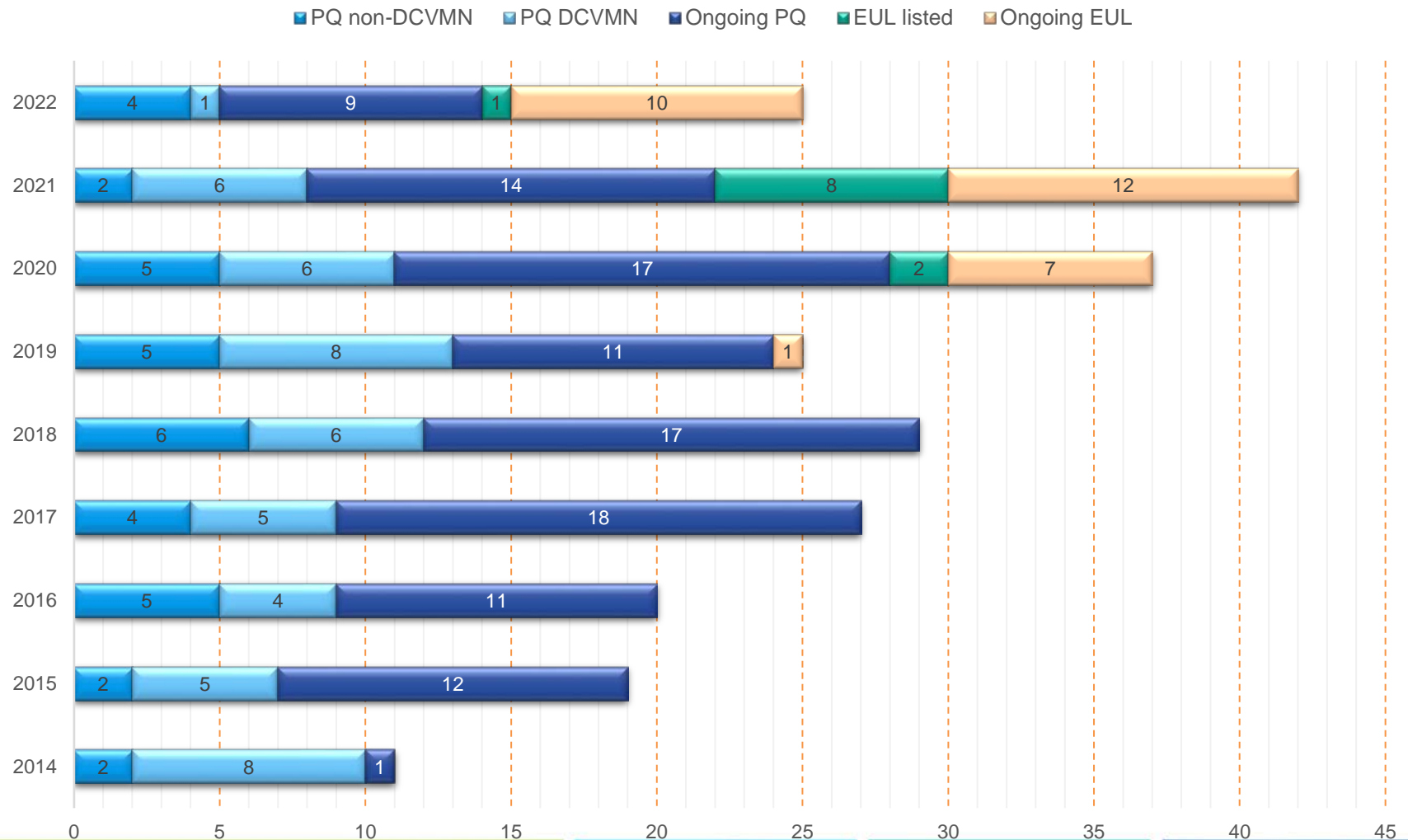
PQ Acceptance Process

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

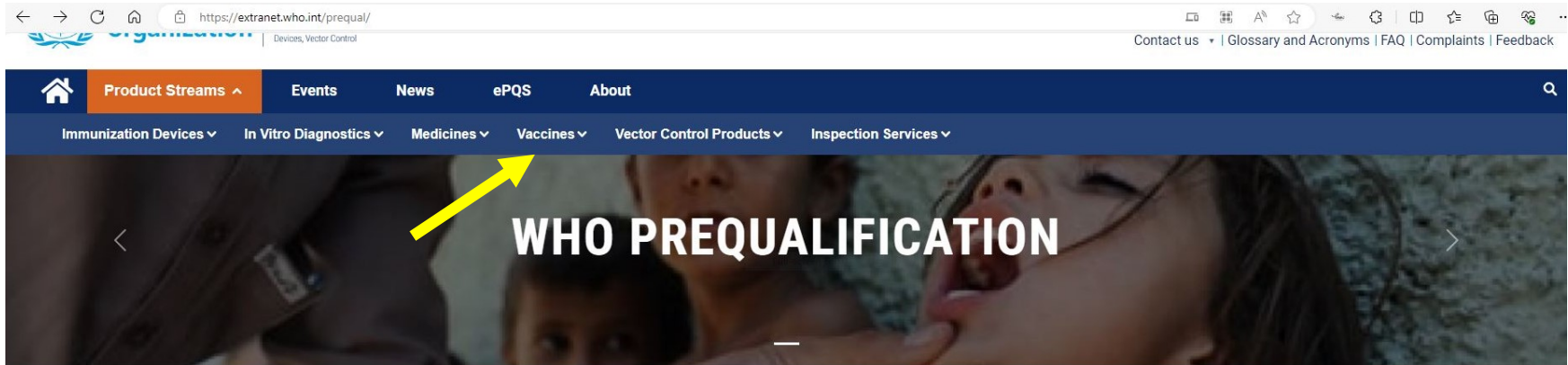


Quality requirements for prequalification (CMC)

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

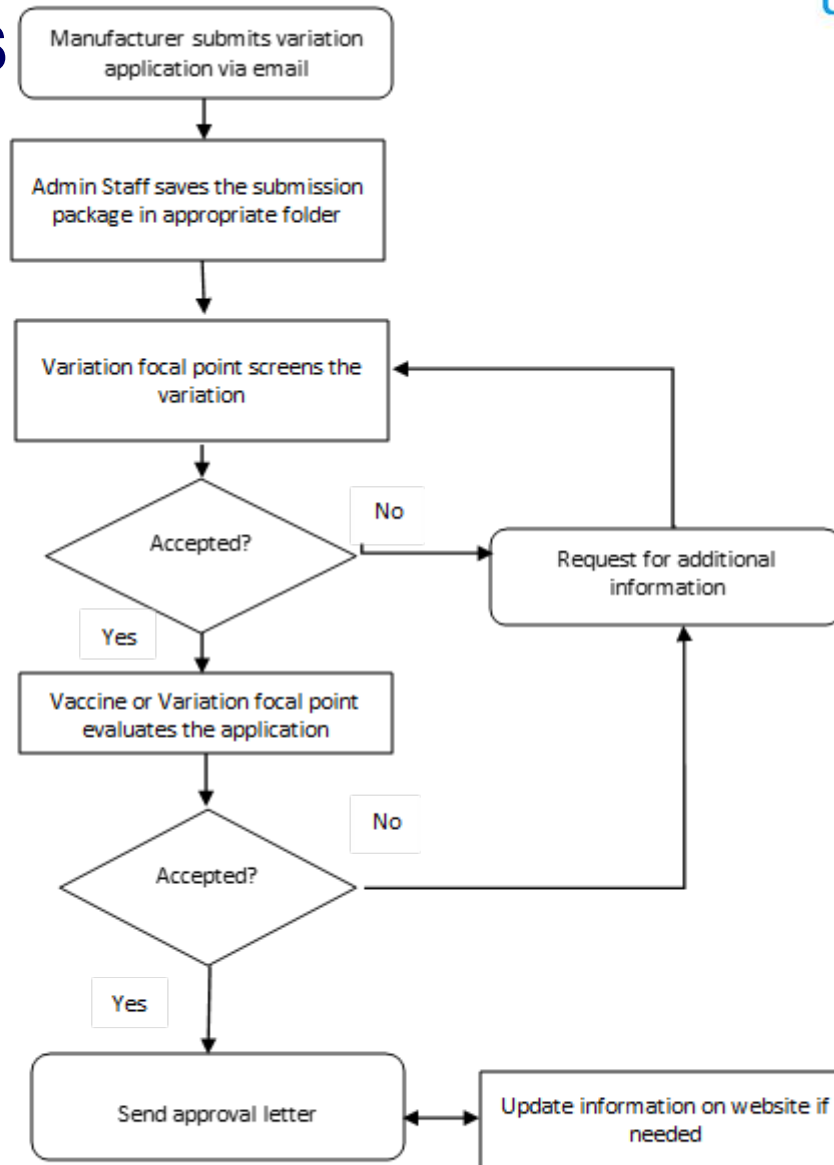
VARIATIONS

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

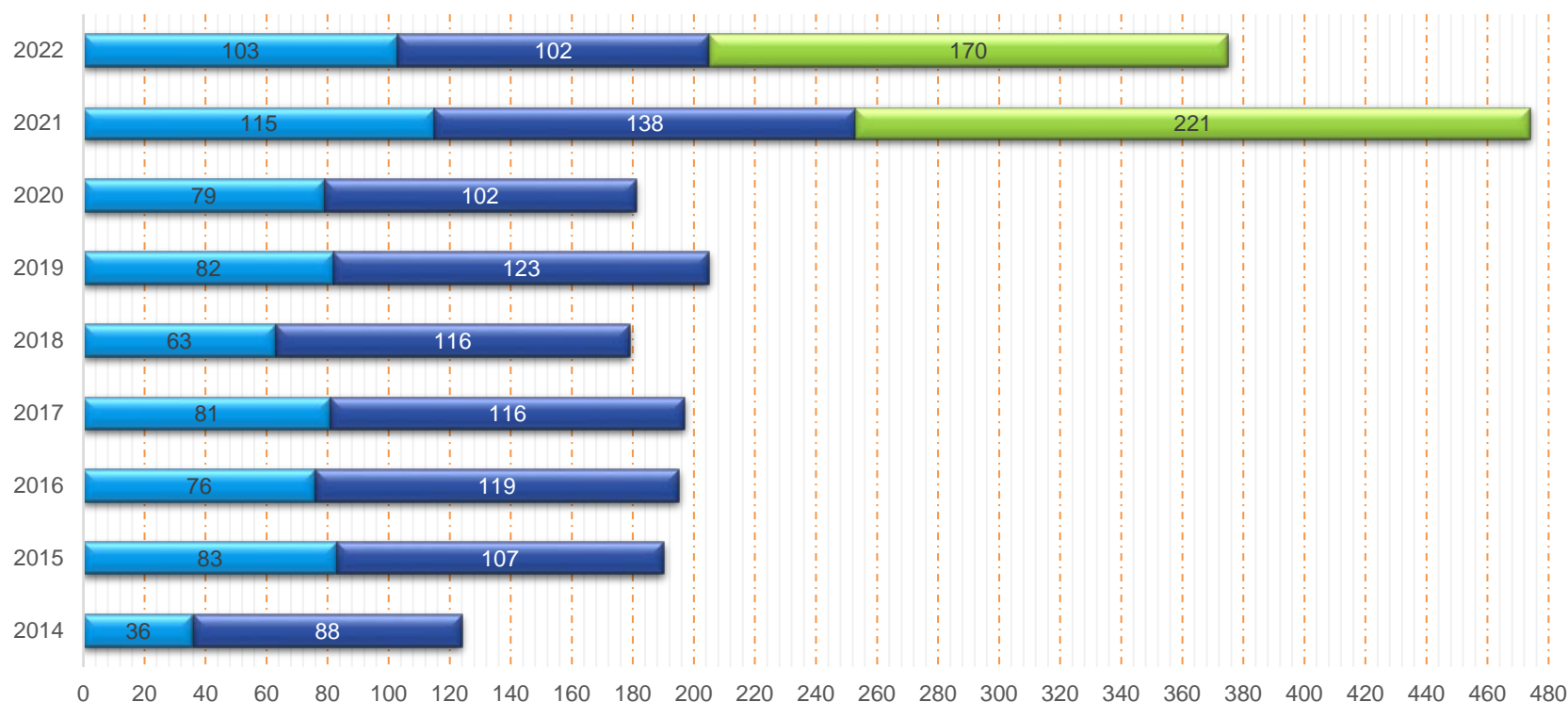
PQVARs is a comprehensive and summarized information on:

- **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

■ PQ Variations ■ PQ annual reports (PQVAR) ■ EUL variations



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**

