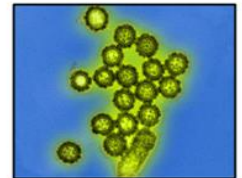


JOINT UNICEF – UNFPA – WHO PREQUALIFICATION UPDATES

Prequalification of Vaccines

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OUTLINE 1

- ✓ **PQ Procedure**
- ✓ **Format and content of a VPQD**
- ✓ **Performance**
- ✓ **Future**

OUTLINE 2

- ✓ **Post PQ Activities**

Prequalification of Vaccines (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

Prequalification of Vaccines (CMC)

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

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

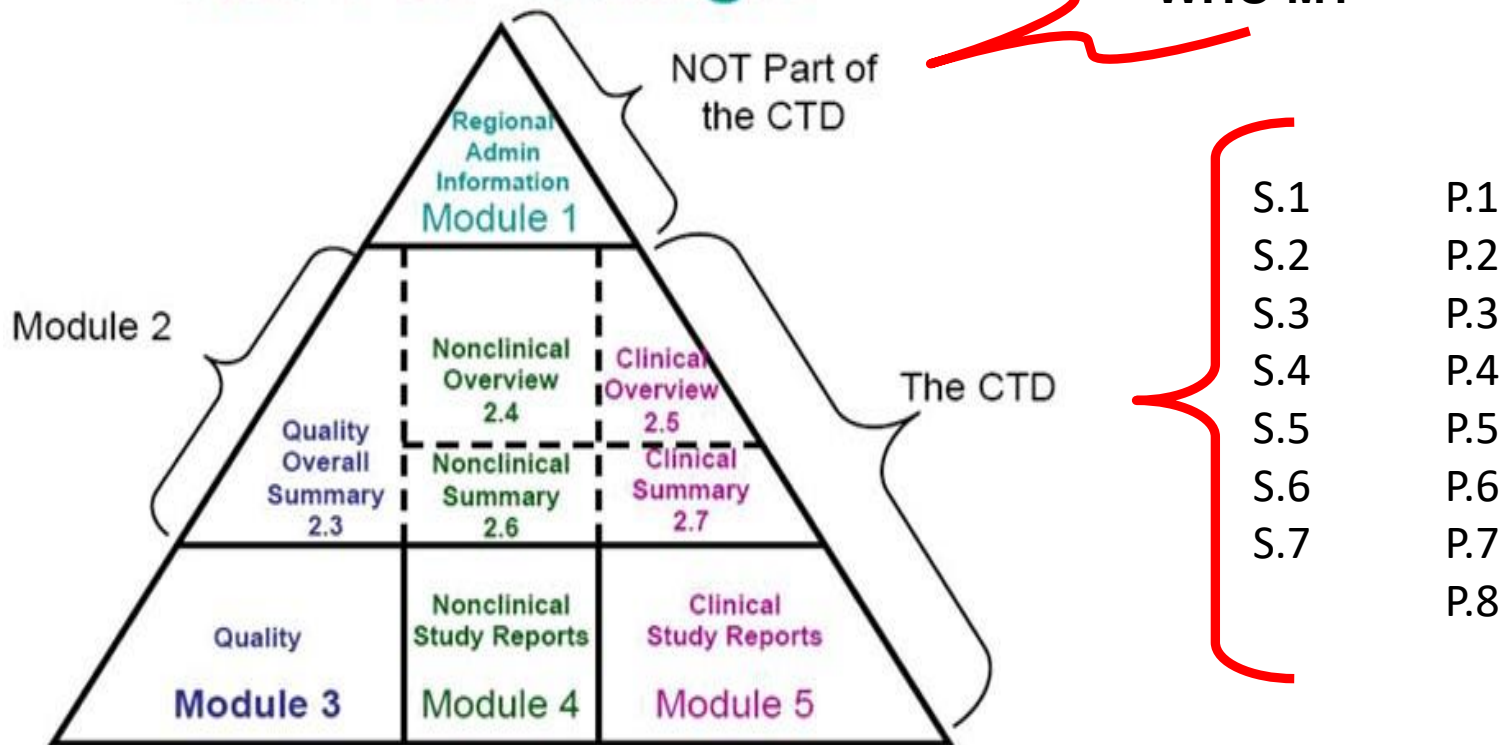
Related links (e.g., WHO Vaccine Position Papers)

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

TRS for vaccines: <https://www.who.int/teams/health-product-policy-and-standards/standards-and-specifications/norms-and-standards/vaccine-standardization>

Format VPQD

The CTD Triangle



Format & Content VPQD

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.*

Format & Content VPQD

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>

Format & Content VPQD

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.

Format & Content VPQD

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.

Format & Content VPQD

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

Format & Content VPQD

Drug product (DP) is a finished dosage form, e.g., solution for injection, that contains a DS, generally, but not necessarily, in association with one or more other ingredients.

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

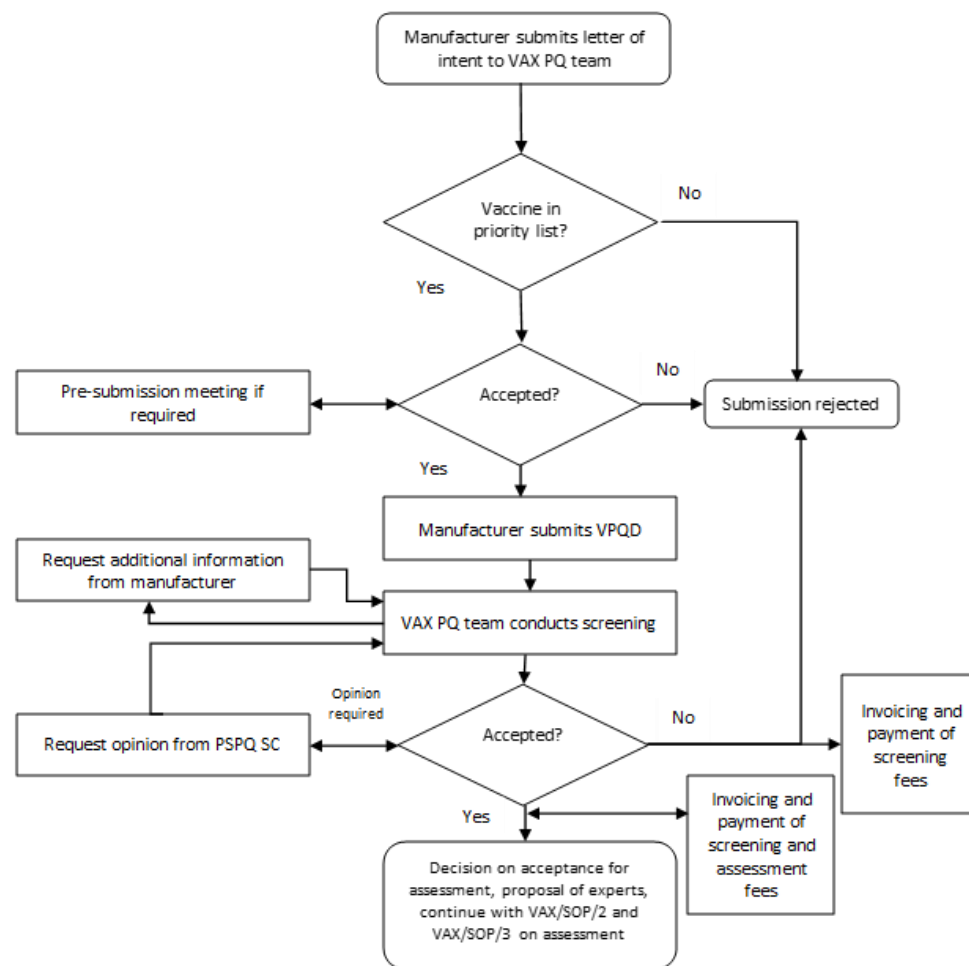
3.2.A APPENDICES: Facilities, equipment; novel excipients; literature.

Format & Content VPQD

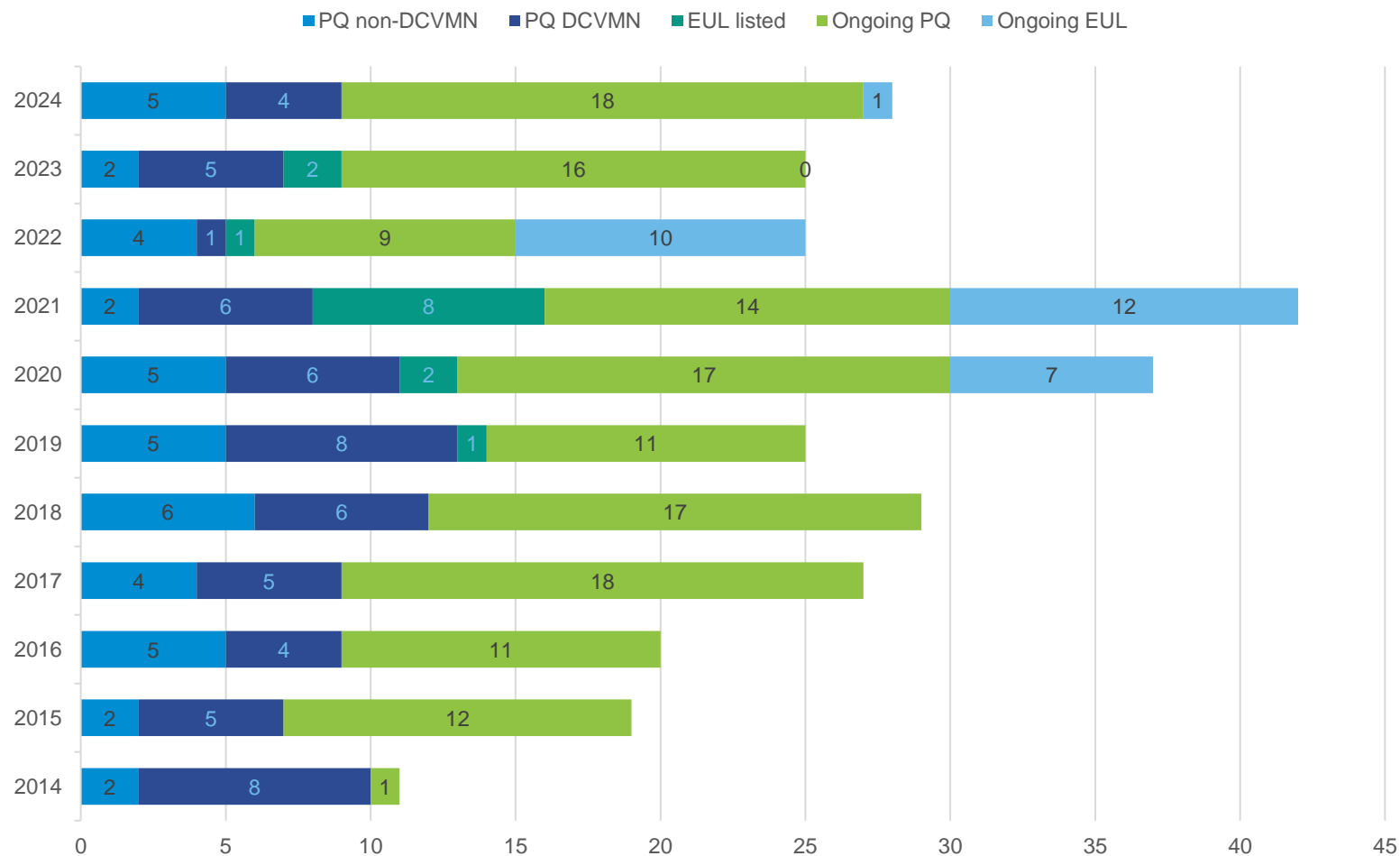
PQ Acceptance Process

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



Performance: PQed and EUL from 2014 to 2024



Prequalification Procedure (CMC)

Messages to take with you:

- Follow guidelines (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



<https://extranet.who.int/prequal/>

Prequalification of Vaccines



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

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

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

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

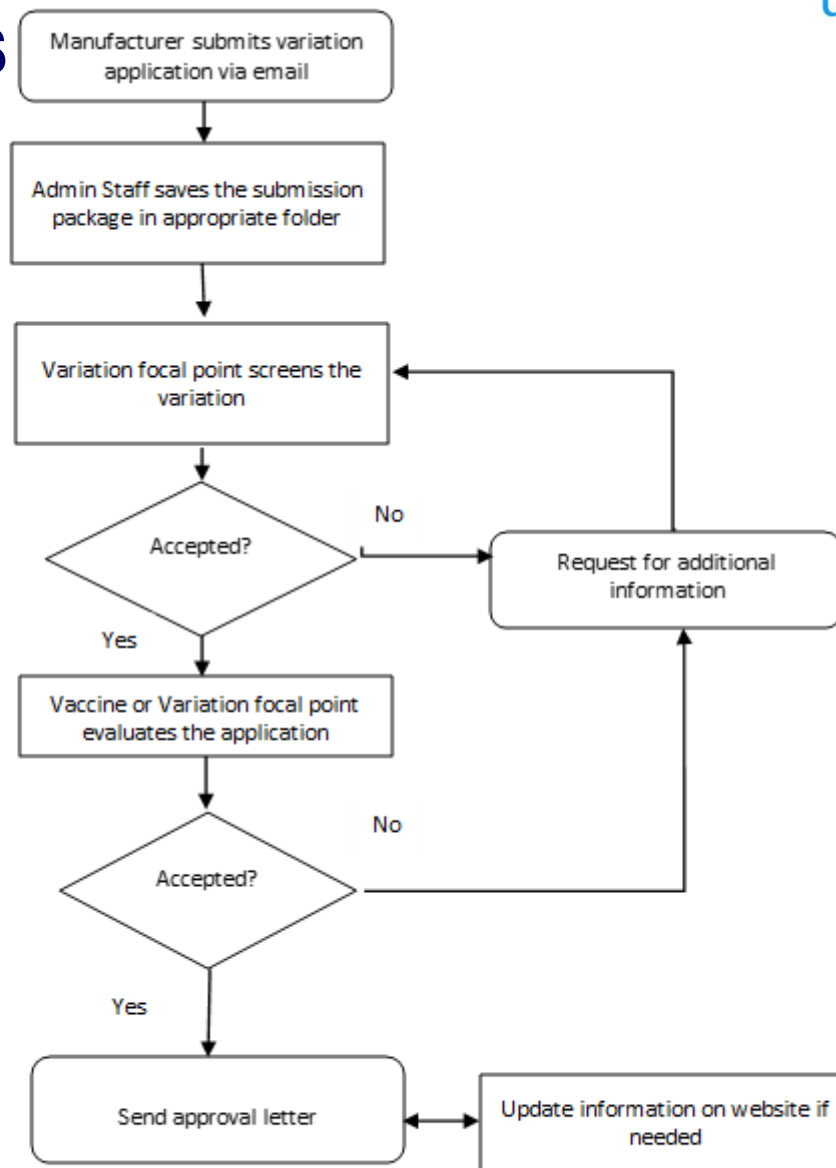
VARIATIONS

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

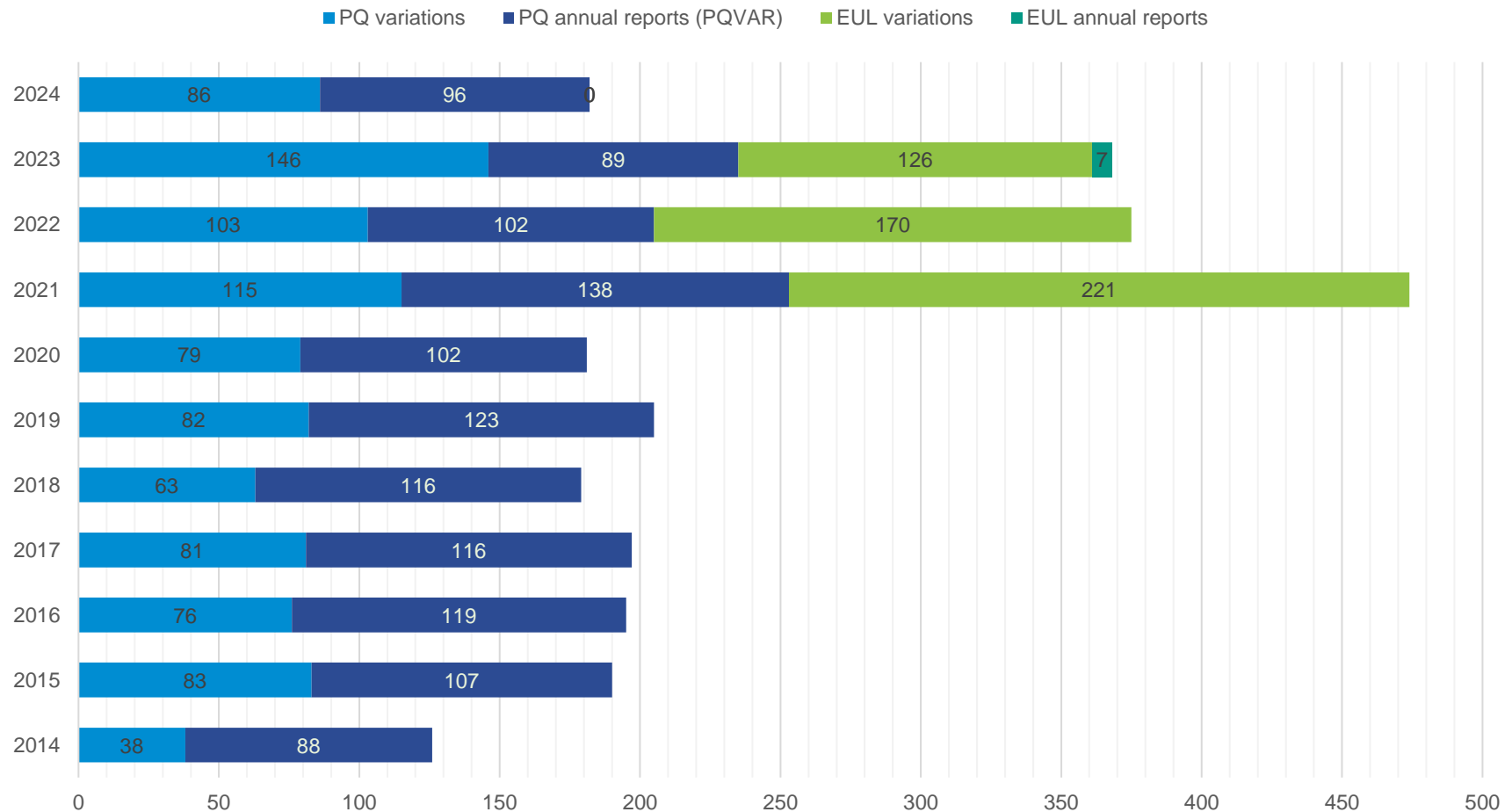
VXA ALWAYS RELY ON THE NRA of RECORD!!!!

VARIATIONS



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

Performance: Post-PQ Activities 2014 - 2024



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).

Post-PQ Activities

Other activities:

- Targeted testing programme
- 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

