Reliance and Collaborative Registration Procedure
Role of WHO Prequalification in facilitating Access to Quality-Assured Vaccines

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Why PQ and Reliance?

In 2022 alone, 6 countries achieved ML 3 or ML4
- ML4 (med & vac): Republic of Korea
- ML4 (med): Singapore
- ML3 (vac): Egypt, China and South Africa
- ML3 (med): Nigeria

Background:
- Over 70% of National regulatory authorities have inadequate regulatory functions

Facts
- 98 countries (51%) have limited capacity to perform core regulatory functions.
- Applicants face a landscape of disparate regulations, frequent delays and limited transparency.

This has implications on:
- Access to quality assured and safe medicines and vaccines in countries at ML 1 & 2 is not guaranteed:
  - high risk of Substandard and Falsified medical products
- Cost of inefficient regulatory systems drives up prices
- Regulators less prepared for public health emergencies
Prequalification: Product types and achievements

In vitro diagnostics (IVD) & male circumcision device (MCD)
- Cholera
- G6PD
- Glucose meter & Test strips
- Haemoglobin POC
- Hep B
- Hep C
- HIV/AIDS
- HPV
- Malaria
- Syphilis
- TB NAT

Finished pharma product (FPP), Active pharma ingredient (API), Quality control lab (QCL)
- BTP/SBPs (Cancer, Insulin)
- Child health
- Covid-19 (BTP, FPP, API)
- Diarrhoea
- Ebola virus disease (BTP)
- Hep B ✓ Hep C
- HIV/AIDS
- Influenza
- Malaria
- MDR bacterial infections
- New-born, young infants
- Neglected tropical diseases
- Nicotine replacement therapy
- Tuberculosis
- Reproductive Health

Vaccines (Vx), Immunization device (ImD) & Cold chain equipment (CCE)
- 24 priority diseases, covering all vaccines required for routine immunization
- Covid-19
- Ebola virus disease
- Malaria

Eligibility criteria for evaluation includes:
- NRA functionality & Programmatic suitability

Vector control products (VCP) & active ingredients
- Larvicides
- Insecticide treated nets
- Indoor residual spraying products
- Space spraying products
- Aircraft disinsection products

Inspection
- IVD
- Medicines: FPP, API
- BTP, SBP
- Vx
- ImD
- Clinical trials
- Bioequivalent studies
- Laboratories
- VCP
- Training

- 105 IVD
- 1 MCD
- 643 FPP
- 161 API
- 170 Vx
- EUL: 12 Vx
- 88 VCP
- 479 inspections in 2020-2022 despite COVID-19 pandemic

(*)Current numbers of PQed/EULed products: March 2023

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### Exhibit 32: Overview of major donors requiring PQ for procurement of vaccines

<table>
<thead>
<tr>
<th>Donor/ procurer perspective on PQ</th>
<th>Contingency approval process</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gavi</strong></td>
<td>Only PQ accepted</td>
</tr>
<tr>
<td></td>
<td>Specific exemption to procure non-prequalified products possible under defined criteria</td>
</tr>
<tr>
<td><strong>UNICEF</strong></td>
<td>Only PQ accepted</td>
</tr>
<tr>
<td></td>
<td>-</td>
</tr>
<tr>
<td><strong>Pan American Health Organization</strong></td>
<td>PQ or SRA approval (PQ preferred)</td>
</tr>
<tr>
<td><strong>Amref Health Africa</strong></td>
<td>PQ or SRA approval or tFDA¹</td>
</tr>
<tr>
<td><strong>ICRC</strong></td>
<td>PQ or SRA approval</td>
</tr>
<tr>
<td><img src="image" alt="International Coordinating Group (ICG) on Vaccine Provision" /></td>
<td>PQ or SRA approval (PQ preferred)</td>
</tr>
</tbody>
</table>

1. Tentative FDA   2. Expert Review Panel   3. Includes a preassessment based on product and manufacturer questionnaires, a Good Manufacturing Practices (GMP) of the manufacturing site, a product evaluation based on product and/or manufacturer questionnaire(s) according to standards set by WHO; and based on a standard Product Questionnaire common to the Interagency Pharmacist Group (UNICEF, ICRC, The Global Fund, WHO procurement center, UNFPA, GDF and MSF) and active monitoring and follow up   4. Details provided based on interviews with WHO colleagues / could not be validated with publicly available information   5. Emergency Use Assessment and Listing

| New compared to 2018 |  |
Objectives/prerequisites of local production

Local production of health products should aim and be trusted to meet the following objectives/prerequisites:

1) Ensure quality/safety/efficacy.

2) Facilitate access.

3) Ensure sustainability.
Definition of a WHO Listed Authority
Adopted by the ECSPP in October 2020, TRS 1033

A WHO Listed Authority (WLA) is a regulatory authority or a regional regulatory system which has been documented to comply with all the relevant indicators and requirements specified by WHO for the requested scope of listing based on an established benchmarking (GBT) AND a Performance Evaluation process.

ML3/ML4 delinked from ML
Exhibit 34: Number of countries that have signed PQ CRP agreements for vaccines and medicines and diagnostics, and SRA CRP agreements for vaccines and medicines between 2018 and 2022

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>2019¹</th>
<th>2020</th>
<th>2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>PQ CRP (medicines and vaccines) Agreements</td>
<td>35</td>
<td>28</td>
<td>47</td>
<td>59</td>
</tr>
<tr>
<td>PQ CRP (diagnostics) agreements</td>
<td>5</td>
<td>21</td>
<td>7</td>
<td>26</td>
</tr>
<tr>
<td>SRA CRP (medicines and vaccines) Agreements</td>
<td>20</td>
<td>31</td>
<td>49</td>
<td>25</td>
</tr>
</tbody>
</table>

¹ PQ CRP for diagnostics started in 2019
Exhibit 37: Cumulative number of accelerated product registrations under PQ CRP for vaccines

Source: Data from WHO FPI team

Cumulative number of product registrations under PQ CRP in an accelerated manner for vaccines, 2018-2022, registrations within 250 days and registrations within 90 days

13 unique products registered as of 2022 for PQ CRP (Vx)

Plateau despite receiving ~40 submissions for prequalified vaccines

For 2018-2022,

- Total # of product registrations: 20
- % of total product registrations:
  - Within 90 days: 80%
  - Within 250 days: 100%

Regional distribution of product registrations completed within 250 days:

- AFRO: 15
- PAHO: 3
- SEARO: 2
**RPQ- Prequalification**

**Summary of achievements**

- 13% more products were prequalified in the last 5-year period (2018-2022) compared to the previous 5-year period
  - If adjusted by removing COVID-19 products – the numbers are the same
- **EUL: 3x more products EUL-listed in the last 5-year period** (2018-2022) compared to the previous 5-year period, almost 100% of them are COVID-19 products
  # Number of IVDs listed in EUL
  Covid-19: 38, Ebola: 6, Zika: 4

- For medicines, COVID-19 products were eligible for PQ - team was able to establish a fast-track process to proceed them achieving median times far lesser than target

- **Increase in the therapeutic areas within PQ scope** - five added for medicines¹, three for vaccines² and three for diagnostics³

**Challenges**

- **Limited human resources** – staff and external experts.
- **Ever increasing workload with expansion of PQ scope** without corresponding increase in resources.
- Competition for capacity of laboratories for PQ Performance Evaluation.
- **Backlog as the result of the impact of the pandemic** on PQ internal and external resources and on timely response of the applicants.
- Immature regulation, harmonisation and diverse stakeholders plus legacy of old programmes in certain product areas (VCPs and IVDs).

**New activities and opportunities**

- **New procedures (CSA, Parallel procedures for Guideline & PQ) and strengthened QMS** – better pipeline scanning, streamlining procedures, etc.
- **Implementation of the new IT system (ePQS)** will facilitate streamlining of workflow, transparency and reporting.
- **Recent independent RPQ impact assessment** – tool for advocacy and continuous improvement
- **Increasing number of WLAs** – will help PQT extend its reliance on the work of others NRAs and a bigger pool for experts.
- **Continued support and recognition** of the work of PQT by stakeholders, including member states, development partners, procurers and clinical departments, as a trusted symbol for safety, quality and efficacy.

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1. Infections in new-born and young infants and childhood pneumonia; Insulins and insulin analogues (BTPs); Certain cancers (BTPs); COVID-19 (BTPs and small molecules); Ebola Virus Disease (BTPs);
2. Ebola, Pneumonia, Malaria;
3. G6PD, Cholera, Syphilis, TB

CSA = Coordinated scientific advise, QMS = Quality Management System, WLA = WHO Listed Authorities
Thank you for your attention
Siyabonga, Dankie, धन्यवाद, Asante

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WHO/MHP/RPQ/PQT

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