WHO RPQ impact assessment: Regulation and prequalification activities

External assessment report on programmes in the Department of Regulation and Prequalification

March 2023
Disclaimer

The contents of this document reflect a consolidation of views gathered through numerous interviews with various stakeholders; they are not the official view of World Health Organization (WHO).

Personal data and confidential elements provided by interviewees for the purposes of this study have been redacted.

Elements in the study may not have been verified or confirmed by WHO and no responsibility is accepted for any decisions or actions taken based on this document. Similarly, recommendations made in the study do not necessarily reflect the views or intentions of WHO.
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# List of abbreviations

AFRO: Regional Office for Africa  
AMA: African Medicines Agency  
AMRH: African Medicines Regulatory Harmonization  
API: Active Pharmaceutical Ingredient  
AVAREF: African Vaccine Regulatory Forum  
BE: bioequivalent  
CARICOM: Caribbean Community  
CEM: Cohort Event Monitoring  
cGMP: Current Good Manufacturing Practices  
CRP: Collaborative Registration Procedure  
DCGI: Drugs Controller General of India  
DCM: Developing Country Manufacturer  
DRAP: Drug Regulatory Authority of Pakistan  
Dx: Diagnostics  
EAC: East African Community  
EMA: European Medicines Agency  
EOI: Expression of Interest  
EPI: Essential Programs on Immunization  
ERP: Expert Review Panel  
EUL: Emergency Use Listing  
EU-M4all: EU Medicines for All  
FPP: Finished Pharmaceutical Product  
GBT: Global Benchmarking Tool  
GHTF: Global Harmonization Task Force  
GMP: Good Manufacturing Practices  
GoE: Government of Ethiopia  
GPW 13: WHO’s 13th General Program of Work  
GreIP: WHO Good Reliance Practices  
GSMS: WHO Global Surveillance and Monitoring System  
HCP: Healthcare Professionals  
HIC: High-income Countries  
HPS: Health Product Policy and Standards  
ICSR: Individual Case Safety Report  
IDP: Institutional Development Plan  
ISF: Incidents and Substandard and Falsified Medical Products  
IVD: In Vitro Diagnostic  
KPI: Key Performance Indicator  
KPIP: Kilinto Pharmaceutical Industrial Park  
ML: Maturity Level  
MSF: Médecins Sans Frontières  
LMIC: Low- and Middle-income Countries  
LNS: Laboratory Network and Services  
LPA: Local Production and Assistance  
MAGHP: Marketing Authorization for Global Health Products  
ML: Maturity Level  
MSF: Médecins Sans Frontières
A Executive summary

A.1 CONTEXT AND OBJECTIVES

An effective regulatory system plays a critical role in ensuring the quality of health products, spanning from their development in the laboratory to their administration in health facilities. This system serves as a cornerstone for achieving high-quality prevention, diagnosis, and treatment and is an indispensable element of the World Health Organization’s (WHO) drive towards universal health coverage (UHC). Moreover, it is a significant contributor to WHO’s objective of reaching the "triple billion" target, which seeks to expand the number of people benefiting from universal health coverage, enhance protection against health emergencies, and promote improved health and well-being for one billion people each.

As of December 2022, there are over 1,580 products – medicines, vaccines, In Vitro Diagnostics (IVDs), vector control, and immunization devices – that are prequalified and have improved public health in low- and middle-income countries (LMICs). Furthermore, there are 13 National Regulatory Authorities (NRAs) that have achieved stable and well-functioning regulatory systems commensurate with maturity level 3 or 4 for at least one product type. The WHO department that is driving the aforementioned impact is the Regulation and Prequalification (RPQ) department whose broader mandate is to “help Member States strengthen regulatory systems through a variety of approaches” and to “ensure medicines, vaccines and other health products for supply to low-income countries are quality-assured, safe, effective and accessible to all populations”\(^1\). The structure of the RPQ department has been included in Appendix 1.

In 2018, an independent impact assessment report of this department was commissioned with three specific objectives:

- Create a fact-based understanding of the value that the PQ and system-supporting activities have created in the global health ecosystem, with a 360-degree view across all stakeholders
- Generate both qualitative and quantitative assessments of the value created by PQ and system-supporting activities
- Create insights that can feed directly into the team’s strategic plan to create greater impact at a country level, driving towards the triple-billion targets laid out in WHO’s 13th General Program of Work (GPW13)

This impact assessment has been one of the inputs that informed the elaboration of WHO’s five-year plan (2019-23)\(^2\) to help build effective and efficient regulatory systems. This strategic plan sets out four strategic priorities for the RPQ department:

- Strengthen country and regional regulatory systems
- Improve regulatory preparedness for public health emergencies
- Reinforce and expand WHO prequalification and product risk-benefit assessment
- Increase the impact of WHO regulatory support activities

At this five-year juncture of the plan considering (a) the value generated by the 2018 assessment report, (b) the shifts that have occurred since its publication in 2019, both in the global health ecosystem (e.g., due to the COVID-19 pandemic) and (c) the changes within the RPQ department - a new independent impact assessment of the scope\(^3\)

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\(^1\) [https://www.who.int/teams/regulation-prequalification/about](https://www.who.int/teams/regulation-prequalification/about) (Link verified on March 31, 2023)

\(^2\) [https://www.who.int/publications/i/item/WHO-MVP-RHT-2019.01](https://www.who.int/publications/i/item/WHO-MVP-RHT-2019.01) (Link verified on March 31, 2023)

\(^3\) Except prequalification of medical devices and vector control products
of the RPQ department has been commissioned. In addition to the RPQ department activities, the activities and impact of the work done by the Health Product Policy and Standards (HPS) department on the topic of norms and standards are also within scope of this assessment considering their close connection to the mandate and activities of the RPQ department.

This new assessment has focused on the last five years (2018-22) and has four specific objectives:

- Generate both qualitative and quantitative assessments of the value created by the RPQ department for its main stakeholders with a focus on country impact in line with the four strategic priorities of the RPQ department
- Create an understanding of the value that the RPQ department activities have created in the global health ecosystem, with a 360-degree view across all stakeholders
- Identify and analyze the main developments since the publication of the previous assessment in 2018
- Develop insights and recommendations that enable both operational quick wins (i.e., allowing for efficiency gains) and long-term improvement

### A.2 SUMMARY OF METHODOLOGY

To create a fact-based understanding of the value that the RPQ department has created across all stakeholders, three main sources of insight were taken into consideration. First, desk research and data analysis provided an objective and fact-based overview of the current ecosystem, case examples, and economic benefits. Second, a total of 28 interviews with WHO stakeholders and 44 interviews with external stakeholders (60 minutes each) provided a more nuanced perspective that is directly linked to the needs and interests of the various stakeholder groups. The external stakeholder interviews covered 9 NRAs (including 2 Stringent Regulatory Authorities (SRAs)), 18 manufacturers (4 Rx, 7 Vx, and 7 Dx), 14 procurers/donors, 2 industry associations, and 1 civil society organization. Finally, a survey was shared with 179 NRAs to collect their perspectives on the relevant WHO activities. A total of 39 NRAs completed the survey.

11 impact themes were assessed with detailed assessment metrics for each:

1. Strengthening regulatory systems (including three quantitative assessment metrics, one perception assessment metric, and one case study)
2. Improving the management of Substandard and Falsified (SF) medical products and incidents (2 quantitative metrics and 2 case studies)
3. Increasing compliance of laboratories with required standards in LMICs (2 quantitative metrics and 1 case study)
4. Strengthening pharmacovigilance (4 quantitative metrics and 1 perception)
5. Enabling faster access to prequalified, SRA-approved and Emergency Use Listed products (5 quantitative metrics and 1 perception)
6. Improving regulatory preparedness for public health emergencies (2 quantitative metrics and 1 case study)
7. Improving access to donor-funded procurement markets (1 quantitative metric and 1 case study)
8. Supporting Member States to build the ecosystem and capacities for high-quality and sustainable local production (3 quantitative metrics, 1 perception metric and 1 case study)
9. Assessing the economic return on investment (RoI) savings generated by PQ (1 quantitative metric)

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*This new impact assessment is an update of the 2018 assessment.*
10. Contributing to saving lives (2 quantitative metrics)

11. Increasing adoption of WHO guidelines and technical standards (1 quantitative metric and 2 perception metrics)

Five limitations of this report should be considered. First, the insights are by no means exhaustive, given that the interviews focus on stakeholder groups that have the highest direct exposure to WHO and have a general understanding of the impact of their activities. Also, no additional stakeholders (e.g., patients or regional regulatory bodies) were interviewed. Second, comprehensive data was not available in some instances (either it was not collected at present or because the information was not publicly available (when related to data for other stakeholders outside of the RPQ department). Third, the scope of this report is limited to specific activities, which is why it does not give an exhaustive review of all RPQ department activities or all the teams within and related to the RPQ. Fourth, the evaluation focuses on the key strategic issues of the RPQ rather than providing a detailed assessment of each activity. Last, there are many projects that the RPQ department has under implementation (e.g., implementation of a new Quality Management System and the electronic PreQualification IT system (ePQS) that have the potential to impact some of the recommendations made in the report. However, since these have not yet been fully rolled out as of December 2022, their impact is not considered within the scope of this assessment.

A.3 SUMMARY OF ASSESSMENT

Based on the combination of quantitative analysis and the insights from the stakeholder interviews across the different metrics, the RPQ department has had meaningful impact. Across all activities, some areas for improvement have been identified that could enhance the impact of the RPQ department.

Overall, the seven key findings of this assessment are:

1. The RPQ department has had significant impact in terms of enabling access to critical health products for the global population:
   a. Increased responsiveness in a global pandemic – The RPQ department has listed 11 COVID-19 vaccines and 42 COVID-19 diagnostic products for emergency use and prequalified 17 COVID-19 related medicines. WHO Emergency Use Listings (EULs) approvals were relied on by more than 170+ Member States and Territories to approve COVID-19 medical products for entry into their markets following facilitation by the WHO through its Regional and Country Offices.

   b. Contributed to averting more than five million deaths during the COVID-19 pandemic – Between 5.1 million and 7.6 million deaths have been averted in LMICs in 2021 thanks to COVID-19 vaccinations. The RPQ department contributed to this positive impact by listing 10 COVID-19 vaccines for emergency use between December 2020 and December 2021. As the large majority of LMICs rely on WHO EULs, the responsiveness of the RPQ department to list COVID-19 vaccines enabled the delivery of hundreds of millions of doses in 2021 (e.g., COVAX delivered over 842 million doses of COVID-19 vaccines in LMICs in 2021; these doses could not have been delivered without an EUL).

   c. Continued progress on improving access to health products: Even with the increased workloads and disruptions to processes (e.g., in-person site inspections) due to COVID-19 overall, the number of prequalified products has increased by 13% in the last 5-year period (2018-22) compared to the previous 5-year period (2013-17), while the number of products EUL-listed has increased by 325%.

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6 From 422 to 439 prequalified. It is worth noting that the number of submissions has decreased by 24% between 2013-17 and 2018-22.
7 From 12 to 51 products EUL-listed. It is worth noting that the number of submissions has increased by 313% between 2013-017 and 2018-022.
2. The RPQ department played a direct and significant role in strengthening regulatory systems globally: between 2018 and 2022, NRAs from 12 Member States (which represent ~30% of the world’s population) have been supported to reach one of the four Maturity Level 3 (ML3)\(^8\) or Maturity Level 4 (ML4)\(^9\) categories, which brings the total number of countries that achieved ML3 or ML4 for at least one medical product type from 1 in 2017 to 13 in 2022 (representing ~50% of the world’s population). Many more have been supported in the strengthening of their regulatory functions, e.g., vigilance systems and marketing authorization during public health emergencies (even though there may not have been an increase in the overall maturity level of the NRA).

3. The RPQ department has expanded the scope of its activities to support Member States, manufacturers, and other stakeholders more comprehensively, some examples include:
   
   d. Increase in the therapeutic areas within scope for prequalification (five therapeutic areas added for medicines\(^{10}\), three for vaccines\(^{11}\) and four for diagnostics\(^{12}\))
   
   e. Development, implementation, and promotion of the concept of reliance, including through the publication of the WHO Good Reliance Practices (GrelP) in 2021 and organization of training sessions and webinars around reliance.
   
   f. Development and launch of the Coalition of Interested Parties (CIP), a WHO Network on regulatory systems strengthening aimed at coordinating efforts by partners contributing to regulatory strengthening and convergence activities at national, regional, and global levels.
   
   g. Expansion of the Collaborative Registration Procedure (CRP) to enable market entry and national marketing authorizations for PQ products:
      
      › Number of Member States that have signed CRP agreements for medicines has increased from 35 to 59 (70% increase), for vaccines from 20 to 49 (150% increase) and for diagnostics, since the launch of the CRP process in 2019, 26 countries have signed CRP agreements
      
      › Number of Member States that have completed product registrations under the CRP agreements has increased by 20% and 25% respectively, for medicines and vaccines. For diagnostics, since the launch of the CRP in 2019, 25% of them have registered products through this pathway.

4. In addition to expanding the scope of its existing activities, the RPQ department has been piloting and testing new processes and support mechanisms to respond to the changing needs of its stakeholders, including but not limited to:

   a. **Pursuant to NRA feedback to replace the previous concept of Stringent Regulatory Authorities (SRA):**
      
      Launch of the first pilots for performance evaluation (currently under way as of December 2022) under the new WHO Listed Authorities (WLA) framework \(^{13}\) which was developed in response to tremendous feedback from NRAs for a transparent and evidence-based pathway for regulatory authorities operating at an advanced level of performance to be globally recognized, thereby replacing the previous concept of SRAs.
   
   b. **Pursuant to the strategic objectives of the department’s 2019-23 strategy:** Development of new approaches to directly support Member States in strengthening their national strategies and capabilities

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\(^{8}\) ML3 confirms that a stable, well-functioning and integrated regulatory system is in place

\(^{9}\) ML 4 (which is the highest level of maturity) is achieved by a regulatory system operating at an advanced level of performance and continuous improvement

\(^{10}\) Infections in newborns and young infants and childhood pneumonia; Insulins and insulin analogues (BTPs); Certain cancers (BTPs); COVID-19 (BTPs and small molecules); Ebola Virus Disease (BTPs)

\(^{11}\) Ebola, Pneumonia, Malaria

\(^{12}\) G6PD, Cholera, Syphilis, TB

\(^{13}\) https://www.who.int/initiatives/who-listed-authority-reg-authorities
around SF products, e.g., (a) supporting Nigeria in procuring handheld devices that have already had tremendous impact in enabling track and trace in the country, (b) collaborating with Tanzania on their national strategy for addressing SF products with the goal of using the lessons learned to develop a handbook for other Member States.

c. **Pursuant to WHO transformation in 2019 and passing of resolution WHA74.6 on strengthening local production of medicines and other health technologies and the 2019 WHO transformation:** Establishing a new WHO initiative “World Local Production Forum” and piloting an ecosystem assessment tool that can support Member States in developing actionable plans to strengthen local production (already piloted in seven countries across AFRO, EMRO, and SEARO).

d. Pursuant to WHO Transformation in 2019, establishing an integrated Pharmacovigilance team in the RPQ department for medicines and vaccines, thereby enabling common tools around reporting and data management across products.

5. **Stakeholders unanimously highlighted the limited resourcing at WHO headquarters as a key constraint across RPQ department’s units and teams.** RPQ department resources have remained stable between 2018 and 2022 (from 114 staff members in December 2019 to 115 in December 2022). However, the scope and the workload across all teams have increased substantially in the same time period (some examples discussed above in points 1-4).

6. **One prominent feedback point that has been shared across all categories of stakeholders interviewed is the need for increased communication, and collaboration between the RPQ department and key stakeholders in the public health ecosystem (NRAs, manufacturers, donors and procurers, other WHO departments).** Stakeholders note that strengthening this aspect can enable even greater impact from the RPQ department as it will not only drive more reliance but also enable the RPQ department to identify where they can leverage other stakeholders (instead of their own limited resources) to scale their impact. In particular,

   a. Mature NRAs are keen for the RPQ department to rely on them to drive capacity-building efforts for their regions.

   b. Manufacturers are keen to have more visibility (e.g., on PQ decision timelines and roadmaps for release of technical standards and guidelines) and more collaboration (e.g., on working with the PQ team to prioritize pipelines for their products).

   c. Donors, procurers, and other WHO departments are keen to collaborate with the RPQ department in setting global public health agendas across different therapeutic areas, regions, and stakeholders, for example by participating in the process of developing planned roadmap and scope for PQ teams.

   d. WHO departments (specifically from the Communicable and Non-Communicable Diseases division) are keen to participate and contribute to the RPQ department’s strategy and priority setting activities. In addition, they are keen to have visibility on the activities and achievements of the department so that they can identify opportunities for collaboration.

   e. All stakeholders are keen to see the RPQ department have a more central role in the PV ecosystem, coordinating, connecting, and collaborating with stakeholders more proactively

7. **Investing in RPQ remains a sound investment:** every USD 1 invested in running PQ contributes to savings of approximately USD 30-40 while acknowledging that PQ operates in the broader ecosystem of Global Health stakeholders contributing towards these savings as well.\(^{14}\)

\(^{14}\) ROI analysis from 2018 assessment report has been leveraged as it is believed that the findings are still valid for the period between 2018 and 2022 - these are discussed in greater detail in Section C.9
A.4 SUMMARY OF RECOMMENDATIONS

Based on this impact assessment, there are five major categories of proposed enhancements. It is also noted that several recommendations from the 2018 Assessment continue to be relevant, especially around the topics of cross-departmental collaboration, PQ, PV, and guidelines and standards.

1. Cross-cutting recommendation on strengthening external and internal coordination and communication efforts

   a. *Towards both internal and external stakeholders:*

      i. **(PQ across all products)** Strengthen the consultation process to collect inputs both from internal and external stakeholders prior to determining the prequalification priorities and developing product pipelines. For example: co-develop multi-year roadmaps for scope of products within PQ with stakeholders; develop a “priority” track to be able to designate “priority” medical products based on global health needs (e.g., a global stockout, pandemic).

      ii. Develop a robust communication strategy to articulate the services provided by the RPQ department to each stakeholder type (National Regulatory Authorities (NRAs), manufacturers, donors, etc.) including what is in scope and what is out of scope. This communication strategy will help manage key stakeholders’ expectations and create visibility both on the activities conducted by the RPQ department – as several new activities have been launched since 2018 – and on the impact these activities generate in terms of public health outcomes.

      iii. **(PQ across all products)** Communicate on a frequent basis the status of all health products within WHO EUL/PQ evaluation process on the WHO website (similar to what has been done for COVID-19 vaccines).

   b. **Towards external stakeholders only**

      i. **(PQ)** Ensure the new ePQS system planned for rollout in May 2023 has the appropriate features and data migration to take action on stakeholder feedback received in the context of this assessment (detailed in Section C.5.6) and of the assessment conducted in 2018.

      ii. **(Regulatory system benchmarking activities)** Increase awareness and understanding of the regulatory system benchmarking process and outcomes for procurers and donors, e.g., through a communication plan that can provide clarity on the purpose of the benchmarking process and tool. This could help address some misperceptions about the purpose of the benchmarking process and tool.

   c. **Towards internal stakeholders only**

      i. **(Across all RPQ teams)** Ensure synchronization of the future strategic roadmap of the RPQ department with the roadmaps of other WHO departments that are developing policies and recommendations on similar topics / products (e.g., IVB department) to ensure consistency of priorities across all departments.

2. Cross-cutting recommendation on readjusting strategic priorities or tracking metrics to drive more focused impact on areas of most need for the ecosystem

   a. **(Pharmacovigilance)** Consider resetting strategic priorities for pharmacovigilance activities to increase alignment with the biggest needs and gaps in the global pharmacovigilance ecosystem. The strategic

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15 Which includes a clear set of key performance indicators
16 The status of COVID-19 Vaccines within WHO EUL/PQ evaluation process is available online and is updated at least once a month (link verified on Feb. 9, 2023)
17 Impact assessment of WHO Prequalification and systems supporting activities (published in June 2019; link verified on Feb. 9, 2023)
priority setting process should include close collaboration with a multi-stakeholder (internal and external) working group.

b. (Local Production and Assistance) Reflect on lessons learned from LPA unit’s PQ Technical Assistance (TA) activities and outcomes over the last three years to reconsider: (a) the process/criteria for identifying manufacturers that receive TA and (b) developing the appropriate Key Performance Indicators (KPIs) for measuring impact of TA (current KPI is number of manufacturers supported with TA).

c. (Incidents and Substandard/Falsified Medical Products (ISF)) Incorporate lessons learned from current Member State pilots and initiatives aimed at developing local regulatory capabilities for SF products into a formal strategic plan and priorities for supporting Member States

d. (Norms and standards) Develop tracking process/methodology to monitor the implementation and the adoption of different guidelines, thereby enabling development of a fact base to determine where and on what implementation support is needed the most

3. Cross-cutting recommendation on optimizing RPQ department’s capacity (in light of resource constraints at headquarters)

a. Leverage capacity of NRAs. Create further opportunities for NRAs to support each other by, for example, strengthening self-sustaining peer learning forums that can be led by mature NRAs in each region (with minimal support from the RPQ department). Based on the findings of this report, some areas where this can be implemented are (a) the self-benchmarking processes and (b) regulatory emergency preparedness.

b. Create capacity in regional offices. Staff dedicated RPQ resources (under the supervision and expertise from the RPQ department in HQ) to drive RPQ department activities where local context and presence may be advantageous. Based on the findings of this report, some areas where this can be implemented are:
   i. (ISF) Provide Member States support in developing ISF strategies and responding to incidents
   ii. (Emergency preparedness) Provide support to countries that want to enhance their regulatory systems and requirements to effectively address public health emergencies
   iii. (LPA) Execution of strategy for strengthening local production
   iv. (QCL) Provide support in leading lab inspections to strengthen lab capacity

c. Optimize allocation of current RPQ department resources in HQ: Once the new strategic priorities and objectives for the RPQ department have been set, consider an independent assessment of the allocation of human and financial resources across RPQ department activities (both technical and non-technical) to ensure allocation matches strategic priorities. This exercise could add value as the scope of activities of the RPQ department has evolved between 2018 and 2022 while its staff has remained stable.

4. Cross-cutting recommendation on improving internal operational efficiency for the RPQ department

a. PQ (across all products): Consider a “teardown” exercise of core PQ processes to identify redundancies. E.g., to be able to map time required for administrative/coordination tasks vs. technical tasks and identify where tasks can be automated (e.g., through automated ePQS notifications) or where tasks can be managed by nontechnical resources out of regional offices (e.g., project managers/leads that are focal points for manufacturers for minutes, document uploads, setting meeting agendas)

b. PQ (Vx and IVD): Improve efficiency of post-approval change notification process. Some examples could be:
   i. Enable dedicated pathway: consider evaluating post-change notifications under a separate dedicated pathway (i.e., different pipeline with dedicated resources and special fit-for-purpose processes)
ii. Consider developing a “priority” track for variations that may be a global health priority

iii. Revise process: consider taking a more risk-based assessment approach (i.e., simple changes to label or color of packaging should not require waiting for WHO approval) more similar to how SRAs (e.g., FDA) evaluate post-approval changes

5. Other recommendations – specific improvements to various activities of the RPQ department:
   a. (Regulatory Systems Strengthening) Organize focus groups with NRAs currently undergoing benchmarking to understand the root cause of the perception that the tool needs more flexibility. Develop an appropriate action plan based on findings (e.g., better communication materials/plan to dispel misinformation about the tool’s purpose and flexibility)
   b. (Pharmacovigilance) Communicate the efficiencies to be gained with an integrated pharmacovigilance system that, where possible, uses the same tools and resources for AEFI and ADR reporting and data management
   c. CRP (Vx): Consider process improvements that can be made to simplify data sharing between the teams that hold the repository of information on PQ assessments and the teams processing/leading CRP registrations, such that information sharing to enable CRP for vaccines does not require significant capacity from the teams.
   d. Reliance: Consider the many different activities being run by the RPQ department on this topic – there is an opportunity for development of clearer strategic priorities, objectives, and KPIs on the impact the department seeks to drive on the topic of reliance
   e. (Emergency preparedness) Introduce systematic measurement of the impact of support from the RPQ department on regulatory capacity preparedness for public health emergencies. For example: request countries that received WHO support to re-evaluate the 11 Global Benchmarking Tool (GBT) sub-indicators related to regulatory preparedness for public health emergencies through self-benchmarking
   f. (Guidelines, norms, and standards) Strengthen implementation support to NRAs and developing country manufacturers (DCMs) to increase adoption (e.g., through a standardized guideline release protocol that includes introductory workshops, online courses that can be self-paced, toolkit and support documentation)
   g. (Guidelines, norms, and standards) Improve accessibility, user friendliness, and transparency to increase adoption (e.g., online, up-to-date, easy-to-navigate platform)
   h. (Medicine QCLs) Develop, communicate, and implement clear end-to-end process for PQ of medicines by Quality Control Laboratories to improve efficiency and better manage timelines for the end-to-end PQ process
   i. (Laboratories) Streamline support to priority regions and LIC Member States – a targeted focus will be key in building global laboratory capacity, especially keeping in mind resource constraints. For example: considering the unique complexities of LICs, develop a targeted action plan and funding to improve LIC participation in medicines QCL PQ
   j. (Pharmacovigilance) Set up incentives for Member States to increase the reporting frequency and quality of adverse events on VigiBase. For example: set up a dashboard of countries reporting performance, enabling peer-to-peer comparison, to foster healthy competition and motivation amongst Member States
   k. (LPA) Strengthen implementation support for NRAs and DCMs. For example: evolve the situational analysis tool in a similar direction as the GBT – where there are clear indicators and Institutional Development Plan (IDP) -like roadmaps that can provide concrete guidance to stakeholders, develop clear
metrics/methodology to be able to track the impact of the ecosystem analysis tool (before its launch in 2025)

I. (Guidelines, norms, and standards) Consider alternate pathways (besides working with/relying on the WHO central website/communications development team) to developing a norms and standards microsite that can have the features that will enable actioning of recommendations from both the 2018 assessment and the current assessment

This section highlights the most prominent measures identified across the assessed metrics. A more detailed list of enhancements is presented at the end of relevant sections and labelled “recommendations”. These recommendations are based on both hard facts/data as well as perceptions from stakeholders.

□ □ □
B Approach and methodology

B.1 SOURCES OF INSIGHT

To enable a fact-based understanding of the value created by the RPQ department across all stakeholders, two main sources of insight were taken into consideration. First, desk research and data analysis provided an objective and fact-based overview of the current ecosystem, case examples, and economic benefits. Second, interviews provided a more nuanced perspective that is directly linked to the needs and interests of the various stakeholder groups. Finally, a survey was shared with NRAs to collect their perspectives on the relevant WHO activities. An overview comparison of the methodology used in the 2018 assessment and current one is shown in Exhibit 1.

Exhibit 1: Comparison of the 2018 impact assessment and the 2023 one

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO staff</td>
<td>8</td>
<td>27</td>
</tr>
<tr>
<td>NRAs</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Manufacturers</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Donors / Procurers</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>Others¹</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>TOTAL</td>
<td>49</td>
<td>71</td>
</tr>
</tbody>
</table>

WHO regional advisors and WHO Directors (of Diseases programmes) have been interviewed

Twice more metrics than in 2019

30 NRAs provided some input

+ 22 stakeholders interviewed vs 2019

B.1.1 Desk research and data analysis

Thorough and systematic desk research was conducted to gather information on donor and procurer policies, regulatory requirements, insights on the impact of COVID-19 on global access to quality health products, and case studies showcasing the impact of RPQ department’s work on low- and middle-income countries’ (LMICs’) health ecosystems. Sources of information included external and internal WHO publications and reports, academic literature, and company websites.

Furthermore, WHO data on the various impact themes described in Section B2 was collected and analysed to gain a deeper understanding of the activities organized by the RPQ department and their impact on the various stakeholders involved. Data analysis was performed to assess, in particular:

- Country participation in and use of WHO tools and systems such as the Global Benchmarking Tool, the global surveillance and monitoring system for SF products, the WHO global database for PV, the WHO ecosystem assessment for quality and sustainable local production
- Country-level adoption of WHO guidance and standards on, e.g., regulatory system maturity levels, functionality of PV systems
- Products that have been prequalified, have been EUL-listed or have been registered under CRP
- Donors’ PQ requirements for procurement and participation in donor-funded pooled procurement mechanisms
• Assistance and training sessions provided to countries and their impact thereon, including on public health emergency preparedness and building quality and sustainable local production

B.1.2 Stakeholder interviews

As shown in Exhibit 1, part of this impact assessment analysed stakeholder perceptions of various RPQ department activities. For this, structured 60-minute interviews with a broad range of stakeholders were held to gather external perspectives on various aspects of the RPQ department as well as other supporting WHO activities, and to identify strengths and improvement areas. Both qualitative and quantitative data was collected to ensure room for discussion and opinion while also allowing for fact-based comparison between stakeholders.

In total, 86 stakeholder representatives across a wide range of stakeholder groups, including: WHO headquarters and regional offices staff, manufacturers, NRAs, donors, procurers, and other implementation partners, were contacted for interviews; 71 agreed to be interviewed. To ensure a comprehensive analysis of perspectives and ideas, stakeholder selection considered backgrounds and operating contexts in which each stakeholder was operating. Therefore, we ensured that the interviewees within stakeholder group were sufficiently diverse.

• Interviews with WHO stakeholders (23 interviewees based at WHO Headquarters and five interviewees from WHO regional offices): staff from various levels and from all teams and units with the RPQ department were selected alongside staff working on supporting activities, e.g., from the WHO Health Product Policy and Standards (HPS) department. WHO directors from various departments and regional advisors from the six WHO regional offices were also selected.

• NRAs (9 NRAs amongst which two SRAs): NRAs from various geographies, income groups, and maturity levels (MLs) were selected.

• Manufacturers (18 manufacturers; 7 diagnostics, 7 vaccines, and 4 medicines): manufacturers of various sizes and types of products were selected (vaccines, diagnostics, and medicines), operating in various geographies and levels of interaction with the RPQ department.

• Procurers and donors (14 procurers/donors): procurers and donors of various sizes, geographies, and levels of interaction with the RPQ department were selected.

• To add further external perspectives, industry associations (2) and a civil society organization (1) were also selected for interviews.

Though the majority of each interview focused on a qualitative discussion, interviewees were also asked to rate their perceptions on a scale of one to five, with five being the highest score. This rating allowed for a quantitative comparison of the various interviewees’ answers while ensuring that there was sufficient context for interpretation.

Finally, the interview questions were tailored to the type of stakeholder and their exposure to the relevant WHO activities, and therefore answers on specific topics (e.g., CRP, Global Benchmarking Tool (GBT), Norms and standards) were only considered when the stakeholder interviewed had direct experience with that topic.

B.1.3 Survey targeting NRAs

In addition to the interviews, a survey has been sent to 179 NRAs to collect their perceptions of RPQ department activities. The distribution by income group and WHO region of the 39 responses received can be found in Appendix 2.

The survey was anonymous, asking only for the region and income level in which the respective NRA was located. In total, the survey covered seventeen questions (see full list of questions in Appendix 5): eleven quantitative (i.e., rating questions on a scale of 1 to 5, with 5 being the highest score) and six qualitative. Amongst those, the survey included the same perception questions as the NRAs interviewed received, followed by text questions where NRAs
could argue why they had chosen a specific rating for the given WHO activity. Similarly to the interviews, if NRAs
did not have exposure to that particular WHO activity, they had the option to not answer the question. Lastly, they
could provide additional feedback at the end of the survey. When applicable, the survey results were compared to
the NRAs’ interview findings.

B.2 ASSESSMENT METRICS

The assessment in this report covers a range of metrics for measuring impact. These metrics are aligned with RPQ
department’s strategic priorities for the time between 2019 and 2023, namely:

- Strategic priority 1: Strengthen country and regional regulatory systems to support the push for Universal
  Health Care
- Strategic priority 2: Increase regulatory preparedness for public health emergencies
- Strategic priority 3: Strengthen and expand PQ and product risk assessment processes
- Strategic priority 4: Increase the scope and impact of WHO’s regulatory support activities

Impact themes were identified focusing on impact at a country level rather than on team mandate. The selection
resulted in the definition of 11 impact themes and 37 related assessment metrics, as set out in Exhibit 2 below.

Exhibit 2: Overview of the impact themes and assessment metrics considered in this report

<table>
<thead>
<tr>
<th>Impact theme no.</th>
<th>Impact theme title</th>
<th>Assessment metrics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Strengthening regulatory systems</td>
<td>A. Number of countries using the GBT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B. Number of NRAs that have reached ML3 or ML4 since 2018 Progress on implementation of WHO-Listed Authority (WLA) initiative NRA and procurer/donor rating and perception of the utility of regulatory system benchmarking activities</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C. Case study on a country that successfully strengthened its regulatory system (Ghana)</td>
</tr>
<tr>
<td>2</td>
<td>Improving the management of SF medical products and incidents</td>
<td>A. Number of incidents and SF products recorded in the global surveillance and monitoring system</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B. Number of global medical product alerts issued by the Incidents and Substandard and Falsified Medical Products (ISF) team</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C. Case study of a country with a national strategy or plan to strengthen prevention, detection, and response for SF medical products (Tanzania)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>D. Two case studies of LMICs that have improved the management of SF incidents (Nigeria and Brazil)</td>
</tr>
<tr>
<td>3</td>
<td>Increasing compliance of laboratories with required standards in LMICs</td>
<td>A. Absolute number and percentage of quality control laboratories (QCLs) for medicines prequalified in LMICs (of the total qualified)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B. Case study of a LMIC that has a prequalified medicines QCL (China)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C. Absolute number and percentage of members of WHO Network of National Control Laboratories (NCL) for Biologicals that are located in LMICs (out of the total members)</td>
</tr>
<tr>
<td>4</td>
<td>Strengthening PV</td>
<td>A. Number of countries with functional PV systems (VL3 and above)</td>
</tr>
<tr>
<td>Impact theme no.</td>
<td>Impact theme title</td>
<td>Assessment metrics</td>
</tr>
<tr>
<td>-----------------</td>
<td>-----------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| 5               | Enabling faster access to prequalified, SRA-approved and EUL-listed products      | A. Number of products that have been prequalified or EUL-listed  
B. Number of major donors requiring PQ for procurement  
C. Number of accelerated product registrations in countries under CRP  
D. Manufacturer, procurer/donor, and NRA/SRA perception of value-add of CRP in streamlining downstream approvals  
E. Number of product registrations that were accelerated for in-country introduction through other FPI pathways  
F. Number of product registrations in countries during public health emergencies that are accelerated using facilitated pathways supported by FPI, such as COVAX and CRP |
| 6               | Improving regulatory preparedness for public health emergencies                    | A. Number of countries assisted and supported in adapting their regulatory requirements to effectively address public health emergencies  
B. Number of countries with improved regulatory capacity preparedness for public health emergencies  
C. Case study on how a country improved its regulatory preparedness for public health emergencies (Pakistan) |
| 7               | Improving access to donor-funded procurement markets                               | A. Ratio of LMICs-to-non-LMIC manufacturers participating in donor-funded pooled procurement mechanisms  
B. Case study of a manufacturer from an LMIC that has recently participated in donor-funded pool-procurement mechanisms (Serum Institute of India) |
| 8               | Supporting Member States to build the ecosystem and capacities for quality and sustainable local production | A. Number of manufacturers and other stakeholders trained by the RPQ department in good manufacturing practices (GMP), other regulatory standards, and quality workshops  
B. Number of manufacturers that received PQ-/EUL-related technical assistance  
C. Number of countries that received ecosystem assessments for quality and sustainable local production  
D. Manufacturer, procurer/donor, and NRA perceptions of general manufacturing practices  
E. Case study on supporting a Member State to strengthen local production and the impact of the WHA74.6 resolution on local production |
| 9               | Assessing the economic RoI savings generated by PQ                                | A. Economic RoI: Savings generated by PQ |
| 10              | Contributing to                                                                    | A. Estimated deaths averted in the first year of COVID-19 |
### Impact theme no.

<table>
<thead>
<tr>
<th>Impact theme title</th>
<th>Assessment metrics</th>
</tr>
</thead>
<tbody>
<tr>
<td>saving lives</td>
<td>vaccinations in LMICs</td>
</tr>
<tr>
<td></td>
<td>B. Patients accessed/lives saved as a result of increased affordability</td>
</tr>
<tr>
<td>11</td>
<td>Increasing adoption of WHO guidelines and technical standards</td>
</tr>
<tr>
<td></td>
<td>A. Manufacturer, procurer/donor, and NRA perceptions of overall WHO guidelines and technical standards</td>
</tr>
<tr>
<td></td>
<td>B. NRA perception of usefulness of specific guidelines</td>
</tr>
</tbody>
</table>

### B.3 LIMITATIONS OF THE STUDY

Five key limitations were identified. First, the stakeholder groups with the highest direct exposure to WHO activities, who have a general understanding of the impact of these activities, were the ones chosen for interview. Priority was therefore given to WHO headquarters and regional offices staff, NRAs, manufacturers, procurers, donors, industry associations, and civil society organizations. Additional stakeholders, such as patients or regional regulatory bodies, were not interviewed. Consequently, the insights in this report are by no means exhaustive. Nevertheless, the key themes discussed in this report emerged consistently, and every effort has been made to fact-check statements.

Secondly, there were several challenges around the availability and quality of data. As far as possible, data was collected from WHO; additional data sources were included where necessary. That said, in some places, comprehensive data was not available (e.g., countries that have completed self-benchmarking in the PAHO region, countries that have experienced improved emergency preparedness and improved SF incident management mechanisms due to support from the RPQ department). In these cases, the most recent data available was used. In addition, certain data was not available either for reasons of confidentiality (e.g., data from donors and procurers in relation to their spend or their supplier base) or because it simply is not collected at present (e.g., number of countries using reliance as a concept, number of countries that have adopted various WHO released norms and standards). In these cases, other mechanisms like the NRA survey or case studies with selected member states were used to demonstrate the impact of the teams.

Thirdly, the agreed scope of this report included the activities of the RPQ department, except for the Vector Control Products Assessment Team and the Medical Devices team, which are both part of the PQ department. Finally, within the WHO Health Product Policy and Standards (HPS) department, only the norms and standards activities fell within the scope of this study. This means that this report is not an exhaustive review of the impact of all RPQ department activities or of all the teams within and related to the RPQ department.

Fourthly, given that the evaluation was performed over a short period of time and covered various teams and topics, it was not possible to perform a detailed assessment of each activity, achievement, and challenge of the RPQ department. Instead, the evaluation focuses on the key strategic issues of the RPQ department.

Lastly, we note that the RPQ department is in the process of implementing two new systems: the ePQS (a new IT system for the PQ process that is expected to begin rollout in May 2023.) and a new Quality Management System (QMS)\(^\text{18}\) based on ISO 9001:2015. These initiatives may tackle many of the recommendations provided in this report. However, considering how early these initiatives and projects are in their implementation, their impact was not considered within the scope of this assessment.

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\(^{18}\) The main objectives of RPQ department’s QMS are: to promote and assure consistency of process outcomes across the RPQ department, to increase effectiveness, transparency and efficiency of RPQ department’s processes, to improve cross-cutting processes between units and teams within the RPQ department, to strengthen collaboration and coordination with WHO entities outside RPQ department.
C Impact theme deep dives

C.1 STRENGTHENING REGULATORY SYSTEMS (THEME 1)

The key metrics covered under this theme for the assessment are set out below.

Exhibit 3: Key metrics covered and the methodology for the assessment under Theme 1

<table>
<thead>
<tr>
<th>Topics</th>
<th>No. Metric</th>
<th>Metric type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strengthening regulatory system</td>
<td>1A Number of countries using the GBT</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>1B Number of NRAs that have reached ML3 or ML4 since 2018</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>1C Progress on implementation of WHO-Listed Authority (WLA) initiative</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>1D NRA and procurer/donor rating and perception of the utility of regulatory system strengthening activities</td>
<td>Perception</td>
</tr>
<tr>
<td></td>
<td>1E Case study on a country that successfully strengthened its regulatory system (Ghana)</td>
<td>Case study</td>
</tr>
</tbody>
</table>

C.1.1 Quantitative assessment of metrics (Metrics 1A to 1D)

Mandated by Resolution WHA67.20, the WHO Regulatory Systems Strengthening (RSS) program implemented in collaboration with the work on Regulatory Convergence and Network (RCN) supports Member States in strengthening their regulatory systems by building their capacity, consistent with good regulatory practices and promoting regulatory cooperation, convergence, and transparency through networking, work-sharing, and reliance.

Overall, the work related to RSS can be summarized in four overarching activities:

1. Develop and maintain policy, tools, and methodology for benchmarking NRAs
   a. Develop, implement, promote, and revise the GBT in collaboration with NRAs and regional offices
   b. Manage and analyze data provided through the GBT
2. Plan and conduct benchmarking of priority NRAs
   a. Promote and implement WLA, including assessment of WLA candidates. This is a new responsibility, as the WLA concept was implemented in 2022
3. Provide support to priority countries in capacity building of regulatory systems
   a. Promote and support countries with the strengthening of their regulatory systems through development of IDP, provision of training sessions, and technical support, in close collaboration with regional offices and sometimes in partnership with other entities
   b. Promote and implement reliance on regulatory systems
   c. Collaborate with partners who also provide support, training, and technical assistance
   d. Ensure participation of NRA experts in PQ assessments and inspections (as further described under theme 8)
Strengthen regulatory capacity to respond to public health emergencies in priority countries.

Between 2018 and 2022, the regulatory system benchmarking activities were expanded to cover regulatory programs for two additional product types – blood products and medical devices, including in vitro diagnostics (IVD) – and were used to assist 12 NRAs in improving their MLs. The RPQ department also developed and launched a new initiative, WLA framework in 2022 to provide for a transparent and evidence-based pathway for regulatory authorities to be globally recognized, to promote access to and supply of safe, effective, and quality medical products, and to optimize the use of limited resources by facilitating reliance. These are discussed in detail below.

**Metric 1A: Number of countries using the GBT**

Over the last few decades, the WHO TPQ department has developed, implemented, and refined a robust model of support: the five-step capacity building strategy. An integral part of this strategy is the GBT, which WHO launched in 2016, and which is the primary means by which WHO objectively evaluates regulatory systems.

The five steps are:

- Develop tools for benchmarking Member States’ regulatory systems.
- Conduct benchmarking of NRAs using the GBT to identify strengths as well as improvement areas.
- Formulate an IDP to build on strengths, address improvement areas, and provide a blueprint for government investment and technical assistance from WHO and other development partners.
- Provide technical support during the implementation of the IDP.
- Continue monitoring progress and outcomes/impact through different follow-up visits.

Since 2018, a total of 22 countries have been formally benchmarked using WHO GBT; a further 71 were supported in performing a self-benchmarking. Few high-income countries (HICs) participated in the benchmarking; they are generally better equipped to strengthen their regulatory systems, and there are not many HICs without a strong regulatory system. Furthermore, WHA Resolution 67.20 mandates that WHO focus on LMICs.

**Exhibit 4: Number of countries using the GBT**

Looking at the data, one notices a dip in usage of the GBT in 2020, which may be due to COVID-19 pandemic requiring that NRAs shift priorities and the WHO postponing planned assessments. Uptake rose very quickly in 2021 due to the launch and availability of the virtual platforms for benchmarking.
Metric 1B: Number of NRAs that have reached ML3 or ML4 since 2018

There are four levels of classification for regulatory systems, called MLs. The lowest level is ML1 and the highest is ML4 and are defined as¹

- ML1: Some elements of regulatory system exist
- ML2: Evolving national regulatory system that partially performs essential regulatory functions
- ML3: Stable, well-functioning and integrated regulatory system
- ML4: Regulatory system operating at advanced level of performance and continuous improvement

Between 2018 and 2022, the RPQ department has assisted and enabled 12 NRAs (that together account for nearly 30% of the world’s population, set out in Exhibit 5 below) to achieve ML3 or ML4 status for at least one medical product stream. This brings the total number of countries that have achieved ML3 or ML4 for at least one medical product type from 2 in 2018 to 13 in 2022, which represents around 50% of the total global population. As evidenced by data, incentives to use the GBT are the greatest for vaccines (given that local manufacturers can only apply for PQ of a vaccine if their NRA is operating at ML3 or ML4: with 7 of the 12 NRAs achieving ML3 for vaccine production¹⁹.

Exhibit 5: Number of NRAs that have reached ML3 or ML4 since 2018

Metric 1C: Progress on implementation of WHO-Listed Authority (WLA) initiative

The framework for designating and publicly listing a regulatory authority as a WLA was “developed in response to Member State requests to develop a transparent and evidence-based pathway for regulatory authorities operating at an advanced level of performance to be globally recognized, thereby replacing the previous concept of SRAs.”²⁰ The WLA initiative is expected “to foster regulatory convergence, harmonization of approaches, and international cooperation, thus contributing to the improvement of good regulatory practices.”²¹

¹⁹ Countries that have received ML3 or ML4 for producing vaccines are compliant with a broader set of regulatory functions than countries who have ML3 or ML4 for vaccines without production. If a country has received ML3 or ML4 for vaccines without production and wishes to include vaccine production in their ML3 or ML4, they must first successfully conduct and pass a mini benchmark for the additional regulatory functions associated with vaccine production.

²⁰ Source: WHO (https://www.who.int/initiatives/who-listed-authority-reg-authorities)

²¹ Source: WHO (https://www.who.int/initiatives/who-listed-authority-reg-authorities)
As illustrated in Exhibit 6, in 2022 the WLA framework was officially launched, and the first three evaluations of candidates kicked off as part of a pilot. However, 57 assessments are still to be completed by 2027, a task that will require substantial resources. To tackle this, the RPQ department aims to finalize the WLA application of all 27 EU Member States as a block in 2023, in collaboration with the relevant agency heads. This would then leave four years to complete the final 30 assessments.

Exhibit 6: Introduction to WLAs and the outlook of the concept

C.1.2 NRA and procurer/donor rating and perception of the utility of regulatory system benchmarking activities (Metric 1D)

Interview results

Exhibit 7: NRA and procurer/donor scoring and perception of the utility of regulatory system benchmarking activities

The following four topics were raised the most during the interviews with NRAs and procurers/donors:

A. Successful development and implementation of a globally accepted benchmarking tool

NRAs confirmed the need for a global benchmarking tool and acknowledged the achievement of the RPQ department in developing a benchmarking tool that allows for a standardized assessment of regulatory systems while ensuring that the tool is widely accepted at a global level. They also appreciated the collaborative process with countries through negotiations and meetings.
“It was great to have the assessment standardized globally. [...] It is an accomplishment of WHO to bring so many countries on board, given that it is incredibly challenging to get global buy-in. WHO had so many back-and-forth negotiations on the tool to get acceptance globally.” (SRA)

“We fully understand how difficult it is to establish such an internationalized tool. They developed it for years. We translated it into [local language] and used it almost like a reference textbook for our agency. We value and we respect the GBT immensely.” (NRA)

“The GBT is a much-needed step to actually get countries motivated to implement the regulations, and to manage regulatory functions by using the guidelines. GBT gives a clear goal on what countries need to decide on basic policy and put in practice elements of governance.” (Procurer)

“The GBT completely changed the way we look at regulatory strengthening: we now have a good tool to measure the success of a country’s regulatory system. For many countries, all the regulatory work will now be focused on achieving ML3.” (Donor)

Next, NRAs recognized the positive impact that the tool and its related activities such as the IDP have had on their regulatory systems. It helped them not only create momentum to start actively addressing the gaps in their regulatory system, but also build relationships with other stakeholders such as manufacturers.

“GBT has created an excitement and momentum for NRAs to invest in their strengthening.” (SRA)

“Best thing that can happen to any regulatory agency. It is a long, detailed process but it is much needed.” (NRA)

“We have developed very good relationship with Vx manufacturers thanks to the WHO GBT. We have improved a lot our regulatory control of vaccine production, we achieved better understanding of the regulatory requirements.” (NRA)

B. Transparency and better usability of the tool for procurers and donors

Procurers/donors are interested in being able to use the GBT for their procurement decisions. To enable this, two themes were most commonly heard. First, procurers/donors are interested in better understanding the meaning of the MLs, including how they are being granted to NRAs.

“It is difficult to understand what the different MLs mean for procurement, therefore, right now we cannot link the MLs with our procurement decisions. We do not know what the different MLs actually mean or what their practicalities are.” (Procurer)

“A clear roadmap on how to get to ML3 or ML4 is important because at the moment procurement processes for non-SRAs take a lot longer.” (Procurer)

“As a procurer, I see the benefits that the GBT offers, but its usage is also unclear for us (...) from our perspective, usability is the main issue.” (Procurer)

Secondly, procurers/donors request that information on NRA’s status and progress be actively made available for their use. Having access to such information would help them understand better the state of a country’s regulatory system and could facilitate procurement decisions.

“There should be a way to make information regarding the current status of an NRA more actively available for procurers.” (Procurer)

C. Perception of low flexibility of the GBT and suitability to local contexts

Some NRAs have raised the concern that the local contexts in which the different agencies across the world operate are different. These differences are driven by many factors, including financial resources available to the agency and the legal/regulatory framework of their country. NRAs are desirous to see more flexibility in the benchmarking
criteria where alternate pathways to meeting criteria can be considered while keeping the NRA’s local context in mind.

- “Some of their requirements are particularly difficult to abide by, particularly the structure of the labs we use for post-market surveillance. Not all NRAs have this capability in house, they need to have flexibility around that.” (NRA)
- “Many elements of the GBT are not applicable to our NRA, it would be helpful if there was flexibility in the design to be more region/country-specific.” (NRA)

Linked closely to the above, NRAs would like opportunities to provide feedback and suggestions for improvement on the GBT to the WHO team. Given that they are the end-users of the tool, they believe that there should be more opportunity for dialogue between the NRAs and the RPQ department to raise concerns and share feedback.

- “Using the GBT is not a teacher-student relationship, it should be used as a platform that is two-way, NRAs should be able to suggest improvements too.” (NRA)

D. Capacity of the RPQ department to support the expected increased demand from NRAs with respect to regulatory system benchmarking activities

Finally, stakeholders have shared their concern for the capacity of the RPQ department to keep up with the demand for formal benchmarking assistance, given that more and more countries and their governments have expressed interest in improving their regulatory systems and achieving ML3. Stakeholders are generally aware of the limited size of the RPQ department and are therefore concerned that with the current size of the team, they could not respond sufficiently to this rise in assistance requests.

- “The WHO will have to try to deal with the increase in request with the same amount of people in the team, as now more and more governments are wanting to achieve ML3.” (Donor)
- “One of the most productive teams, amazing what they do with the limited number of staff. However, they need more full-time staff.” (SRA)

This concern also becomes important as many NRAs are relatively small agencies and do not have the capacity internally to go through a rigorous process like GBT benchmarking. For such agencies to strengthen their regulatory systems and achieve increased MLs, significant support will be required externally (including from the RPQ departments).

- “The downside of GBT is that it is very cumbersome and very complicated. For a small agency, it is a lot of work, they need someone who is very driven to make the assessment happen.” (SRA)

This concern for the team’s capacity is validated by the data as well. As of the end of 2022, about 70% of NRAs do not meet the GBT requirements for ML3 (50% maturity level 1 and 20% maturity level 2) – all will require support over the coming years from the RPQ department on their maturity journeys.

Survey results

The survey results are displayed in Exhibit 8. The spread of survey responses across the scale of 1 to 5 is similar to that found in the interviews with a largely positive response (60%+ respondents rating it a 4 or 5).
C.1.3 Case study on a country that successfully strengthened its regulatory system (Ghana) (Metric 1E)

Context

In May 2020, Ghana (Ghana Food and Drugs Authority (FDA)) became the second country in WHO African Region to attain regulatory system “ML3” – the second highest in the four-tiered WHO classification of national medicines regulatory systems.

Approach

A first set of evaluations of Ghana FDA – the national regulatory body for medical products in Ghana– was carried out in 2014 and 2015.

However, the RPQ department has had a long-standing relationship with Ghana FDA since 2006 – several of Ghana FDA’s assessors participated in the medicines team assessments since 2006 as well as 3-month rotations in PQ team at HQ, demonstrating RPQ department’s early and ongoing support to the authority.

In 2019, the authority was evaluated again using the GBT. The GBT evaluation started in March 2019, when WHO shared a first draft of the GBT benchmarking and findings, including the conclusion that 29 sub-indicators did not meet ML3 levels. Between July 2019 and April 2020, the WHO team and Ghana FDA worked together to execute the implementation of Ghana’s IDP. The support provided by the RPQ department included for instance the organization of a WHO good distribution practices workshop in March 2019, reviews, and follow-up on the IDP implementation status every three months, and placement of its regulators in a more mature NRA. Various WHO units and teams and WHO partners have been supporting Ghana FDA to enhance its regulatory capacity for several years.

As a result of the collaboration, the Ghana FDA attained ML3 status in April 2020.

Impact and outcome

Ghana was able to improve its ML from ML1 to ML3 in six years, showing the long investment and collaboration between WHO and the Ghanaian government. This makes Ghana one of two agencies in African region to get ML3 status and enables Ghana to apply in the future to become a WLA.

Having achieved ML3, Ghana was able to, for instance:
Support other countries with their benchmarking activities, now that it is recognized by other countries in the region as a mature NRA

Prove its worth when preparing to deploy COVID-19 vaccines, as it was the first country outside India to receive vaccines through the COVAX facility

Improve capacity to quickly develop specifications and guidance, and to establish a fast-track for marketing authorization, which enables Ghana to secure vital supplies at a time of acute scarcity across the region

Stakeholders from Ghana and WHO are both very satisfied with the work that has been realized:

Minister for Health, Hon. Kwaku Agyeman-Manu: “The President and the Government of Ghana are proud of this achievement.” He also made a passionate appeal to other regulatory agencies to “strategically partner with the FDA to learn and adapt best practices.”

Dr. Matshidiso Moeti, WHO Regional Director for Africa: “This is a milestone achievement. Strong national regulatory systems are critically important to ensure that when people seek treatment, they receive effective medication and are safe from harm. Access to healthcare is incomplete without guaranteed quality.”

Lessons learned

Ghana’s achievement reaffirms the collaboration between WHO and governments toward realizing the targets of universal health coverage and sustainable development goals. Furthermore, it showed that buy-in and involvement of senior leadership at the NRA are critical: in this case there was tremendous commitment and support from leadership at FDA Ghana that was the driving force behind this achievement.

C.1.4 Recommendations

Based on desk research and interviews, set out below are some options that the RPQ department can consider for actioning the key opportunities for improvement mentioned earlier in this section (referred to as “recommendations” in the table below). It is noted that the feedback shared by stakeholders in the 2018 Assessment was not raised at all during this assessment – indicative of the team having acted on the feedback and recommendations from the 2018 Assessment.

<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendation</th>
<th>Example initiatives</th>
</tr>
</thead>
</table>
| 1.  | Create self-sustaining opportunities for NRAs to support each other in the process of improving their ML by leveraging the willingness of mature NRAs to support other NRAs in the context of limited capacity of the RPQ department teams | a. Launch NRA peer learning forums more systematically: create peer learning forums where NRAs can learn from each other and advise each other on GBT processes (e.g., a mature NRA could coach a less-mature NRA). It would be key to ensure these forums are self-sustaining (i.e., can be organized and run with minimum involvement from the RPQ department teams)  
b. Launch an NRA peer coaching program: identify mature NRAs that can be paired with less-mature NRAs undergoing benchmarking  
c. Encourage NRAs to publish their success stories and experiences for other NRAs to use/learn |
<p>| 2.  | Conduct a short stakeholder consultation to understand NRA                      | a. Organize short focus groups in each region with NRAs currently undergoing self-benchmarking or formal |</p>
<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendation</th>
<th>Example initiatives</th>
</tr>
</thead>
</table>
| 2   | Concerns around the flexibility of the GBT | Benchmarking to understand pain points or perceived pain points  
  b. Based on the findings from focus groups, identify pain points that may just be perceived (due to misinformation or lack of information) versus those that may need resolution from the RPQ department team. For the former, consider releasing a FAQ (or updating existing FAQs). For the latter, consider whether revisions may be needed in the next iteration of the tool  
  c. Tailor support for smaller NRAs (e.g., those with limited resources) – special training that can be done in an expedited manner, better supporting documents, peer programs with NRAs in the region to augment staff, e.g., through secondments or rotations |
| 3   | Increase understanding of the regulatory system benchmarking process and outcome for non-NRA stakeholders (donors and procurers) | a. Consider if there is any information that can be made currently available to procurers and donors (without compromising on confidentiality under GBT-linked constraints), e.g., detailed understanding of the metrics underlying the different maturity levels and how NRAs are assessed against these |
| 4   | Improve access to the GBT, SharePoint, and results for relevant internal and external stakeholders | a. NRAs/internal: allow multiple users from each NRA to be able to access the tool and SharePoint  
  b. Internal: Ensure more awareness and increased use of existing processes that allow the RPQ department members to access and use GBT-related data (e.g., for the pharmacovigilance team to be able to access vigilance levels for Member States) |

C.2 IMPROVING THE MANAGEMENT OF SUBSTANDARD AND FALSIFIED (SF) MEDICAL PRODUCTS AND INCIDENTS (THEME 2)

The four key metrics covered under this theme for the assessment are given below.

**Exhibit 9: Key metrics covered and the methodology for the assessment under Theme 2**

<table>
<thead>
<tr>
<th>Topics</th>
<th>No.</th>
<th>Metric</th>
<th>Metric type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improving the management of Substandard and Falsified (SF) medical products and incidents</td>
<td>2a</td>
<td>Number of incidents and SF products recorded in the global surveillance and monitoring system</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>2b</td>
<td>Number of global medical product alerts issued by the Incidents and Substandard and Falsified Medical Products (ISF) team</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>2c</td>
<td>Case study of a country with a national strategy or plan to strengthen prevention, detection, and response for SF medical products (Tanzania)</td>
<td>Case study</td>
</tr>
<tr>
<td></td>
<td>2d</td>
<td>Two case studies of LMICs that have improved the management of SF incidents (Nigeria and Brazil)</td>
<td>Case study</td>
</tr>
</tbody>
</table>

Within the Regulation and Safety unit, the Incidents and Substandard and Falsified Medical Products (ISF) team is in charge of safeguarding the public from falsified products, or products that fail to meet their quality standards...
and/or specifications. This team follows the “prevention, detection, and response” strategic pillars through its various activities. The prevention pillar is centred around ensuring quality across the supply chain as well as securing the supply chain over time. Detection refers to the identification of SF products, which are often built to deceive. Finally, response is focused on preventing the spread of risk to the population. ISF activities can be described as follows:

- Build capacity in NRAs focusing on market control and surveillance activities, notably by supporting the development and implementation of national action plans to combat SF products.
- Manage the global surveillance and monitoring system (GSMS) database.
- Launch global medical product alerts.
- Act as technical unit of the Secretariat to the Member State Mechanism.

Since 2018, on the capacity-building front for NRAs the RPQ department has provided direct technical assistance to Tanzania in developing a national strategy for the management of SF medical products. This is part of the ISF’s evolution towards direct country support, as they are currently working on the development of a handbook destined for NRAs to then launch pilot projects in two to three countries. The ISF team has also been working on multiple pilots to develop new tools to support Member States, e.g., a web-based tool for risk-based Post Marketing Surveillance (PMS) and reference medicine, and vaccine spectral “fingerprint” technology focusing on COVID-19 medical products and aimed at rapidly identifying SF products with a handheld field device.

Additionally, in the five-year period between 2018 and 2022, the number of incidents reported to the GSMS in a five-year period has increased almost twofold (from 616 to 1,204), with reports coming in from all six WHO regions. The increase in reporting has resulted in an increase in the number of global medical product alerts issued. This number almost doubled from 20 in 2017 to 38 within the same five-year period in 2022. This is discussed in detail below.

According to survey results (please see Section B.1.3 for more details) demand for support for improving the management of SF medical products is expected to increase significantly with 58% respondents noting that they have received support from the RPQ department on this topic between 2018 and 2022 and 84% noting that they will need support in the next five years.

### C.2.1 Quantitative metrics for substandard and falsified products (Metrics 2A and 2B)

#### Metric 2A: Number of incidents and SF products recorded in the global surveillance and monitoring system

Launched in 2013, the GSMS for incidents and SF medical products is a database built to analyse and react quickly to tangible or emerging risks. Through this tool, “WHO can link cases and connect focal points around the world” to better understand risks. Furthermore, this database allows the RPQ department to notify NRAs and provide technical assistance, and also “identify weaknesses in systems and vulnerabilities in the supply chain.” Findings from the GSMS will then “inform more direct PMS, but also the work of the Member State Mechanisms” to support stakeholders’ collaboration on these issues.

The GSMS records both instances of incidents and the products involved in those incidents.

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22 Source: WHO (https://www.who.int/health-topics/substandard-and-falsified-medical-products#tab=tab_1)
23 Source: WHO (https://www.who.int/teams/regulation-prequalification/incidents-and-SF/mechanism#:~:text=In%202012%2C%20the%20World%20Health,considerations%20of%20intellectual%20property%20rights)
25 Source: Ibid.
26 Source: Ibid.
The following exhibit shows the total number of incidents, and products involved between 2013 and 2017 as well as between 2018 and 2022. These incidents are then broken down into WHO regional counts.

Exhibit 10: Number of products and incidents recorded on the GSMS between 2013 and 2022, and the geographical breakdown between all six WHO regions in the 2018 to 2022 period

Compared to the period between 2013 and 2017, in the last five years, the number of incidents recorded on the GSMS has almost doubled, which is indicative of growing awareness about the database as well as the benefits of reporting into the database.

Furthermore, the share of recording across WHO regions has also become more balanced in the last five years. In 2018, AMRO and EURO regions each contributed a third of the reporting into the GSMS. By 2022, that split was more balanced, with almost all regions (except AMRO and SEARO) contributing between 15% and 20% of the reports. This is a move in the right direction, indicating that the increase in awareness of the database and benefits of reporting is well-spread globally (and not just prevalent in one or two regions).

Metric 2B: Number of global medical product alerts issued by the Incidents and Substandard and Falsified Medical Products (ISF) team

The RPQ department issues global alerts when a “serious risk to public health in a wide geographic area” has been discovered. There are criteria that define whether a global alert should be issued for a particular product, which include assessment and validation that the product is SF, evidence of recent or continued circulation beyond a single country, or evidence that adequate steps have not been taken to inform healthcare professionals (HCPs) and consumers to remove these products from the supply chain. Alerts often involve multiple SF products in circulation.

Such alerts are publicly available on the WHO website or through a newsletter. These alerts contain advice for public authorities and photos of the SF products concerned.

Set out below are two graphs: the first displays the number of alerts between 2018 and 2022 and the second shows the geographic spread of these alerts.

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27 Source: Ibid. (on previous page)
28 Source: Ibid. (on previous page)
Between 2018 and 2022, the number of global product alerts almost doubled compared to the period between 2013 and 2017, from 20 alerts to 38 alerts issued.

The alerts have impacted and benefited all six WHO regions, with many alerts impacting more than one region and two alerts impacting all regions.

C.2.2 Case study of a country with a national strategy or plan to strengthen prevention, detection, and response for SF medical products (Tanzania) (Metric 2C)

The case set out below is an illustration of how WHO ISF works to provide technical assistance and help NRAs develop national strategies to strengthen their prevention, detection, and response against SF products. This project was done with the Tanzania Medicines and Medical Devices Authority (TMDA).

Context

TMDA's mission is to protect and promote public health by ensuring quality, safety and effectiveness of medicines, medical devices, diagnostics and other health-related products. Until 2017, TMDA was working on SF incidents, and this was done in a traditional way, more reactive to particular events. In 2012, WHO adopted Resolution 65.19, requiring Member States to develop national strategies on combatting SF products. This is what eventually led TMDA to develop a structured approach and establish five years 2017/28 – 2021/2022 national strategy against SF medical products.

Approach

Before developing that strategy, TMDA conducted assessments to evaluate the buy-in from stakeholders and check the numbers from the previous 10 to 12 years. These assessments led to enough evidence for TMDA to launch its strategy which relied on three pillars (prevention, detection, and response).

These pillars follow the WHO ISF "Prevention, Detection, Response" framework. For each of these pillars, three specific objectives were set up: to prevent entrance and consumption of falsified and substandard medicines; to detect falsified and substandard medicines and to respond to reported incidents of falsified and substandard medicines.
Each of these specific objectives were linked with targets, activities, key performance indicators and budget. TMDA then conducted a SWOT analysis for each of the three pillars and analysed the data from the past 10 years to best solve the problem of SF medical product, using the three pillars. As part of the national plan working, starting from 2017, TMDA and WHO collaborated on several activities:

- **Guidance and continuous collaboration.** TMDA interacted and received on and off support from WHO, both from the Headquarters in Geneva, and from the WHO regional and country office. For the action plan development phase in 2017-2018, TMDA appointed a focal person working with WHO to get guidance on the strategy, and consequentially the three pillars were developed and concretized with assistance and guidance from the WHO. There was full engagement, including day to day consultation with WHO.
- **Mobile phone application for reporting SF medical products.** In 2017, Tanzania became one of two countries (alongside Indonesia) to whom WHO piloted use of mobile phones for reporting SF medical products in public and private healthcare facilities.
- **Trainings.** From 2017, WHO funded and provided technical assistance and training to inspectors for the identification and reporting of SF medical products. In 2022, TMDA collaborated with WHO to pilot use of an e-tool (epione) for planning, implementing and reporting on risk-based post market surveillance.
- **Quality control.** WHO provided TMDA with approximately 25 mini field laboratory kits to be used quality assurance of medicines on market and specifically to detect SF medical products for medicines of public health importance including anti-tuberculosis, antimalarials and ARV imported into Tanzania.

**Impact and outcome**

The three pillars cemented the activities of TMDA regarding SF medical products, and also structured their work. As a result, Tanzania has not encountered any SF products for the past two years.

Additionally, TMDA has developed the capacities to conduct targeted investigative inspections twice to thrice a year, based on intelligence collection, and these have been very successful. TMDA has also been able to have inspectors posted at all 32 land border controls, which is a considerable achievement considering the size of the country. In 2020, TMDA developed a whistle-blower policy help TMDA stakeholders to report issues that might impact TMDA reputation among them being manufacturing, packaging, repackaging, relabelling, stocking, selling or distributing of SF medical products. The buy-in from police, customs, and other government agencies has also been a success. Lastly, TMDA has developed and for many years being implemented communication and public education strategic plan which helps the authority to air programs and campaign on TV and newspaper to increase the public’s awareness of SF medical products.

This collaboration between TMDA and WHO on the five-year plan has improved and structured the management of SF products in Tanzania. Although the planned mid-term review has not been achieved, TMDA now hopes to conduct a full assessment of the collaboration by June 2023.

**C.2.3 Two case studies of LMICs that have improved the management of ISF incidents (Nigeria and Brazil) (Metric 2D)**

**(a) Brazil case study on collaboration with ANVISA**

The case study set out below illustrates how Brazil, through ANVISA, has been able to improve its management of ISF incidents, through collaboration with the RPQ department.

**Context**
A universal healthcare system was established by law in Brazil in 1990. ANVISA, the Brazilian health regulatory agency was established in 1999, and since its inception has made preventing SF products from entering, being manufactured, or circulating in Brazil a priority. Most SF products found in Brazil are usually brought in from other countries, and thus pose an important threat to the national healthcare system. Protecting the Brazilian population against SF products entering the supply chain had been a priority for ANVISA.

**Approach**

ANVISA and the WHO ISF team have been collaborating since the ISF team’s inception in 2013. This collaboration is exemplified by active participation in the Member State Mechanism. Brazil has been (a) the acting Vice Chair for the Americas in the MSM steering committee (alongside the US) and (b) the Chair of the working group for strengthening the capacity of national/regional regulatory authorities for the prevention and detection of, and response to, SF medical products.

Due to the threat of SF products entering Brazil, international cooperation, and coordinated mechanisms for prevention, detection, and response are important for ANVISA.

In the past five years, ANVISA has taken multiple steps to strengthen their ISF systems and processes:

- In 2019, ANVISA became a nominated member of the National Committee to Fight Piracy and Crimes against Intellectual Property, to prevent the trade and spread of illicit products, focusing on medical products.
- In 2021, an automated tool was launched to continuously detect and monitor falsified medical products distributed via the internet.
- In 2021, Brazil established a regular process of self-assessment of the Inspection and Enforcement Office based on related indicators of the WHO GBT.

More specifically, ANVISA, through its cooperation and collaboration with the WHO ISF team, was able to achieve the following:

- WHO supported ANVISA in building regulatory and technical capacity.
- WHO helped ANVISA establish a strategic internal procedure for the notification of SF medical products to the GSMS. Reporting on the GSMS has now become a priority topic within ANVISA.
- WHO conducted investigations of SF medical products detected in Brazil, with widespread international distribution, to issue global alerts. One of such alerts was the Medical Product Alert N°5 in 2020 regarding Defibrotide. This product was manufactured and emerged outside Brazil, and then reached the country. The response to this alert was delayed due to the lack of international cooperation between the country of emergence of the product and Brazil.

**Impact and outcome**

Since the beginning of the relationship between ANVISA and WHO ISF, the collaboration has contributed to capacity building in Brazil, and provided a global system for notification of incidents. In global markets, the international articulation and the technical support provided by the ISF team play a critical role in the fight against SF medical products by NRAs.

The development of the GSMS has given ANVISA a way to systematically report potential incidents for evaluation, and this has been included as part of their strategic priorities. ANVISA has also highlighted the role of global alerts in dealing with real threats with wide geographic coverage.

**Learning points:**
ANVISA has highlighted international cooperation and collaboration amongst NRAs as an important future step for the WHO ISF team and would be ready to support WHO ISF with further developments in that area. The aforementioned Defibrotide global alert showed that cooperation, or the lack thereof, between countries is essential for stopping the spread of SF products. Participating in the MSM processes has permitted ANVISA to share its experiences and improve its international influence in public health.

(b) Case study with Nigeria TruScan program in collaboration with WHO ISF

**Context**

- NAFDAC has set itself the goal of reducing the prevalence of SF products in Nigeria to 5% by 2025. In 2004, the prevalence of SF products in Nigeria was 16.7%
- NAFDAC has been highly proactive and vigilant toward curbing SFs in the country and made all efforts to safeguard the health of the Nigerian populace. In a determined effort to combat falsified medicines, NAFDAC has deployed multifaceted strategies.
- NAFDAC and WHO have collaborated often and on many topics in relation to combating the prevalence of SF products in Nigeria including most recently in relation to procurement and deployment of handheld barcode scanners for traceability of medical products
- The android-enabled hand-held scanner is used to capture traceability event data by scanning GS1 standard barcodes when there is change of custody of medical products with the aim of securing the legitimate medicine supply chain and preventing infiltration of counterfeit medicines.

**Approach**

- In 2021 NAFDAC approached WHO for funding and technical assistance to procure and deploy android-enabled mobile scanners
- WHO accepted the proposal, and since then, WHO and NAFDAC have worked together to:
  - In early 2022, WHO funded the procurement of 74 scanners. In June 2022 support provided for training, and the deployment of 74+ health and warehouse workers to pilot the scanners. This has had tremendous impact already. NAFDAC was able to use these scanners for COVID-19 vaccines and was the only NRA to be able to do so
  - In continuation of WHO intervention, USAID procured an additional 74 scanners in August 2022, and completed a joint USAID/UNICEF/NAFDAC training program for 128+ health, regulatory and warehouse workers
- In this project collaboration with WHO has been especially impactful for NAFDAC in providing visibility of medicines from plant to patient, increased data quality to support pharmacovigilance, improved capacity to detect infiltration of substandard and falsified (SF) medications, and ultimately increased patient safety.

**Impact and outcome**

- 74 scanners procured
- 74 health and warehouse workers trained
- One instance already of speedy redressal by NAFDAC that has enabled identification and recall of a batch of SF products
- Increased traceability scanning coverage to 36 States and the Federal Capital Territory.
- The impact of the project was concretely felt when the agency was able to use the scanners to trace and remove from circulation a batch of COVID-19 vaccines that failed NAFDAC’s two-week sterility test. The
visibility provided from data capture by scanning during the distribution assisted in the prompt recall of the defective batch

Lessons learned

There is need for sustained stakeholder engagement to provide understanding of the requirements of traceability for medical products and build capacity to comply with proper use of scanners – this will improve adoption and improved data capture and quality.

C.2.4 Recommendations

Based on desk research and interviews, set out below are some options that the RPQ department can consider for actioning the key opportunities for improvement mentioned earlier in this section (referred to as “recommendations” in the table below).

<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendations</th>
<th>Example initiatives</th>
</tr>
</thead>
</table>
| 1.  | Deepen focus on capacity building at a country level to ultimately enable better prevention detection and response at a global level | a. Formalize lessons learned and feedback from work done to date with NRAs on capacity building (e.g., with Nigeria and Tanzania) to develop strategic priorities and programs for capacity building at local level.  
b. Ensure capacity building programs have a direct and clear link to global reporting and active participation in Member State Mechanisms.  
c. Ensure alignment of priority regions/member state of support in line with other RPQ department teams including for example the teams involved in RSS activities. |
| 2.  | Consider alternate pathways to bolster team capacity – critical considering increase in reporting and increase in support to Member States – both will require more capacity from team | a. Consider if data management activities/capabilities can be housed externally, e.g., with a vendor or a model like the one used for Uppsala Monitoring Centre (UMC) to manage VigiBase.  
b. Build capacity and capability in WHO regional offices. |

C.3 INCREASING COMPLIANCE OF LABORATORIES WITH REQUIRED STANDARDS IN LMICS (THEME 3)

The RPQ department provides support to improve the capacity of national quality control/reference laboratories for medicines, vaccines, and in-vitro diagnostics to meet international and/or prequalification standards. A selection of compliant laboratories is contracted to contribute to the WHO prequalification activities. Key activities that the RPQ department undertakes in relation to this theme include:

1. Strengthening capacity of laboratories in Member States through (a) provision of specialized technical support to individual national quality control laboratories based on direct requests from Member States or arising out of a Member State’s IDP generated from the formal benchmarking or self-assessment), or as part of the EoI to become a prequalified QCL, (b) provision of training on best practice, technical procedures, QMS, maintenance of equipment.

2. Strengthening capacity of laboratories in Member States through inspection of quality control laboratories before they are prequalified and regularly to monitor their continues compliance. The inspections confirm not only the existence of a system in compliance with WHO standards but also is there proficiency and capacity to
execute specific analytical methods. This contributes to regulatory capacity of the country and regions and provides tools for Members States to make robust, science-based regulatory decisions.

3. Promoting reliance on outputs from national control laboratories (NCLs), through building networks with confidential knowledge sharing data hubs, building mutual confidence, fostering harmonization of standards and test procedures, reduce redundant testing, including animal testing

4. Supporting the PQ team pre- and post-PQ by: “organizing and coordinating laboratory testing as dictated by various needs (e.g., pre/post prequalification, following complaints, quality surveys, support of national regulatory approvals, development of WHO standards and guidelines, resolution of ad hoc issues related to quality).”

Exhibit 12 below provides an overview of the different QCL-related activities undertaken across the RPQ department and how these vary across the three types of labs. Both commercial and national medicine QCLs can express their interest to receive PQ status, which enables them to “participate in WHO prequalification monitoring projects that are undertaken periodically to assess the quality of medicines procured by UN agencies. Each monitoring project focuses on a particular therapeutic area and medicines assessed include both WHO-prequalified and non-WHO-prequalified medicines”.[29] The List of PQ-ed medicines QCL is also of interest for manufacturers and for MS with limited national laboratory capacity, that seek to outsource some of their testing needs.

Exhibit 12: Key WHO RPQ activities related to medicines QCLs, vaccine NCLs and IVD Reference Labs

Between 2018 and 2022, the RPQ department has inspected 86 medicine QCLs and prequalified 15 medicine QCLs and increased the network of vaccine NCLs by 32 members

According to survey results (please see Section B.1.3 for more details) demand for support for increasing compliance of labs is expected to double with 32% respondents noting that they have received support from the RPQ department on this topic between 2018-22 and 66% noting that they will need support in the next five years.

The key metrics covered under this theme and the methodology for the assessment are set out in Exhibit 13.

29 Source: WHO ([https://extranet.who.int/pqweb/medicines/information/quality-control-laboratories](https://extranet.who.int/pqweb/medicines/information/quality-control-laboratories))
C.3.1 PQ for medicine QCLs (Metrics 3A and 3B)

Metric 3A: Absolute number and percentage of quality control laboratories (QCLs) for medicines prequalified in LMICs (of the total qualified)

Prequalified medicine QCLs are involved in (a) monitoring quality of prequalified products through pre-shipment and post-shipment testing of prequalified products as part of QA policies by procurers and NRAs and analysing samples from market survey that are conducted from time to time by the RPQ department in collaboration with NRAs to review quality of products on the market.

To become a prequalified QCL for medicines, the QCL has to go through four overall steps:

1. A QCL submits an expression of interest (EOI) to WHO for PQ.
2. The RPQ department verifies whether the lab is eligible for PQ. If the QCL is indeed eligible, they are invited to submit an application, including a laboratory information file (LIF), in accordance with the prequalification procedure for QCLs.
3. The RPQ department reviews the LIF (and quality manual) and requests any additional information if necessary. If the information provided is satisfactory, the information is shared with PQ INS team, who then organizes an inspection of the QCL.
4. If the QCL has successfully passed the PQ inspection and is deemed to be compliant with the PQ requirements, the lab is informed about its PQ status and is added to the WHO list of prequalified QCLs for pharmaceuticals.

To maintain its PQ status, the medicines QCL has to report annually on its activities and needs to report any changes in the LIF. This information is re-evaluated annually. In addition, a reinspection is usually scheduled every three years, by the PQ team INS team (routine post PQ inspection) or at an earlier point in time based on the recommendation of the inspection report (other post PQ inspection).

The WHO LNS team offers technical assistance to QCLs that are challenged by the PQ process and want to improve their capabilities, either before or after the PQ team inspection. Exhibit 14 provides a full annual overview of the medicine QCLs that were prequalified between 2018 and 2022.
Between 2018 and 2022, 15 medicine QCLs have received PQ-10 are located in LMICs (none in LICs), representing 67% of all QCLs that were prequalified between 2018 and 2022. Overall, as of December 2022, 53 medicines QCLs are currently prequalified (45% of which are located in LMICs and only 1 QCL is located in LICs).

No medicine QCLs were prequalified in 2021 due to the pause in on-site QCL inspections in March 2020. Exhibit 15 below sets out the details of the inspections conducted for medicine QCLs and how they were impacted by COVID-19 disruptions.

Exhibit 15: Number of inspections completed (by type of inspection) for medicines QCLs

This pause/disruption has also contributed to a lower total number of labs prequalified between 2018 and 2022 (15 labs) compared to the five-year period before that (20 medicines QCLs prequalified between 2013 and 2017). During this period, the LNS team was able to pivot and continue to provide technical support to QCLs in the PQ pipeline through using virtual technology and local partners to prepare them for inspections.
Delisting

Besides additions to the list of prequalified QCLs for medicines, seven QCLs were delisted between 2018 and 2022. They were delisted for two reasons:

- Relocation to new sites (which required a new application and inspection, etc.) – two medicine QCLs: one located in Ghana (delisted in 2021) and one in Pakistan (2022)
- Noncompliance with PQ requirements to provide the annual report – five medicines QCLs: one in Thailand (2020); one in Algeria (2019), one in India (2020), and two in the Netherlands (both 2020)

Time to prequalify

Exhibit 16: Time to receive PQ in months by country and by lab between 2018 and 2022

As illustrated in Exhibit 16, between 2018 and 2022, the median time for a QCL to be prequalified is 26 months and has varied substantially, ranging from one year to five years\(^a\). This is driven, among others, by the amount and type of adjustments needed for the lab to receive PQ, by resources available to the QCLs (e.g., LICs generally require more technical support to reach PQ standards), and by the levels of engagement from the QCL and its senior management. The RPQ department has already started to consider process changes to improve operational efficiency and use of the team’s resources in the most impactful manner, e.g., for labs that may require significant technical assistance to complete PQ, they are first being directed to seek the technical assistance before they submit an EOI, or their application is closed. A new EoI can be submitted after the QCL is ready for PQ.

Metric 3B: Case study of an LMIC that has a prequalified medicine QCL (China)

Context

An expression of interest to become a prequalified medicines QCL was received from the deputy director/quality manager of the Shenzhen Institute for Drug control (SZIDC) on May 17, 2014. To become WHO-prequalified, the QCL must be able to demonstrate that it adheres to WHO good practices for pharmaceutical quality control laboratories, and the relevant parts of WHO GMP.

Approached collaboration between the WHO LNS team and SZIDC

\(^a\) Not including Ghana FDA QCL, a significant outlier
For this purpose, the applying QCL has to submit an LIF. The screening of the LIF identified some deficiencies and SZIDC was requested to address them. In June 2015, SZIDC was accepted into the PQ pipeline after they managed to rectify the deficiencies identified during the screening of their application.

The next step involved an inspection from the PQ inspection team. However, as SZIDC did not yet feel confident to undergo a formal PQ inspection, they submitted a request for technical assistance in the form of a peer audit. In the peer audit, a team of experts, including laboratory staff and quality managers from other WHO-prequalified QCLs and international consultants, organized a mock audit in August 2016. They identified areas that needed to be improved, and further technical assistance was provided in the form of training to address specific deficiencies.

SZIDC implemented the recommendations from the peer audit and had their PQ inspection in January 2018. After review of the corrective action plan, PQ team INS informed LNS that SZIDC was deemed compliant, SZIDC was prequalified in May 2018.

Impact and outcome

Medicine QCLs play a vital role in testing and verifying that finished pharmaceutical products (FPPs) continue to meet international standards of quality and safety. If they fail, QCLs alert regulators, procurers, and manufacturers of the need for corrective action. This role is especially important when the FPPs concerned are imported or produced locally for treating life-threatening diseases or for promoting maternal and child health in vulnerable populations. But it can only be carried out successfully if the relevant QCL operates according to international standards. A WHO-prequalified QCL is such a lab: its services can be used with confidence.

Since their PQ in 2018, SZIDC has been involved in two WHO testing projects, namely the AFRO antibiotics and antimalarials testing in 2019 and the antimalarials testing in 2021. In addition, some SZIDC staff were part of the team conducting the WHO peer audit of the QCL of the Shanghai Institute for Food and Drug Control in March 2021, sharing their knowledge. Both activities bring recognition and prestige to the SZIDC; at the same time, they also come with the pressure to keep standards high.

To maintain their status, WHO-prequalified QCLs for pharmaceuticals are requested to submit annual reports of their activities and any changes in their lab operations. The annual reports submitted by SZIDC have indicated that besides playing an important role in the capacity building of QCLs in China through participation in peer audits, seminars, and WHO projects, SZIDC also plays an important role in providing testing services to local manufacturers.

C.3.2 Absolute number and percentage of members of WHO Network of National Control Laboratories for Biologicals that are located in LMICs (out of the total members) (Metric 3C)

Part of the activities of the RPQ department is to build and support regional and global collaboration and networks of laboratories with the aim to harmonize procedures meeting international standards and promote reliance. For vaccines, WHO has set up the Network of NCLs for Biologicals (NNB) which was established in 2017 with the aim to harmonize procedures for vaccine lot release testing in accordance with WHO’s international standards, build confidence, and promote reliance. The network includes two types of members:

1. Full members: national regulatory authorities (NRAs)/NCLs from countries producing WHO-prequalified vaccines who have responsibility for lot release of those vaccines.

2. Associate members: NRAs or NCLs of countries that are vaccine-recipient countries

The network is used for various purposes, including for instance:

- Foster sharing of quality and technical information on prequalified vaccines to ensure reliance, avoid redundant testing, save cost, and reduce risk
- Organize annual NNB meetings to discuss common points of interests, such as reducing and refining the R3 principles
- Support strengthening of NCLs through capacity building, implementation of harmonized testing methodologies, collaborative studies, and information sharing of lot release results (depending on consent of manufacturers)
- Promote reliance practices, promote harmonization of standards and testing, and develop best practices
- Organize workshops and training sessions to make sure that countries using different methodologies are aware of the latest harmonized technologies and procedures. For these training sessions, the WHO LNS team works together with the full members of the network or the NCLs of countries with ML3, who train the other members

Exhibit 17: Number of members of WHO Network of NCLs for Biologicals that are located in LMICs by region

As presented in Exhibit 17, as of December 2022, 47 NCLs are currently members of this network. Out of the 47 NCLs, 22 are in LMICs, representing 47% of all members. This share has remained relatively constant between 2019 and 2022. Apart from European countries, NRA/NCLs in African countries are moderately represented (nine members, or 20% of all members). However, due to low levels of biologicals production in Africa, there are only limited number of NCLs on the continent, given most vaccines are supplied via bilateral agencies such as the United Nations or Gavi. This situation may change in the coming years and efforts need to be made to strengthen the capacity of the NRAs and/or NCLs in view of this.

C.3.3 Recommendations

Based on desk research and interviews, set out below are some options that the RPQ department can consider for actioning the key opportunities for improvement mentioned earlier in this section (referred to as “recommendations” in the table below). There were no specific recommendations for increasing compliance of labs in the 2018 Assessment as this was out of scope.

<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendation</th>
<th>Example initiatives</th>
</tr>
</thead>
</table>
| 1.  | Increase efficiency PQ submission reviews by ensuring that QCLs only apply/are accepted when there is a readiness to meet | a. Develop, communicate, and implement clear end-to-end process for PQ of medicine QCLs to improve better management of timelines, e.g.:  
  - Clear criteria/checklist for acceptance of application in the PQ pipeline (currently, timeline is tracked from receipt of first EOI); |
<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendation</th>
<th>Example initiatives</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PQ criteria</td>
<td>perhaps this should be tracked after acceptance and receipt of the LIF)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Mandatory post submission meeting after receipt of an EOI, to estimate readiness for PQ</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Setting clear response time expectations with labs to be able to maintain their spot in the PQ pipeline</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Work with the PQ team inspection team to schedule inspections at a realistic timeline aligned with the readiness of the QCL</td>
</tr>
<tr>
<td></td>
<td>b. Reassess annual reporting requirements to consider if the reporting burden can be reduced (this is key because five out of the seven labs that were delisted between 2018 and 2022 were due to failure to meet annual reporting requirements)</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Consider alternate pathways to bolster team capacity to meet increasing demands for support in strengthening lab capacities</td>
<td>a. Harness regional expertise from PQ-ed QCLs to support peer audits/direct technical assistance to increase preparedness for a formal PQ team inspection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b. Continue to leverage the expertise of the NNB members to provide training and capability-building activities to associate members. Leverage other labs in the region where possible (use train-the-trainer approach), go-and-see visits, etc.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>c. Return to provide hands-on lab training in collaboration with partners to increase technical competencies of the lab analysts</td>
</tr>
<tr>
<td>3.</td>
<td>Streamline support to priority regions and Member States – a targeted focus will be key in building global lab capacity especially keeping in mind resource constraints</td>
<td>a. Continue to increase the number of the participating labs in the respective networks to enable a supportive environment, as today less than 30 % of WHO MS are included</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b. Considering the many complexities that QCLs in LICs face, develop a targeted action plan and funding to improve LIC participation in medicines QCL PQ</td>
</tr>
<tr>
<td></td>
<td></td>
<td>c. Specific focus on ensuring spread of lab capacity within and across regions – especially critical as access to compliant QCLs is a critical indicator in the GBT for an NRA</td>
</tr>
</tbody>
</table>

### C.4 STRENGTHENING PHARMACOVIGILANCE (THEME 4)

The key metrics covered under this theme and the methodology for the assessment are set out below.

Exhibit 18: Key metrics covered and the methodology for the assessment under Theme 4

<table>
<thead>
<tr>
<th>Topics</th>
<th>No.</th>
<th>Metric</th>
<th>Metric type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strengthening pharmacovigilance</td>
<td>4A</td>
<td>Number of countries with functional PV systems (VL3 and above)</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>4B</td>
<td>Number of case safety reports in the WHO global database</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>4C</td>
<td>Number of countries that have websites meeting WHO best-information-practice criteria</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>4D</td>
<td>Number of countries implementing active surveillance mechanisms</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>4E</td>
<td>Manufacturer, procurer/donor, NRA perception of the utility of PV activities</td>
<td>Perception</td>
</tr>
</tbody>
</table>
C.4.1 Quantitative assessment of Pharmacovigilance impact metrics (Metrics 4A to 4D)

As part of the Regulation and Safety unit within the RPQ department, the PV team’s mandate is to detect, assess, understand, and prevent adverse effects or other issues linked to vaccines and medicines. An integrated WHO PV team was established in 2020 to combine work related to the safety of medicines and vaccines within the RPQ department. Key activities that the PV team conducts to deliver on its mandate include:

- Supporting countries in developing functional pharmacovigilance systems including active surveillance mechanisms
- Promoting the reporting of adverse events to the WHO global database, VigiBase and supporting the early detection of previously unknown safety problems of medicines
- Establishing and convening two safety advisory committees, to review the safety of prequalified medicines and vaccines that are recommended by WHO programs (IVB, HIV, TB, Malaria, etc.) - timely recommendations from whom help manage negative perceptions about priority medicines and vaccines
- Promoting and enabling the exchange of reliable information and countering misinformation on vaccines and medicines

Between 2018 and 2022, WHO PVG has:

- Assisted 14 new countries in developing functional pharmacovigilance systems (Vigilance Level (VL) 3 or above)
- Supported (technically or financially) at least 12 countries in implementing active surveillance mechanisms
- Implemented the Smart, Safety, Surveillance (3S) concept in six countries to enhance their ability to collect, assess, and act on safety data
- Evaluated and added 49 websites to the Vaccine Safety Net (VSN), a network of websites providing credible information on vaccine safety
- Other elements of note:
  a. Established an integrated Pharmacovigilance team within the RPQ department for medicines and vaccines – to enable common tools around reporting and data management across teams. Since 2021, (a) data management tools (e.g., VigiFlow) have been made available to Essential Programs on Immunization (EPI) program managers (and not just the NRA) to report vaccines-related adverse events; (b) EPI program managers (and not just NRA) have access to the WHO global database of individual case safety reports, VigiBase, to be able to monitor performance of AEFI systems and to identify signals
  b. Increased the frequency of the meetings of the Vaccines (GACVS) and Medicines (ACSoMP) Safety Advisory Committees to review adverse events on priority products, including COVID19

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32 “The 3S concept was applied to 6 countries to enhance their ability to collect, assess, and act on safety data on products of relevance to these countries. Although each country varied in the capacity to monitor safety of medicinal products at the start of the project, the study has demonstrated that the 3S strategy can be applied equally to pharmacovigilance (PV) systems with different capacities.” Source: Iessa et al., 2021 (https://link.springer.com/article/10.1007/s40264-021-01100-z)


34 Source: WHO (https://www.who.int/groups/global-advisory-committee-on-vaccine-safety)

35 “ACSoMP was established in 2003 to provide advice to WHO, including its Collaborating Centre for International Drug Monitoring (the UMC), and through it to the Member States of WHO, on safety issues relating to medicinal products.” Source: WHO (https://www.who.int/groups/ACSoMP/sub-committee)
vaccines and therapeutics. Webpages for GACVS and released statements have had ~420,000 unique views in the last 2 years.

c. Established a new COVID-19 subcommittee under GACVS: Established by the RPQ department in December 2020 to provide timely input to the SAGE for their Policy recommendations on all the new COVID-19 vaccines. The GACVS met weekly for 6 months in Q1/Q2 2021, followed by 8 monthly meetings in 2022 and comprised of 10 Experts and EMA representatives. The RPQ department supported this committee with:

- safety reviews, press briefing notes/FAQ for the WHO senior leadership and DCO on serious adverse events reported with the new COVID-19 vaccines
- developed a new guideline for the case management of TTS\(^{36}\) and updated an existing guideline on the management of anaphylaxis with new COVID-19 vaccines

d. Established a new the nOPV2\(^{37}\) sub-committee under GACVS: Established by the RPQ department in January 2021 to advise WHO and its Member States on safety outcomes following the use of the new vaccine, during the EUL period, prior to the availability of Phase III clinical trial results. This is to ensure that the overall decision to accelerate the timeline to roll out nOPV2 from its initial to wider use under EUL and beyond, will be informed and based on sound evidence. The RPQ department has supported this committee by:

- establishing safety criteria for nOPV2 surveillance standards for routine passive surveillance and AESI Surveillance; and
- together with the WHO Polio secretariat, organizing the subcommittee meetings to review the analyses of routine safety data from the field, during the initial use of nOPV2

e. Developed and launched 3 new e-learning courses (listed in rows 2, 4 and 5 in the table below), updated 2 existing ones (listed in rows 1 and 3 in the table below) and made these available on the WHO Open and iLearn Platforms (available in many languages including those in addition to the 6 WHO languages like Bahasa, Kazakh, Vietnamese, and Portuguese). Additional details in table below.

<table>
<thead>
<tr>
<th>E-learning course</th>
<th>Learning objective</th>
<th>Languages the course is available in</th>
<th>No. persons enrolled(^{38})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Vaccine safety basics(^{39})</td>
<td>To introduce participants to the foundations of vaccine pharmacovigilance - to provide healthcare professionals whose work involve vaccine safety issues, with essential knowledge about vaccines and their safety aspects. These professionals can include nurses, midwives, community health workers, as well as pharmacists, medical doctors and immunization programme or vaccine safety communication officers.</td>
<td>English, Bahasa, French, Spanish, Russian and Ukrainian</td>
<td>40,000 +</td>
</tr>
</tbody>
</table>

\(^{36}\) thrombosis with thrombocytopenia syndrome (TTS) following vaccination to prevent coronavirus disease (COVID-19)

\(^{37}\) A type 2 novel oral polio vaccine (nOPV2) that became the first vaccine authorized by WHO for use under Emergency Use Listing (EUL) in November 2020

\(^{38}\) At the time of this assessment, data for no. of learners that have completed the courses was not available

\(^{39}\) [https://openwho.org/courses/vaccine-safety-basics](https://openwho.org/courses/vaccine-safety-basics)
2. AEFI Causality assessment courses[^40][^41] To understand the complex nature of causality assessment in Individual Case Safety Reports (ICSRs) and the value of structured approaches. And then for the learner to be able to apply the theoretical concepts for individual case causality assessment using examples. English, Portuguese and Spanish 12,000 +

3. Principles and Processes of AEFI Casualty Assessment[^42] To guide the learner to undertake a systematic and standardized process for assessing causality of a serious adverse event following immunization (AEFI) using the WHO methodology. English 5,000+

4. Recognizing and managing anaphylaxis[^43] To provide practical guidance to the frontline health care providers and vaccinators key information on its identification, differentiating it from other clinical conditions such as fainting and other stress related responses. It also provides step by step guidance on the case management at the site of the event and the process of referral. English, Arabic, Chinese, Kazakh, Vietnamese, Portuguese, Russian 18,000+

5. Vaccine Safety Communication[^44] To amongst other things, enable learners to respond to vaccine safety rumours and formulate a vaccine related crisis communication plan. Chinese 3,800+

f. Supported WHO priority public disease treatment programmes through signal analysis – for example, the review of neural tube defects with dolutegravir (HIV), review of reports of ocular events with miltefosine (leishmaniasis), hallucinations in children with delamanid (TB).

The key developments and achievements from above are discussed in further detail in the impact metrics below.

**Metric 4A: Number of countries with functional PV systems (VL3 and above)**

PV is one of the nine core sections of the GBT. It leads the evaluation of NRA’s VL and supports the development of functional PV systems[^45] through this benchmarking exercise[^46]. PV does this by first assisting NRAs in their self-benchmarking (or formal benchmarking) to identify gaps and then developing a clear plan to bridge the gaps including providing technical assistance and capacity-building support as needed. On the latter, the team supports capability building for NRAs in a few different ways (e.g., organizing and sponsoring visits to NRAs that have a more advanced functional PV system, developing and sharing data management tools, etc.).

Exhibit 19 shows the countries that have developed functional PV systems (as measured by the GBT).

[^40]: https://learning.who-umc.org/visitor_catalog_class/show/34308
[^41]: https://learning.who-umc.org/visitor_catalog_class/show/37752
[^42]: https://gvsi-aefi-tools.org/elearning.html
[^43]: https://openwho.org/courses/anaphylaxis
[^44]: https://openwho.org/courses/vaccine-safety-basics-communication-zh
[^45]: An NRA with a functional PV system is VL3 or above, which corresponds to the following criteria: establishing, monitoring, and reporting functions; post-marketing vigilance; and access to reliable information. Source: WHO ([https://www.who.int/publications/i/item/9789240020245](https://www.who.int/publications/i/item/9789240020245))
[^46]: Source: WHO ([https://www.who.int/publications/i/item/9789240020245](https://www.who.int/publications/i/item/9789240020245))
### Number of new countries achieving VL3/4 per year, 2016-2022

<table>
<thead>
<tr>
<th>Year</th>
<th>LIC/LMICs</th>
<th>LMICs</th>
<th>HICs</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>2022</td>
<td>4</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2021</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>2</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2019</td>
<td>2</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td>2</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Exhibit 19: Number of new countries achieving VL3/4 per year between 2018 and 2022

Between 2018 and 2022, 14 NRAs developed functional PV systems, with 79% of them being low- or middle-income countries (11 of 14). Almost all (13 of the 14) NRAs received technical assistance and support from the RPQ department to achieve this. Additionally, six of the 14 countries that have achieved VL3/4 between 2018 and 2022 have done so in 2022. This is likely driven by the clearing of an assessment backlog due to COVID-19.

It is worth noting that the RPQ department also supports countries through other mechanisms, notably via international platforms and networks such as WHO Program for International Drug Monitoring (PIDM), established pursuant to WHA16.36. The number of countries in the WHO PIDM supported by WHO has increased from 163 in 2018 to 175 in 2022.

**Metric 4B: Number of case safety reports in the WHO global database**

The RPQ department strengthens the culture of reporting globally by helping NRAs understand and appreciate the benefits of reporting and supporting them with tools and training sessions to enable them to take decisions based on the data collected.

WHO monitors individual case safety reports (ICSR) through the VigiBase global database. This database is maintained by WHO Collaborating Centre for Drug Monitoring. Established in 1968, the database has collected over 30 million ICSRs since then. VigiBase’s mission is to ensure that safety problems in medicines are rapidly identified and reported; it is the largest database of its sort in the world.

Exhibit 20 below highlights the evolution of ICSRs (for both medicines and vaccines) on VigiBase between 2018 and 2022. This exhibit also displays the split between reporting for LMICs and HICs.
The total number of ICSRs logged on VigiBase more than doubled between 2018 and 2022, compared to 1968 to 2017 (49 years), indicating a significant increase of reports on VigiBase. This is largely driven by an increase in reports for COVID-19 vaccines which contribute to 14% of reports in the entire database. HICs contributed to more than 80% of the reports between 2018 and 2022 as well since the inception of VigiBase (1968 to 2022). Within HICs, the US represents the highest share (41% of all ICSRs to date). China is the middle-income country with the highest share of reporting (8%) – most reports for medicines. Reporting by LMICs saw an increase between 2018 and 2020 (where they nearly doubled each year) and remained unchanged at 900,000 between 2020 and 2022.

Metric 4C: Number of countries that have websites meeting WHO best-information-practice criteria

Following a request from governments, key nongovernmental organizations, and UNICEF, WHO initiated the VSN to counter misinformation about vaccines in 2003. The RPQ department undertakes the following activities to enable access to best information on vaccine safety for internet users around the globe:

1. Website membership registration: the PV team assesses and evaluates candidate websites on a rolling basis. If a website meets the eligibility criteria, then the PV team conducts a formal assessment. During this evaluation, the website is assessed against content, credibility, design, and accessibility criteria. Following implementation of the recommendations addressed, the website can join the VSN and be added to the list of websites with reliable information on vaccines safety.

2. Capability building: the PV team helps develop tools and activities to improve high-performing online vaccine safety information and communication interventions. The VSN website’s package is one of the tailor-made tools aiming to encourage more institutions of limited resources to build websites meeting the good information practices criteria and disseminating reliable vaccine safety information.

3. The PV team established partnerships to facilitate availability of online science-based safety information to combat misinformation. In this connection, together with NewsQ and in collaboration with the Wikimedia Foundation DC, VSN members and Wiki editors created eight articles and edited 461 existing articles, resulting in 455,000 views within the first month. The program so far has generated two million article views from the 61 articles edited and 28 new articles created.

4. Maintenance of the VSN membership: to ensure continuous adherence to the good information practices criteria, the PV team reevaluates the VSN members’ websites every two years.
Exhibit 21 sets out the number of countries represented by websites on the VSN as well as the total number of websites.

**Exhibit 21: Number of websites represented in the VSN**

Between 2018 and 2022, 49 additional websites joined the VSN, leading to a total of 104 websites bringing access to credible, correct, and timely information. There has been a positive trend in the representation of low- and middle-income countries: only 28% of the websites were LICs, LMICs, or UMICs before 2018, but as of 2022, 43% of the websites have been from these countries.

The number of visits increase with the number of websites; however, this is not a proportional increase as some websites grab a large share of the visits, including the US-CDC, Immunization Action Coalition, Somos Mamas, or Public Health England.

While the overall growth trend of the number of websites in the VSN is positive, the growth between 2018 and 2020 (38%) was faster than between 2020 and 2022 (16%). This slower growth occurred during the COVID-19 pandemic – likely due to resourcing constraints and reprioritization of the team’s tasks due to these constraints. Additionally, most websites’ owners are healthcare providers or policy makers. With the COVID-19, those teams did not have enough means to engage with WHO and implement recommendations to improve their websites.

These websites are available in 36 languages, including four of the five most spoken languages in the world (Mandarin, English, Spanish, French), and other major regional languages such as Russian or Arabic.

Of the ten most populated countries in the world, three (Pakistan, Indonesia, and Bangladesh) do not host a VSN member website.47

**Metric 4D: Number of countries implementing active surveillance mechanisms**

ICSRs give an overview of the situation related to safety problems with medicines; these are spontaneous measurements that have no denominator and thus do not enable calculation of rates and frequency. Hence, active surveillance is used by the PV team for intensive monitoring, and gain understanding of potentially unknown adverse events. This type of monitoring is shorter term and more resource intensive than standard reporting.

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47 List of the ten most populated countries: China, India, the US, Indonesia, Pakistan, Brazil, Nigeria, Bangladesh, Russian Federation, and Mexico. Source: World Bank (https://data.worldbank.org/indicator/SP.POP.TOTL?most_recent_value_desc=true)
Currently, the WHO PV team supports the implementation of various forms of active surveillance methods, including two of the most used globally:

1. **Cohort event monitoring (CEM)** is a form of drug-based monitoring in which the effects of a new drug are analyzed for a group of people taking it over a defined period.

2. **Sentinel sites (SS)** is a type of setting-based monitoring. There, designated institutions are selected based on their specialization to monitor the effects of drugs in those particular areas.

Exhibit 22 introduces the number of LICs, LMICs, and UMICs that implemented and/or experienced CEM and/or SS between 2017 and 2022 as well as the disease programs they cover.

Exhibit 22: Number of LICs, LMICs, and UMICs that implemented and/or experienced some form of active surveillance

```
Number of LICs, LMICs, UMICs that have implemented and/or experienced some form of active surveillance, # LICs, LMICs, UMICs in 2017 and 2022, # of SS and CME

<table>
<thead>
<tr>
<th></th>
<th>2017</th>
<th>2018-2022</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sentinel Sites</strong></td>
<td>9</td>
<td>21</td>
</tr>
<tr>
<td><strong>Cohort Event Monitoring</strong></td>
<td>0</td>
<td>16</td>
</tr>
</tbody>
</table>

XX1: xx of the countries are in very early stages
XX2: xx of the countries are in very early stages

Source: Interview with WHO PVG team (Dec 5, 2022), WHO Data, Vaccine Safety Net
```

In between 2018 and 2022, out of the 37 cases of implementation of CEM and SS in low- and middle-income countries, 25 new low- and middle-income countries implemented or experienced CEM and SS mechanisms compared to 2017 numbers – 848 of them were supported by the PV team (either technically or financially) in 2022.

---

48 Three countries in SS implementation (Indonesia, Nepal, Lebanon) and five countries in CEM implementation (Iran, Jordan, Egypt, Philippines, Bangladesh)
C.4.2 Manufacturer, procurer/donor, and NRA perception of the utility of PV activities (Metric 4E)

Exhibit 23: Manufacturer, procurer/donor, NRA perception of utility of PV activities

Overall, the perception of the RPQ department’s PV activities is mixed. Stakeholders who have worked directly with the PV team acknowledge the importance of the team’s support – especially when it comes to training sessions.

- “The work we did [on Pharmacovigilance] with the technical experts and the team from WHO, especially with the review of the risk-benefit plan [...]. Training is always great to have as we increase our own capabilities, also awareness.” (NRA)
- “The 3S program has helped tremendously – its focus on training our staff has helped us a lot [...]. There was good collaboration with NRAs on this project.” (NRA)

However, many stakeholders note (even those with positive perceptions) that the global trends in the last few years – particularly driven by the COVID-19 pandemic – have left stakeholders desirous of seeing the RPQ department play a stronger role in PV activities. On pharmacovigilance, stakeholders have noted opportunities for the RPQ department to (a) play a more central and proactive role and (b) to support even more in building capabilities at a country level. More specific insights about the kind of roles and topics are shared below.

A. Taking on a more central and proactive role in the PV ecosystem – drive coordination and build coalitions

During the interviews, stakeholders have noted that there are many different organizations active in the PV ecosystem – each deploying their own set of mechanisms, e.g., manufacturers are developing public awareness and NRA capacity-building programs so that they can collect better safety data on their products. Almost all NRAs acknowledge that they have PV programs, but many are not yet coordinating or working with the RPQ department on this topic.

- “[There is a] need for a central coordinating body that can bring together all the work happening between different stakeholders – this is a big gap in the ecosystem.” (Vx Manufacturer)

Stakeholders note that the RPQ department could play a more active part in the PV ecosystem. As an example, they note that while the RPQ department has a presence on the information collection side, there is lack of visibility or clarity on how that data is used to strengthen the system.

- “PVG is more reactionary than systemic, the team steps in when something is wrong.” (Procurer)
- “The PV activities from WHO are more passive … [...]. The downside to a passive approach is that it is very dependent on country reporting.” (Procurer)
- “Exchanging information could be useful for us, but right now, we are more providers than beneficiaries of this exchange of information.” (NRA)
B. Playing a more focused role in building Member State capabilities

As noted above, NRAs find the RPQ department’s training-related support impactful. Stakeholders note the benefit of strengthening local capabilities – it will not just strengthen regulatory systems across the world but also positively impact safety reporting as NRAs develop appreciation about the benefits for safety reporting to them and also develop the tools needed to do it efficiently.

- “Right now, there are [low] local PV capabilities, so very little is being captured and very little being reported. WHO is pushing global reporting and capturing of data […], but perhaps a focus on building capabilities at a country level would be more impactful.” (Vx manufacturer)
- “We [NRAs] could use some help with materials, strategies, and implementation guide to increase awareness on safety reporting.” (NRA)

Additionally, NRAs note that capability building needs to be done not just for NRAs but also for doctors, healthcare workers, and others that may become eventual reporters of safety events.

- “More needs to be done to train the many different stakeholders in Member States – more for the actual reporters – especially in the local languages.” (NRA)
- “Materials even like video graphics need to be made available to the people [in Member States] that do the reporting, like healthcare workers.” (NRA)

Survey results

The survey results are displayed in Exhibit 24. Compared to those interviewed, more NRAs had exposure to PV activities (only 10% responded that that had no exposure compared to interview respondents where 50% or more had no exposure); however, perception continues to be mixed, with 1/5th of the respondents rating the area as one where there is opportunity for improvement.

Exhibit 24: Survey results on how the WHO’s PV activities have impacted NRAs

<table>
<thead>
<tr>
<th>On a scale from 1 to 5, how would you rate the impact WHO’s PVG activities have had in your country?</th>
<th>Number of responses, n=38</th>
</tr>
</thead>
<tbody>
<tr>
<td>High/some opportunity for improvement</td>
<td>8 (21%)</td>
</tr>
<tr>
<td>Mixed perception</td>
<td>6 (16%)</td>
</tr>
<tr>
<td>Very positive/positive opinion</td>
<td>20 (53%)</td>
</tr>
<tr>
<td>No exposure</td>
<td>4 (10%)</td>
</tr>
</tbody>
</table>

1. 5 being the best
2. One grade disregarded due to reference to ESF products in comment

C.4.3 Recommendations

Based on desk research and interviews, set out below are some options that the RPQ department can consider for actioning the key opportunities for improvement mentioned earlier in this section (referred to as “recommendations” in the table below). The recommendation to increase cross-functional collaboration (point 1
below) and focus on building local capabilities (point 2 below) are similar to those made at the time of the 2018 Assessment.

<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendation</th>
<th>Example initiatives</th>
</tr>
</thead>
</table>
| 1.  | Evolve team priorities toward a more active surveillance and more visible coordination role in the ecosystem to reflect the change in expectations and needs from various stakeholders (driven largely by COVID-19) | Work with a multi-stakeholder working group (internal and external) to:  
   a. Identify the biggest gaps in the PV ecosystem and the most impactful role(s) that WHO can play  
   b. Identify where the RPQ department should play a direct role and where the role of a coordination and coalition builder  
   c. Conduct a retrospective study to understand what the biggest shifts in requirements have been in the last five years  
   d. Find what might the team deprioritize from current activities – keeping in mind the resource constraints  
   Based on the assessment, some potential areas of focus for the team going forward could include:  
   a. Deepening focus on building capabilities for NRAs and DCMs  
   b. Systemizing collaboration mechanisms internally and externally  
   c. Concertizing focus on incentivizing the frequency and quality of Member State reporting into VigiBase by using the VigiBase data to detect safety signals and share information back with the ecosystem |
| 2.  | Set up incentives for Member States to increase the reporting frequency of adverse events on VigiBase | a. Make it a strategic priority to finalize the WHO Data Access Policy and relevant tools that will support stakeholder access to data and insights on adverse events reported to the WHO Global Database, VigiBase  
   b. Set up a dashboard of country reporting performance, enabling peer-to-peer comparison, to foster healthy competition and motivation amongst Member States |
C.5 ENABLING FASTER ACCESS TO PREQUALIFIED, SRA-APPROVED, AND EUL-LISTED PRODUCTS (THEME 5)

The key metrics covered in this theme for the assessment are set out below.

Exhibit 25: Key Metrics covered and the methodology for the assessment under theme 5

<table>
<thead>
<tr>
<th>Topics</th>
<th>#</th>
<th>Metric</th>
<th>Metric type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prequalification of medical products</td>
<td>5A</td>
<td>Number of products that have been prequalified or EUL-listed</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>5B</td>
<td>Number of major donors requiring PQ for procurement</td>
<td>Quantitative</td>
</tr>
<tr>
<td>Collaborative Registration Procedure</td>
<td>5C</td>
<td>Number of accelerated product registrations in countries under CRP</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>5D</td>
<td>Manufacturer, procurer/donor, and NRA/SRA perception of value-add of CRP of streamlining downstream approvals</td>
<td>Perception</td>
</tr>
<tr>
<td>Product registrations through other FPI pathways</td>
<td>5E</td>
<td>Number of product registrations that were accelerated for in-country introduction through other FPI pathways</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>5F</td>
<td>Number of product registrations in countries during public health emergencies that are accelerated using facilitated pathways supported by FPI, such as COVAX and CRP</td>
<td>Quantitative</td>
</tr>
</tbody>
</table>

C.5.1 Number of products that have been prequalified or EUL-listed (Metric 5A)

WHO prequalification aims to ensure access to key health products that meet global standards of quality, safety, and efficacy/performance in order to optimize use of health resources and improve health outcomes. The key PQ-related activities performed by the RPQ department include:

- Dossier assessment
- Inspection of manufacturing and testing sites/facilities
- Sample testing/independent performance evaluation

The above activities are performed in collaboration across the three PQ assessment teams and the PQ inspection team.

In addition to the above-mentioned core prequalification activities, the RPQ department also performs the following related activities:

- Maintain and monitor prequalified products
- Evaluate health products and/or assess risk to support health emergencies, shortages, and other needs outside the scope of PQ
- Provide scientific advice to manufacturers and other stakeholders
- Build the capacity of regulators and harmonize
- Support product evaluation activities at international, regional, and national levels, including reliance
- Provide technical advice to other WHO programs

Between 2018 and 2022, 439 products were prequalified by the RPQ department across medicines, vaccines, and diagnostics. In the previous 5 years (2013 to 2017), a total of 422 products were prequalified. Additionally, 51 products were EUL-listed between 2018 and 2022 (vaccines and diagnostics), against 12 between 2013 and 2017.

Between 2018 and 2022, the RPQ department completed 758 inspections in support of the PQ dossier assessments. Additional details below in Exhibit 26.
(a) Medicines

PQ for medicines/Finished Pharmaceuticals Products (FPPs) was launched in 2001. In 2001, only HIV products were in scope for PQ. Since then, the scope has been increased to 13 therapeutic areas, with 5 of the 13 being added in the scope between 2018 and 2022.

The types of products within scope have also been broadened. In 2011, WHO prequalification was broadened to Active Pharmaceutical Ingredients (API) and in 2017, it was further broadened to biotherapeutics, including biosimilars (the first biosimilar PQ occurred in 2019).

FPPs and biotherapeutic products can go through two types of assessment pathways as part of the PQ process: full assessment and abridged assessment (for products approved by an SRA or approved in the future by an ML4 WLA). An EUL pathway for medicines exists, although there has not been a need to launch this path so far, since all medicines considered for review have been eligible for prequalification.

Set out below in Exhibit 27 are the details of the number of FPPs and APIs prequalified between 2018 and 2022.

---

HIV/AIDS, Tuberculosis, Malaria, Reproductive health, Influenza, Neglected Tropical Diseases, Diarrhea disease, Hepatitis B and C, Infections in newborn and young infants and childhood pneumonia, Insulins and insulin analogues (BTPs), Certain cancers (BTPs), COVID-19 (BTPs and small molecules), Ebola Virus Disease (BTPs)

Infections in newborn and young infants and childhood pneumonia, Insulins and insulin analogues (BTPs), Certain cancers (BTPs), COVID-19 (BTPs and small molecules), Ebola Virus Disease (BTPs)
Between 2018 and 2022, the RPQ department prequalified a total of 343 products (272 FPPs and 71 APIs). These included 17 COVID-19-related products (10 FPPs and 7 APIs). Overall, even with COVID-19, the team was able to maintain PQ numbers at a level higher than in the previous 5 years.

COVID-19 applications were all eligible for prequalification (therefore, there was no need to launch an EUL process) and the team was able to establish a fast-track process to deal with the demands of a health emergency by putting in special processes. Some examples include early engagements with potential applicants to advise whether bio waiver is feasible or not, rolling submission of quality data while the bioequivalent (BE) study is progressing, handling of new and additional data submissions as top priorities (uninterrupted assessment, independent of the regular scheduled assessment sessions), etc. Exhibit 28 includes details on the median times for COVID-19 applications.

Exhibit 28: Median time for abridged assessment and full assessment for COVID-19 and non-COVID-19 FPPs and APIs
While there was no specific perception question on PQ, many interviewers raised the topic themselves. Those who had first-hand experience with the PQ medicines process and team were unanimously positive, with a high regard for the PQ Medicine team’s responsiveness.

- “PQ Meds team has been very forthcoming, and they have been very responsive when we reached out to them.” (Rx Manufacturer)
- “We have a transparent and open relationship with the PQ Meds team; they never hesitate to discuss any questions.” (Rx Manufacturer)

In addition to the positive feedback, some stakeholders also pointed out opportunities for strengthening the PQ process in all three teams; these are shared in Section (d) below.

(b) Vaccines

PQ for vaccines was launched in 1987 to provide advice to UN procuring agencies on the acceptability of vaccine for international procurement for Bacillus Calmette-Guérin (BCG) and Yellow Fever. Since its establishment in 1987, the procedure has been revised several times to introduce improvement and adapt to upcoming needs. The scope of vaccine PQ has been expanded to 26 unique disease types. Several vaccines were developed in recent years (Ebola, pneumonia, malaria), thus expanding the scope of PQ. The PQ vaccine team has two assessment pathways: full assessment and abridged assessment (for products approved by an SRA or in future WLA).

WHO has developed the time-limited EUL (in 2015 and its revision in 2020) to expedite the availability of medical products needed in public health emergency situations, to assist interested UN procurement agencies and Member States on the acceptability for use of specific products in the context of a public health emergency. The EUL procedure has been used to assess nOPV2 vaccine to address the rising cases of a vaccine-derived polio strain and for COVID-19 vaccines that were developed to address the COVID-19 pandemic.

Exhibit 29: Number of vaccines prequalified or EUL listed and prequalified between 2013 and 2022

Between 2018 and 2022, the RPQ department prequalified 46 vaccines and approved 12 vaccines for EUL listing (11 Covid-19 vaccines and 1 nOPV2).

At least 101 countries relied on the EUL of COVID-19 vaccines developed by the PQ vaccines team and relied on it to grant local authorizations and approvals in less than 15 days. Indeed, 101 countries (out of 145) approved AstraZeneca or Serum Institute of India vaccines within these 15 days after WHO EUL, and allocated doses in the
first COVAX allocation round. A case study on the EUL of AstraZeneca and Serum Institute of India COVID-19 vaccines and the resultant impact is available in the Appendix 3 of this report.

While there was no specific perception question on PQ, many interviewees raised the topic themselves. For those with exposure to the PQ vaccines process and team, the perception was unanimously positive with a lot of appreciation for the PQ vaccine team’s technical expertise, collaboration, and efforts during the COVID-19 pandemic.

- “The team is very small, but they are very collaborative and have an accessible environment compared to usual situations [...] They are also very flexible, they ask to fix things already during the review to save time. They did anything that was humanly possible to smooth the EUL granting.” (Vx Manufacturer)
- “They will bring in technical experts, this is tremendously helpful.” (Vx Manufacturer)
- “Even though their capacity is so stretched, they do still seem to be willing to engage in meetings with other health authorities to represent the rest of the world.” (Vx Manufacturer)

In addition, some constructive feedback for the PQ teams in general was shared by interviewees and is integrated in Section (d) below.

(c) Diagnostics

The first diagnostic product that benefited from the PQ label dates back to 2010. As of December 2022, nine disease areas\(^{51}\) are within the scope of the PQ diagnostics process, four of which\(^ {52}\) were included between 2018 and 2022. Similar to FPPs, APIs, and vaccines, PQ for diagnostics has two assessment pathways: full assessment and abridged assessment (for products approved by an SRA)\(^ {53}\).

EUL was first introduced and used for diagnostics in 2014 during the Ebola crisis.

Exhibit 30: Number of diagnostics products EUL listed and prequalified between 2013 and 2022

<table>
<thead>
<tr>
<th>Application decisions(^ {1})</th>
<th>Variations approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>45</td>
</tr>
<tr>
<td>45</td>
<td>50</td>
</tr>
</tbody>
</table>
| 122                           | 122                 | 122

Source: Data from WHO PQ IHO Assessment Team

1. This data includes the failed and listed products. It does not include the withdrawals and renewals.

<table>
<thead>
<tr>
<th>Year</th>
<th>Covid related</th>
<th>Emergency use listed</th>
<th>Prequalified</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2019</td>
<td>0</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>2020</td>
<td>10</td>
<td>27</td>
<td>10</td>
</tr>
<tr>
<td>2021</td>
<td>2</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>2022</td>
<td>10</td>
<td>8</td>
<td>10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>Covid related</th>
<th>Emergency use listed</th>
<th>Prequalified</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>9</td>
<td>43</td>
<td>16</td>
</tr>
<tr>
<td>2019</td>
<td>0</td>
<td>23</td>
<td>17</td>
</tr>
<tr>
<td>2020</td>
<td>13</td>
<td>26</td>
<td>14</td>
</tr>
<tr>
<td>2021</td>
<td>30</td>
<td>71</td>
<td>19</td>
</tr>
<tr>
<td>2022</td>
<td>19</td>
<td>56</td>
<td>22</td>
</tr>
</tbody>
</table>

\(^{51}\) HIV, Malaria, Hepatitis C, Hepatitis B, HPV, G6PD, Cholera, Syphilis, TB

\(^{52}\) G6PD, Cholera, Syphilis, TB

\(^{53}\) Source: https://apps.who.int/iris/bitstream/handle/10665/350642/9789240033146-eng.pdf
Between 2018 and 2022, the RPQ department prequalified 50 products and approved 39 for EUL (all EUL products are COVID-19 products). The focus on EUL for COVID-19 products has slowed PQ assessments and approvals for all other disease areas, with only eleven products being prequalified in the last two years. Overall, even with COVID-19, the team was able to maintain PQ numbers at a level higher than in the previous five years.

While there was no specific perception question on PQ, many interviewers raised the topic themselves. For those with exposure to the PQ diagnostics process and team, the perception was that efforts on the EUL process were particularly valuable during the COVID-19 pandemic. Furthermore, a lot of appreciation was given for the quality of the PQ diagnostics team’s work:

- “They are victims of their own success, people value the outcome of the assessment, especially organizations that are trying to figure out which tests are worth buying.” (Donor)
- “The value of emergency use listing use is very clear – if we compare it to PQ, it is already half or one third of normal time” (Dx Manufacturer)

However, concerns were raised about the slowdown in PQ approvals for other disease areas over the last three years. The same stakeholders also noted that this issue goes hand in hand with the larger issue around resource constraints in the PQ team which is discussed further in Section (d) below.

(d) Manufacturer, Donor/Procurer, NRA perception of the overall work on PQ assessments

While there was no specific perception question on PQ in the interviews, many interviewees raised the topic themselves. As shared above in sections (a), (b), and (c), stakeholders are appreciative of PQ’s effort and hard work in light of not just the increased demand due to COVID-19, but also resourcing constraints. Donors and procurers continue to rely heavily on PQ team’s assessments and decisions for guiding their procurement decisions. Manufacturers acknowledge the criticality of PQ’s timelines and how this can facilitate their work.

- “At a higher level, our collaboration with the PQ team is very important. Having a close interaction and engagement with them is very valuable.” (Donor)
- “PQ is absolutely fundamental for our activities.” (Procurer)
- “The RPQ department has been very fast, dedicated, and quick to respond to questions. It feels like they have gone through the approval process faster than the timelines they have set.” (Rx Manufacturer).

However, almost all stakeholders raised opportunities for improvement. Four themes emerge most commonly: (a) transparency on setting of PQ team’s strategic and workflow priorities; (b) operational efficiency; (c) specifically for vaccines and diagnostics, post-approval change notification process, and (d) resourcing and team capacity.

A. Transparency of setting of PQ teams’ strategic and workflow priorities

Donors, procurers, and manufacturers highlight considering the significant impact of the PQ teams’ activities on procurement decisions and business operations; currently, there is insufficient visibility on how the teams determine their strategic and day-to-day workflow priorities.

Stakeholders highlight an opportunity for a broader coalition building and collaboration between the RPQ department, other WHO departments, donors, procurers, and manufacturers to set global health priorities.

- “A pattern I have noted over the years is that the PQ department tries to set world priorities, and that can be frustrating for manufacturers or procurers who see other priorities.” (Procurer/Donor)
- “[The department] needs to become less opaque.” (CSO)
- “We need a seamless routine to communicate our [WHO department] priorities and RPQ department’s priorities; sometimes our department prioritizes a medical product and the RPQ department deprioritizes...”
it. We are not synchronized. We could have constructive co-consultation between manufacturers, the [disease department] and RPQ department, instead of having siloed conversations.” (Colleague from a WHO department)

- “They should reach out and collaborate with us more if they need to prioritize their pipeline with respect to our applications, we can provide inputs based on our business priorities.” (Procurer/Donor)

Manufacturers especially are keen to collaborate more with the PQ team to help prioritize their own pipeline of applications, thereby enabling them to match PQ process timelines better with their business priorities. While the more proactive manufacturers or manufacturers with larger teams/resources currently do this by, e.g., setting up quarterly meetings with the PQ team to review their pipeline – there is an opportunity to do this more systematically.

- “We recently started asking for quarterly meetings with WHO, that has really helped relationship building but also helped them prioritize what is important from a business perspective.” (Dx Manufacturer)

B. Operational efficiencies to increase information sharing and updates in the assessment process

Many stakeholders shared that there is an opportunity to improve overall operational efficiency in the PQ process. Similar feedback was raised in the 2018 Assessment as well.

Firstly, Vx manufacturers felt that responsiveness to requests in regular correspondence could be improved. This can relate to queries on the receipt, completeness of dossiers, or confirmation of meeting requests and minutes.

- “.... for instance, WHO has not confirmed the meeting minutes from a meeting that we held six months ago.” (Vx Manufacturer)

- “We would like to see an improved response time on, e.g., endorsements, submissions for changes, minute endorsements. Right now, it takes a long time to get feedback.” (Vx manufacturer)

Secondly, stakeholders are keen for the transparency of the PQ process to be improved – mainly with regard to the current status of PQ products. The RPQ department currently publishes a list of prequalified medicines, vaccines, and diagnostics; however, stakeholders are looking for a more end-to-end life cycle management approach to the information available, i.e., the status of prequalified products, including variations, approval status in countries, rejection, or delisting.

- “The PQ database is easy and fine to access, but there is some important lag, some products have been prequalified and we have been waiting for more than a year to see them on the database.” (Vx Manufacturer)

- “Right now, we are working through the WHO server, but we would appreciate it if there was a specific software that could be used for data transfer.” (Rx manufacturer)

C. Post-approval change notification process (specially for vaccines and diagnostics)

Most vaccine and diagnostic manufacturers have highlighted the need for better life cycle management of prequalified medical products. They note that current processes can take significant time and impact their operations significantly. As an example, shelf life of their product starts running out while waiting for an approval from PQ team and this may disqualify them from participating in tenders. Donors and procurers share this concern as well.

- “For us, this [change notifications] has huge impact, we and the suppliers are always worried about the next change, they don’t know whether they should secure their products.” (Procurer)
“During the whole process, the batches of the new medicine are sitting on the shelves, losing shelf life. Therefore, batches are often wasted, or we lose tenders as they need to have a minimum shelf life left to be sold.” (Vx Manufacturer)

The concern on timelines coupled with the concern on transparency and lack of a “single source of truth” for PQ products and their status further compounds the lack of clarity. Stakeholders suggest that there is potential to redesign the process for change notifications by reconsidering the information submission requirements as well as by considering a more risk-based approach like SRAs.

“Change notification process needs to be revamped, it takes far too long, and their expectations about what information needs to be shared tend to be very unreasonable.” (Dx Manufacturer)

D. Resourcing and team capacity

Stakeholders have unanimously noted that the PQ team’s inability to expand team size in Geneva is a constraint that underlies the improvement areas that they have highlighted. However, they also acknowledge that there is need to consider what can be some alternate ways to combat this constraint. This has been especially noted for the vaccine and diagnostics teams.

“There is no way they can continue performing like this if staying at the same head count, external people have to advocate for growth to have the RPQ department function accordingly.” (Donor)

“If this [delays due to resource constraints] remains, then it will actually become a barrier rather than a facilitator.” (Vx Manufacturer)

“We did not get a response from PQ team for two years, the communication completely stopped. This was probably due to the pandemic but nevertheless caused long delays, leading to us and other manufacturers sometimes losing tenders.” (Dx Manufacturer)

C.5.2 Number of major donors requiring PQ for procurement (Metric 5B)

PQ offers a helpful tool to donors when making procurement decisions. Therefore, some donors have integrated PQ requirements into their procurement policies for medicines, vaccines, and/or diagnostics. As of January 2023, at least 16 major donors require PQ for their medicine, vaccine, and/or diagnostic procurements.

(a) Medicines

Donors require most often PQ for the procurement of medicines: 13 donors have requirements for medicines for at least one of the conditions included in this report, i.e., HIV/AIDS, tuberculosis (TB), malaria, and rhesus disease (RH) (see Exhibit 31). Compared to 2018, five additional donors require PQ for procurement of specific medicines as of December 2022, i.e., Médecins Sans Frontières (MSF), UNDP, PAHO, the International Committee of the Red Cross (ICRC) and the International Planned Parenthood Federation (IPPF).

Furthermore, most donors consider PQ approval as equivalent to SRA approval for medicines. However, for HIV/AIDS medicines, some US-based donors, such as President’s Emergency Plan for AIDS Relief (PEPFAR) and USAID, rely on the USFDA tentative approval (tFDA) for their procurement. This process permits products that are not approved for marketing in the US to be purchased by PEPFAR and distributed in resource-constrained settings.

Many donors have in place a contingent approval process that allows donors to consider procurement of medicines that are not prequalified and do not have SRA approval. For instance, if a stakeholder (e.g., an NRA) requests a


specific medicine to be procured that is not on the list, the donor can rely on its contingent approval process to assess the medicine. Some donors, such as UNFPA and PAHO, have set in place their own processes, but most use an expert review panel (ERP). This panel consists of independent experts who balance the risks and benefits associated with the medicine and advice donors on whether it is safe to be procured56.

Exhibit 31: Overview of major donors requiring PQ for the procurement of medicines

(b) Vaccines

With six major donors requiring PQ for procurement of vaccines, fewer donors have included PQ requirements in their procurement policies for vaccines compared to medicines and diagnostics (see Exhibit 32). Compared to 2018, 1 additional donor requires PQ for procurement of vaccines as of December 2022 (i.e., the International Coordinating Group on Vaccine Provision)57. Some donors rely on PQ for vaccines procurement exclusively, such as Gavi and the International Coordinating Group (ICG) on Vaccine Provision.

As with medicines, most donors consider SRA approvals equal to PQ, although Gavi and UNICEF Supply accept only prequalified vaccines for procurement. Furthermore, contingent approval processes rely less on ERPs and more on tailored processes for each donor. For instance, if specific vaccines are not available for procurement, Gavi requires the approval of the NRAs (which must be fully functional) in the country of production and the country of delivery58. Also, MSF has developed its own qualification process, which includes a preassessment based on various sources, such as product and manufacturer questionnaires, a GMP of the manufacturing site, a product evaluation based on product and/or manufacturer questionnaire(s) according to standards set by WHO, and an Inter-Agency Product Questionnaire.

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(c) Diagnostics

At least 11 major donors require PQ of diagnostics for at least one of the medical conditions included in the report, i.e., HIV/AIDS, TB, malaria, and rhesus disease. Compared to 2018, 2 additional donors require PQ for procurement of specific diagnostics as of December 2022, i.e., USAID and the International Planned Parenthood Federation (IPPF). Furthermore, no PQ requirements could be identified for the Clinton Health Access Initiative, which had such requirements in 201859.

Although many donors consider SRA approval equal to PQ, some donors – especially UN agencies – have stricter requirements for diagnostics than for medicines, accepting only prequalified diagnostics for procurement. Given that TB was only recently (Q4 2022) included as a therapeutic area that is within the scope for PQ of diagnostics, most donors continue to require alternative approvals, such as the WHO endorsement, recommendation, or FDA recommendations.

In terms of contingent approval processes, many of the donors rely on ERP or Global Harmonization Task Force (GHTF) authorization. Under the GHTF, IVDs can be approved by one of the regulatory authorities of the founding members of GHTF, which includes the EU, the US, Canada, Australia, and Japan. Diagnostics that are not IVDs must only meet ISO 9000 manufacturing requirements.

C.5.3 Collaborative Registration Procedure (Metric 5C and 5D)

CRP was launched with the aim of facilitating the introduction of products in countries, notably resource-limited NRAs. To address this challenge, WHO launched the Collaborative Registration Procedure (CRP) for FPPs prequalified by WHO in 2013. In 2016, the CRP was extended to vaccines. A major evolution for CRP between 2018 and 2022 was the expansion of those agreements to FPPs approved by SRAs in 2018 and to diagnostics prequalified by WHO in 2019.

The CRP relies on the collaboration of manufacturers (applicants), NRAs, and WHO, thus reducing duplication by giving NRAs access to applicant dossiers submitted for prequalification (including assessment and inspection outcomes). In turn, participating NRAs commit to reaching their decision in an accelerated way within 90 days of receiving access to the assessment and inspection information, as to whether it will register the FPP, and to communicate its decision to WHO and the applicant within a further 30 days.

The exhibit below highlights the evolution of countries that have entered PQ CRP agreements for vaccines and medicines, PQ CRP agreements for diagnostics, and SRA CRP agreements for vaccines and medicines. In addition, this exhibit shows the number of countries that have registered products using CRP agreements.
Between 2018 and 2022, there has been significant growth in the number of countries that have signed CRP agreements; however, the number of countries that have used the CRP to register a product has grown at a slower rate. This can be partly explained by the fact that the most important uptake in the number of countries signing CRP agreements occurred in 2022 and are starting to register products.

- For PQ CRP medicines – number of Member States that signed PQ CRP agreements increased by ~70%; in the corresponding period, number of countries that registered a product using CRP increased by 20%

- For PQ CRP vaccines – number of Member States that signed PQ CRP agreements increased by 150%; in the corresponding period, number of countries that registered a product using CRP increased by 25%

- For PQ diagnostics – number of Member States that signed PQ CRP agreements since its launch in 2019 is 26; however, only five of those have registered a product using CRP
The exhibit below shows the regional distribution of countries that have signed CRP agreements.

**Exhibit 35: Breakdown of number of countries that have signed various CRP agreements between 2018 and 2022 by WHO region**

<table>
<thead>
<tr>
<th>Region</th>
<th>2018</th>
<th>2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMRO</td>
<td>10%</td>
<td>4%</td>
</tr>
<tr>
<td>EURO</td>
<td>4%</td>
<td>15%</td>
</tr>
<tr>
<td>WPRO</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>SEARO</td>
<td>51%</td>
<td>49%</td>
</tr>
<tr>
<td>AFRO</td>
<td>31%</td>
<td>21%</td>
</tr>
<tr>
<td>PAHO</td>
<td>49%</td>
<td>73%</td>
</tr>
</tbody>
</table>

The numbers shown here highlight that industry players have prioritized the AFRO market for product introduction and have looked for mechanisms to do this in a facilitated and accelerated manner.

**Metric 5C: Number of accelerated product registrations in countries under CRP**

Between 2018 and 2022, 571 product registrations in countries have occurred using CRP (PQ and SRA). Out of 571 registrations, 516 (90%) were accelerated (completed within 250 days) when compared to the average time taken by national procedures, and 404 (71%) were completed within the 90-day timeline committed under the CRP Agreements. Out of these 516 accelerated registrations, 455 (88%) were in the AFRO region. These are discussed in detail below.

**(d) PQ CRP medicines registered in countries in an accelerated way**

Exhibit 36 shows the total number of medicine registrations done in an accelerated way compared to national procedures, and within 90 days, in countries under PQ CRP per year between 2017 and 2022.

---

60 The sum is greater than in previous Exhibit 33 as PAHO is counted as 15 countries in this one, but as 1 country in the previous one.
Between 2018 and 2022, 454 products have been registered in countries using PQ CRP agreements for medicines. Of these, 74% of the registrations met the 90-day timeline committed under CRP and another 18% were completed within 250 days. This has been consistent with the trend observed pre-2018 – as of 2017, 70% registrations were done within the 90-day timeline and another 23% within 250 days.

Out of the accelerated in-country registrations (2018-22) within 250 days, 80% took place in the AFRO region.

PQ CRP for medicines represents the largest pool of products across all CRP agreements, with 218 unique products registered.

(e) PQ CRP vaccines registered in countries in an accelerated way

Exhibit 37 below shows the total number of vaccine registrations done in an accelerated way compared to national procedures, and within 90 days, in countries under PQ CRP per year between 2017 and 2022.

Exhibit 37: Cumulative number of accelerated product registrations under PQ CRP for vaccines
Between 2018 and 2022, 20 products have been registered in countries using PQ CRP agreements for vaccines. Of these 80% of the registrations met the 90-day timeline committed under CRP and the remaining were completed within 250 days.

However, it is noticed that PQ CRP in-country registrations have plateaued since 2020, with no new product registrations, despite the RPQ department having received ~40 submissions for prequalified vaccines in this period. This is largely due to resources being focused on assessment of products under EUL and to facilitate their national authorization for use. 12 vaccines under 19 EULs were listed and over 500 reports shared with countries to facilitate national authorization for use. It is understood that the RPQ department has recently (Q4 2022) held a workshop with stakeholders to discuss a plan on how to gradually revitalize CRP activities for vaccines.

Similar to PQ CRP for medicines, the majority of accelerated registrations (2018-22) for vaccines were done in the AFRO region (70%).

(f) PQ CRP diagnostics registered in countries in an accelerated way

The CRP for prequalified products was extended to prequalified diagnostics in 2019.

The exhibit below shows the total number of diagnostics that were registered in an accelerated manner (90 days) out of the total number of diagnostics registered in countries using CRP. The benchmarking against average timeline for national procedures is not used for PQ CRP for diagnostics.

Exhibit 38: Cumulative number of accelerated product registrations under PQ CRP for diagnostics

Between 2019 (PQ CRP for diagnostics was launched in 2019) and 2022, 18 products have been registered in countries using PQ CRP agreements for diagnostics. Of these, 100% of the registrations met the 90-day timeline committed under CRP. Out of these registrations, 80% took place in the AFRO region.

(g) SRA CRP medicines and vaccines registered in countries in an accelerated way

CRP for SRA-approved vaccines and medicines was introduced in 2015 and enables signatories to rely on the assessment done by an SRA (currently, the 5 SRAs participating are EMA, Medicines and Healthcare products Regulatory Agency, TGA, Dutch Medicines Evaluation Board, Swissmedic) for in-country accelerated product registration.

The exhibit below shows the total number of product registrations done within 250 days (i.e., in an accelerated way compared to national procedures), and within 90 days under the SRA CRP, per year between 2018 and 2022.
Between 2018 and 2022, 79 products have been registered under SRA CRP agreements. Of these, 43% of the registrations met the 90-day timeline committed under CRP and 78% were completed within 250 days. 75% of registrations achieved within 250 days were done in the AFRO region.

**Metric 5D: Manufacturer, procurer/donor, and NRA/SRA perception of value-add of CRP of streamlining downstream approvals**

**Interview results**

Exhibit 40: Manufacturer, procurer/donor, NRA/SRA perception of the added value of CRP in streamlining downstream approvals

Interviewees almost unanimously note that the CRP is great in theory and when it works and would like to give it the highest rating. It is perceived as a tool that has strong potential to accelerate the introduction of products into countries. Procurers and manufacturers in particular see the benefit of CRP as an initiative that facilitates access and reduces timelines.

- “The introduction of CRP was a big relief for us. It was something we had been looking forward to. It is a great initiative and we have already seen the timelines reduce considerably.” (Rx Manufacturer)
“Conceptually, CRP is a good idea, we are impressed that WHO wants to take the next step in helping the NRAs. [...] We are encouraged by the general direction WHO is going, particularly with CRP, as manufacturers have been asking for this for years.” (Dx Manufacturer)

“...I consider it very important for the role of WHO to introduce this in the regulatory framework of countries, this can truly facilitate access to products.” (Procurer)

Yet stakeholders feel that in reality, CRP has not been able to adhere to the strict 90-day registration target, and that NRAs are not provided with enough guidance to improve this. Stakeholders have also noted inconsistencies on how these timelines are applied between product types. As such, stakeholders have raised opportunities for the RPQ department regarding CRP to (a) focus on meeting the expected 90-day timeline better, (b) improve country-level support beyond registration by providing clearer guidance, and (c) improve consistency across medical products.

A. Ensure that the 90-day target is met more consistently for CRP Vaccines

During interviews, stakeholders have noted that the expected 90-day target for registration is not always met.

Stakeholders have noted that this issue applies particularly to vaccines (more than to medicines).

- "Timelines are a lot longer than expected. In 2019, we started applications through CRP with the expectation that we would receive approval within a day, given the product already received PQ. Today, 4 years later, we still have 5 applications outstanding.” (Vx Manufacturer)

- “Many agencies today are reluctant to use CRP for vaccines and find it hard to meet timelines. It seems like agencies are not comfortable working with CRP for vaccines, although it has been working very well for pharmaceuticals.” (Industry Association)

- “It needs to be expedited, the process is slow and delayed.” (NRA)

It is suggested that the delay (for vaccines) may be caused by delays in sharing of PQ assessments/reports

- “CRP today is working great for medicines. But not for vaccines. The issue is that it has been hard to get access to the PQ assessments/reports for vaccines. Countries ask for the assessment files, but PQ team doesn’t share them, then the manufacturer ends up having to do local registrations in that country.” (Vx Manufacturer)

B. Increasing country-level support by providing clearer guidance and coordinate more efficiently with NRAs

Industry stakeholders see benefit in CRP going beyond registration to support NRAs in gaining better understanding of the procedure itself, and the benefit it offers. From their perspective, NRAs lack comprehension and guidance to better use CRP, and thus to facilitate accelerated registrations. NRAs have noted that they also struggle to see the benefit of participating in CRP. Some say that there is a lack of clarity around what they can bring to the process, and how the process benefits them.

- “NRAs lack full understanding of the CRP procedure. More advocacy on awareness needs to be done, and sessions need to be better organized. Right now, even in those meetings, there is not much alignment. WHO says one thing and countries say another.” (Industry Association)

Local focal points in NRAs are in charge on enabling the in-country registration of products through CRP. These focal points often change frequently, making it more difficult for manufacturer and NRAs to coordinate in the process. Some interviewees see an opportunity for the RPQ department to provide standardized support and training sessions to reduce local subjectivity. Respecting timelines depends on the work of focal points at a country level – having more structured guidance could improve accelerated registration across the board.
“The current central focal point of the CRP is at country level. However, these people do not know the procedures as they have not been trained properly, leaving them all in dilemmas about what to do when.” (Vx Manufacturer)

“WHO needs to include principles of CRP in local guidance to reduce subjectivity. This will help give countries clear guidance.” (Industry Association)

“WHO should support the countries to implement CRP, not just enable registration. That is where they can add value.” (Procurer)

Survey results

The survey results are displayed in Exhibit 41. It shows a higher exposure to CRP activities across the survey respondents (only 30% no exposure) compared to interview respondents (60% no exposure), with lower perception scores from survey respondents (30% NRAs scored the CRP <4, compared to 0% NRAs in interviews).

Exhibit 41: Survey results on how the collaborative procedure for CRP have had in streamlining downstream approvals

<table>
<thead>
<tr>
<th>Type of Perception</th>
<th>Number of Responses</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>High/some opportunity for improvement</td>
<td>9</td>
<td>23%</td>
</tr>
<tr>
<td>Mixed perception</td>
<td>3</td>
<td>8%</td>
</tr>
<tr>
<td>Very positive/positive opinion</td>
<td>13</td>
<td>33%</td>
</tr>
<tr>
<td>No exposure</td>
<td>14</td>
<td>36%</td>
</tr>
</tbody>
</table>

1. Excluding NA
2. 1 being the best
C.5.4 Product registrations through other FPI pathways (Metric 5E to 5H)

Beyond CRP, PQ, and EUL, the RPQ department also contributes to introducing quality and safe products in an accelerated manner via other mechanisms like reliance approaches, and joint activities at the national, regional, and international levels.\(^{61}\)

For its reliance activities, the WHO RCN team has been developing, implementing, and promoting the concept of Reliance since 2019. The concept underpins the RPQ department’s CRP and abridged assessment processes, as well as the GBT assessment. It is also central to the development and implementation of the new WLA program: the designation of regulators as WLAs will provide a transparent and evidence-based pathway to help agencies understand on whom they can rely as a reference agency. Between 2018 and 2022, the team has published the WHO Good Reliance Practices (GreIP) and organized training sessions and webinars around Reliance. Exhibit below provides an overview of the key activities related to Reliance conducted by the WHO RCN team.

Exhibit 42: Timeline of the introduction and implementation of Reliance

Exhibit 42: Timeline of the introduction and implementation of Reliance

Timeline of the introduction and implementation of reliance

<table>
<thead>
<tr>
<th>Year</th>
<th>Key Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020</td>
<td>Throughout: development of WHO GreIP including two public consultations.</td>
</tr>
<tr>
<td>2021</td>
<td>October: approval of practices by the WHO Expert Committee on Specification for Pharmaceutical Products.</td>
</tr>
<tr>
<td>2021</td>
<td>June: webinar on GreIP and implementation plans.</td>
</tr>
<tr>
<td>2022</td>
<td>October: launch of dedicated e-learning course.</td>
</tr>
</tbody>
</table>

In addition to these Reliance activities, the RPQ department has been involved in supporting product introduction in NMRAs between 2018 and 2022 via the following key initiatives:

- **Zazibona, ASEAN (Association of Southeast Asian Nations), and EAC (East African Community) Regional Joint Assessments** which led to the joint assessment of 261 products.
- **EU-Medicines for all (EU-M4all)**\(^{62}\) and Swissmedic’s Marketing Authorization for Global Health Products (MAGHP)\(^{63}\) which led to the assessment of 24 products (between 2020 and 2022).
- **Piloting a new approach/process to improve the process for market authorizations for post-approval changes:** pilot in collaboration with Sanofi, which includes 21 countries across all six WHO regions. Training sessions for assessors and support for implementation of facilitated registration pathways: 20 countries received personalized training sessions for assessors, and 3 received technical support for the implementation of facilitated registration pathways (Bangladesh, Bhutan, East Timor)

The RPQ department also strengthens regional harmonization and convergence by providing technical support to many regional networks and organizations like African Medicines Regulatory Harmonization (AMRH), African

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Vaccine Regulatory Forum (AVAREF), African Medicines Agency (AMA) and Southeast Asia Regulatory network (SEARN).

**Metric 5E: Number of product registrations that were accelerated for in-country introduction through other FPI pathways**

**a. Regional Joint Assessments**

The FPI team supports countries in their work-sharing and collaborative initiatives, where countries cooperate to “assess common applications submitted to the NRAs, inspect manufacturing facilities, or contract research organizations” \(^{64}\). WHO supports these countries with technical assistance, and also conducts GMP inspections in the target areas.

Zazibona Regional Joint Assessment, ASEAN Regional Joint Assessment, and EAC Regional Joint Assessment are examples of such initiatives to support product assessments at a regional level. These three initiatives involve 24 countries in total (the Democratic Republic of the Congo and the United Republic of Tanzania are involved in both Zazibona and EAC). Below is a more detailed introduction to these programs:

- **Zazibona** \(^{65}\) is a Regional Joint Assessment developed in 2013, initially by Zambia, Zimbabwe, Botswana, and Namibia with WHO support. The goal of this initiative is for Member States to collaborate in assessments and GMP inspections for medicines across 13 disease areas to “reduce workload, reduce timelines to registrations, develop mutual trust and confidence in regulatory collaboration, and establish a platform for training and collaboration in other regulatory fields” \(^{66}\). The specific role of the RPQ department in this involves participation in and provision of technical assistance, expertise, and support during the Joint Assessment. The RPQ department also participates in heads of NRA meetings which oversee the Joint Assessment. Appendix 6 contains additional details on this joint assessment process.

- **ASEAN Regional Joint Assessment** was started in 2015 with WHO and aimed at strengthening harmonization between all 10 ASEAN countries \(^{67}\). Assessment work is carried out simultaneously in all countries, enabling better coordination between Member States \(^{68}\). The RPQ department coordinated the recent revision of the ASEAN Regional Joint Assessment Procedure. It also provides technical assistance during the assessment and for drafting the final assessment report and is involved in the meetings that oversee the Joint Assessment.

- **The EAC Regional Joint Assessment** was launched in 2014 by the seven EAC member NRAs \(^{69}\) with the objective of “harmonizing technical requirements and standards for medical product regulation” and conducting joint reviews of dossiers \(^{70}\). The specific role of the RPQ department in this involves the provision of technical assistance, expertise, and support during the procedure. It also participates in the Steering Committee meetings which oversee the Joint Assessment.

The exhibit below shows the number of products submitted to these three Joint Regional Agreements, and the number of products recommended by each Joint Regional Assessment.

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\(^{65}\) Member States are: Zambia, Zimbabwe, Botswana, Namibia, Democratic Republic of the Congo, Malawi, Mozambique, Tanzania, South Africa

\(^{66}\) Source: Zazibona (https://zazibona.com/)

\(^{67}\) Member States: Brunei Darussalam, Cambodia, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Singapore, Thailand, Viet Nam


\(^{69}\) Members NRAs: Kenya, Uganda, United Republic of Tanzania (Tanzania Mainland and Tanzania Zanzibar), Burundi, Rwanda, South Sudan

Exhibit 43: Number of in-country registrations of quality-assured products jointly assessed and recommended by countries via the ASEAN, EAC, and Zazibona Regional Joint Assessments since 2018

![Graph of cumulative number of quality assured products jointly assessed and recommended by countries via Regional Joint Assessments since 2018, number of in-country registrations for ASEAN, EAC, Zazibona, 2018-2022](image)

Source: Data from WHO FPI team

b. SRA Joint Assessments

EU-M4all and MAGHP are two global health pathways for the introduction of quality-assured medical products. Both allow participants to take part in the assessments conducted by two SRAs; the EMA and Swissmedic. They offer the possibility for target NRAs to participate in the assessments from the relevant SRAs (in this case, EMA and Swissmedic) with a view to building capacity, increasing confidence, and accelerating registration.

- **EU-M4all**[^1]: EMA, in collaboration with WHO provides scientific opinions on high-priority human medicines, including vaccines, which are intended for markets outside the EU.
- **MAGHP**[^2]: MAGHP aims to make the Swissmedic authorization procedure and the procedure for providing scientific advice accessible to representatives of regulatory authorities in selected countries as well as to WHO.

The abovementioned pathways enable accelerated access in two ways:

- Firstly, other countries can use and rely on the results of the assessment to accelerate their own assessment/market authorization processes. In this, the RPQ department is responsible for program-wide coordination of the procedure, including communication with the different stakeholders (through a dedicated generic electronic mailbox), confirmation of the eligibility of the specific products for the EU-M4all procedure (through respective disease programs) and nomination of WHO and Member States experts for participation in the procedure.
- Secondly, the results of the assessments can be used by manufacturers to apply for market authorization in an accelerated manner including under the SRA CRP process which is facilitated by the RPQ department.

Exhibit 44 below shares the details of the above-mentioned procedures/assessments.

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Exhibit 44: Products reviewed under EU-M4all and MAGHP between 2020 and 2022

Metric 5F: Number of product registrations in countries during public health emergencies that are accelerated using facilitated pathways supported by FPI, such as COVAX and CRP

In addition to prequalification and facilitating product introduction, the RPQ department has also facilitated and coordinated the interactions across global and local agencies on the regulatory approval of COVID-19 vaccines. For example:

- The RPQ department regularly liaises with UNICEF, Gavi, and WHO Regional Offices to facilitate the registration of products in countries.
- The RPQ department has been providing regulatory expertise to countries and UNICEF for ACT allocations of non-prequalified COVID-19 antivirals/therapeutics, in order to facilitate the registration of the products in countries and alignment on regulation.

As part of this effort on COVID-19, 5,074 authorizations for COVID-19 products in over 190 countries/territories (Exhibit 45 below) and four COVID-19 antivirals/therapeutics in 11 countries, as well as all CARICOM, have been granted.
C.5.5 Recommendations

Based on desk research and interviews, set out below are some options that the RPQ department can consider for actioning the key opportunities for improvement mentioned earlier in this section (referred to as “recommendations” in the table below).

<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendations</th>
<th>Example initiatives</th>
</tr>
</thead>
</table>
| 1.  | PQ (across all products): collaborate more with internal and external stakeholders to determine and communicate priorities and pipelines for PQ | a. Consider developing a “priority” track for medical products that may be a global health priority e.g., to help with a stockout, public health impact (e.g., a new treatment that is cheaper/faster). Diverse set of stakeholders (from other WHO departments as well as procurers/donors/NRAs) should be able to provide input on these  
b. Consider if there are any lessons learned from the process already in place for the PQ (diagnostics) team to collaborate with internal and external stakeholders that can then be used while actioning point (a) above |
| 2.  | Ensure successful deployment of ePQS to improve PQ process                      | Note: As of December 2022, the RPQ department is in the process of migrating to a new IT system (ePQS) which is expected to begin rollout in May 2023. An assessment of the features of the ePQS system against the recommendations below has not been conducted.  
a. Redesign processes: consider mapping the PQ process end-to-end to identify redundancies and points in the process with high time needed and high impact; redesign these processes leveraging digital tools and automation  
b. Improve automation: related to the point above, improve the automation and use of digital tools for supporting PQ processes, e.g., manufacturer- or application-specific dashboards that can reduce tedious update-related emails and meetings for both the PQ team and manufacturers  
c. Improve the communication process and protocols with manufacturers, e.g., designate point persons within the team by |
<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendations</th>
<th>Example initiatives</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>manufacturer, establish system of periodic (e.g., quarterly) touchpoints with manufacturer.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>d. Develop offshore nontechnical support teams (that are not impacted by hiring caps at the Headquarters): consider setting up an offshore support team comprising project managers, administrators, assistants, data managers, etc. that can take on administrative and process-related tasks (e.g., data management and updates, acting as focal points for manufacturers, sharing minutes for manufacturer meetings, helping the PQ technical team in Geneva to prioritize, supporting data collection and following up with manufacturers and NRAs).</td>
</tr>
</tbody>
</table>
|     |                                                                                 | e. Set up an automated, live, publicly available PQ database: expand the currently existing PQ list containing the applicant, PQ date, and therapeutic area; develop an easily accessible database with a more end-to-end lifecycle view and a – real-time status update on prequalified products/candidate products. The database should be offered across medicines, vaccines, and diagnostics. It should include: i. Full PQ status: pending PQ, prequalified, rejected, delisted  
ii. Status on post-approval changes  
iii. Countries where the product is marketed  
iv. Approval status in countries  

f. Validity of inspection report (clarification that it has not expired) |
| 3   | PQ (Vx and IVD): improve efficiency of post-approval change notifications       | a. Dedicated pathway: consider evaluating post-change notifications under a separate dedicated pathway (i.e., different pipeline with dedicated resources and special fit-for-purpose processes)  
b. Revise process: consider taking a more risk-based assessment approach (i.e., simple changes to label or color of packaging should not require waiting for WHO approval) more similar to how SRAs (e.g., FDA) evaluate post-approval changes  
c. Consider developing a “priority” track for variations that may be a global health priority, e.g., to help with a stockout, public health impact (e.g., a new treatment that is cheaper/faster) |
| 4   | CRP (Vx) and PQ (Vx): simplify collaboration and file sharing process          | a. Consider process improvements that can be made to simplify data sharing between the teams that hold the repository of information on PQ assessments and the teams processing/leading CRP registrations, such that information sharing to enable CRP for vaccines does not require significant capacity from the teams. |
| 5   | Development of clear strategic priorities, objectives, and impact metrics related to the concepts of reliance | Considering:  
- The RPQ department currently has only one KPI for its activities on Reliance\(^74\) and data for this KPI was unavailable; and  
- The many activities linked to reliance and regional agency/network strengthening undertaken by the RPQ |

\(^{73}\) This was a recommendation last time as well.  
\(^{74}\) Number of countries implementing regulation through the concept of reliance and network
<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendations</th>
<th>Example initiatives</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>department teams (most specifically those currently undertaken by the RCN team) It is recommended that clear strategic priorities, objectives, and KPIs be developed for the impact the department seeks to drive on the topic of Reliance as well as support provided to regional networks/agencies. This is especially critical when the teams are operating under resource constraints.</td>
</tr>
</tbody>
</table>

### C.6 IMPROVING REGULATORY PREPAREDNESS FOR PUBLIC HEALTH EMERGENCIES (THEME 6)

WHO strives to establish regulatory systems that have the capacity and capabilities necessary to establish access to quality and safe medical products in all circumstances, including public health emergencies. To realize this objective, WHO supports NRAs to, e.g., strengthen their regulatory preparedness plans and regulatory capabilities by helping them identify the current gaps and strengthen these capabilities through different approaches such as developing different guidelines and standards, training, and in-country technical support. In addition, participation of NRA regulators in EUL assessments and regional workshops, facilitated by PQ teams also contributes to building regulatory capacity for public health emergencies.

Given that many LMICs are still inadequately prepared for public health emergencies and in response to the 2009 influenza outbreak, increasing regulatory preparedness for public health emergencies was defined as a strategic priority for WHO. It was therefore included in its five-year plan (2019-23) to improve global regulatory systems. As part of this five-year plan, WHO aimed to improve the regulatory infrastructure for public health emergencies in at least ten countries by 2023.

These targets were already achieved by 2022: between 2018 and 2022, the RPQ department supported 84 countries in adapting their regulatory requirements to address public health emergencies and tracked and confirmed improvements in regulatory capacity preparedness for public health emergencies in 16 countries. Further details are given below.

In addition, COVID-19 provided an opportunity to provide tailored technical assistance and support to Member States to enhance their preparedness for public health emergencies. Shortly after the WHO DG announced COVID-19 disease as a PHEIC, the PV team, anticipating the introduction of several new COVID-19 vaccines worldwide, convened a global group of experts, to develop a COVID-19 Vaccine safety Surveillance Manual the manual is available in 3 UN languages and has been downloaded at least 71,000 times. The manual provides guidance to EPI managers, NRA and small vaccine developers in submitting their risk management plans.

Exhibit 46 summarizes the three-impact metrics that were assessed in this section.

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75 Source: [https://www.who.int/publications/i/item/9789240032781](https://www.who.int/publications/i/item/9789240032781)
C.6.1 Quantitative assessment of support provided to countries to improve regulatory preparedness for public health emergencies (Metrics 6A and 6B)

Metric 6A: Number of countries assisted and supported in adapting their regulatory requirements to effectively address public health emergencies

The RPQ department supports countries in enhancing their regulatory capacity for various functions and topics, including preparedness for public health emergencies. The support related to regulatory capacity preparedness for public health emergencies includes various functions, such as market authorizations, vigilance, and PMS. Details are set out in Exhibit 47 below.

Exhibit 47: Number of countries assisted and supported in adapting their regulatory requirements to effectively address public health emergencies

Between 2018 and 2022, the RPQ department supported 84 countries\(^{76}\) in strengthening their regulatory requirements for public health emergencies. This included 18 LICs, 37 LMICs, 25 UMICs, and 4 HICs. 50 countries received support for more than one year, 33 countries received support for two years and 1 country received support for three years.

---

\(^{76}\) The 84 countries include countries that received support to enhance regulatory capacity beyond public health emergencies as well as countries that received support focused particularly on enhancing regulatory capacity for public health emergencies only.
In 2022, given the prioritization of the GBT and the WLA concept, the RPQ department had less capacity to support countries in enhancing their regulatory systems. This resulted in a lower number of countries being supported compared to 2021.

**Metric 6B: Number of countries with improved regulatory capacity preparedness for public health emergencies**

The ultimate objective of the RPQ department’s support is to effectively improve regulatory capacity and prepare for public health emergencies. At present, the RPQ department does not systematically track the impact of all their support activities (as discussed above under Metric 6A). However, for the purposes of this report the team tracked impact for at least 16 countries by analysing changes in their performance on emergency-preparedness-related indicators in WHO GBT. Additional details are given in Exhibit 48 below.

**Exhibit 48: Number of countries with improved regulatory capacity and preparedness for public health emergencies**

At least 16 countries (out of the 84 supported between 2018 and 2022\(^7\)) improved their regulatory capacity preparedness for public health emergencies between 2021 and 2022. Emergency-preparedness-related indicators were only included in the GBT in 2019 (following the influenza outbreak); given that it takes time to track improvements, data on this point is only available for 2021 onwards.

The high number of countries in 2021 illustrates the importance of regulatory preparedness during pandemics specifically COVID-19 pandemic. Countries made significant investments in improving their regulatory capacity to ensure timely access to high-quality COVID-19 vaccines. As stated under Metric 6A above, limited resources and competing priorities in 2022 resulted in fewer countries being supported on emergency preparedness, which is reflected in the lower number of countries that showed improvement on this metric.

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\(^7\) The actual number may be higher. For 16 countries, the team was able to confirm strengthening by observing changes in the performance of emergency-preparedness-related indicators in the GBT.

\(^7\) As discussed in Metric 6A above.
**C.6.2 Case study on how a country improved its regulatory preparedness for public health emergencies (Pakistan) (Metric 6C)**

**Context**

During the COVID-19 pandemic, Pakistan had the challenge of ensuring people's access to medicines in general and COVID-19-related medical products in particular. Multiple factors constrained the emergency response, including technical capacity and human resource limitations.

**Approach**

In 2019, various IDPs were identified during the self-assessment of the Drug Regulatory Authority of Pakistan (DRAP) using the GBT after preparatory visit by the WHO in 2018. Under the RS 04.05, DRAP identified preparation of Health Emergency Preparedness and Risk Management Plan (HEP&RM). The draft plan helped the authority to prioritize and focus on regulatory functions in the health emergencies.

In 2020, due to COVID-19, the IDPs related to emergency preparedness in the regulatory system were more focused, and DRAP and WHO worked together to strengthen this area. Some examples of activities undertaken are below:

- Developed and enhanced relevant guidelines and procedures for drugs and medical devices through organization by DRAP of different workshops and technical support in the area of regulatory preparedness.
- Strengthened clinical trial application review and approval processes and approved multi-center trials for COVID-19 vaccines.
  
  — An example is the local trial of the Can Sino vaccine: on the basis of the results, EUA was granted, setting an example of evidence-based decision-making.
- Improved regulatory preparedness in market authorization through the adoption of reliance mechanism into the EUA methodology using Good Reliance Practices. As a result, DRAP approved EUAs for three vaccines – Pfizer, Moderna, and Astra Zeneca.
- Granted EUA to two vaccines based on clinical trial data evaluation i.e., Sinovac (multi-center trials) and Can Sino (local trials).
- Upgraded PV system, which was linked with Uppsala Monitoring Centre, and strengthened reporting, assessment, and communication activities in particular.
- Started a causality assessment of the reported data for four provinces, two states, and one region that report to National Pharmacovigilance Centre (ongoing as of January 30, 2023), which strengthened the data collection of AEFI in the country.

**Impact and outcome**

Due to improved regulatory preparedness, a success rate of about 90% was achieved in the population vaccination. The efforts of the DRAP in ensuring timely availability and access to COVID-19 medicines and vaccines were praised by the National Command and Control Centre – a national body established to supervise the emergency response. According to Asim Rauf, Chief Executive Officer of the DRAP, “the steps taken by the DRAP during the pandemic have ensured the availability of treatment options and contributed towards access to quality-assured medicines and vaccines through clinical trial evaluation, EUA, and reporting of AEFIs.”

Furthermore, the DRAP’s assessor worked with WHO on the Moderna vaccine dossier evaluation, for which WHO Regional Offices and headquarters praised their competency.
Finally, a series of consultative meetings were held on the promotion of domestic manufacturing of mRNA vaccines. WHO has also selected Pakistan as a hub for mRNA manufacturing.

**Lessons learned**

Based on the above experiences, four lessons learned were identified

- Due to scarcity of evaluation reports for various vaccines, timelines for EUA were further stretched. Since then, DRAP has been actively networking with other regulatory authorities for timely sharing of information.
- Regulatory framework must have enabling legal provisions for EUA.
- EUA was successfully implemented by amending SOPs and guidelines in a very short time through a group of experts, thereby increasing the scope of DRAP’s technical resources, which are now an addition and have a direct input for more transparent decision-making.
- The experience has allowed Pakistan’s NRA to support other countries with the EUQ process of medicine.

**C.6.3 Recommendations**

Based on desk research and interviews, set out below are some options that the RPQ department can consider for actioning the key opportunities for improvement mentioned earlier in this section (referred to as “recommendations” in the table below). It is noted that there were no specific recommendations on the topic of regulatory preparedness in the 2018 Assessment as this topic was not within scope of the assessment.

<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendations</th>
<th>Example initiatives</th>
</tr>
</thead>
</table>
| 1.  | Create self-sustaining opportunities for NRAs to support and lead capability building in their regions – especially relevant in light of the constrained capacity of the RPQ department | Consider these pathways to reduce workload pressure on RPQ department’s teams:  
  a. Establish systemic and periodic peer learning forums in each region which can be led by mature NRAs in the region (with light support from the RPQ department teams)  
  b. Build capacity by staffing focal points from regional offices |
| 2.  | Introduce systematic evaluation of the impact of the RPQ department support on regulatory capacity preparedness for public health emergencies | a. Follow up with countries on the impact of WHO support on the country’s preparedness for public health emergencies: e.g., ask countries that received WHO support to reevaluate the 11 GBT sub-indicators related to regulatory preparedness for public health emergencies through self-benchmarking |

**C.7 IMPROVING ACCESS TO DONOR-FUNDED PROCUREMENT MARKETS (THEME 7)**

To increase access to medical products for LICs and LMICs, donor-funded procurement and pooled-procurement processes are used to ensure the affordability of medical products. A pooled procurement process is “a formal arrangement where financial and other resources are combined across different purchasing authorities, to create a single entity for procuring health products on behalf of individual purchasing authorities.” Donors frequently fund the procurement of health products, which are purchased in larger quantities and in a wider range of products. This, together with sharing of resourcing and more streamlined procurement processes, enables donors to procure at a
lower price point and therefore helps increase the purchasing power of the countries participating in the procurement pool. \(^{79}\)

To ensure that health products are supplied to all who need them, the participation of LICs and LMICs in such donor-funded pooled procurement mechanisms is key. Data from the Global Drug Facility, UNICEF, and Gavi indicates that the ratio of LMICs participating in their pooled procurement mechanisms has increased between 2018 and 2022, although at a relatively slow rate. Furthermore, given that many donors require PQ for their procurement, manufacturers who produce prequalified processes have the possibility to participate in pooled procurement mechanisms and can supply their products to LICs and LMICs. These topics are further discussed below.

Exhibit 49 provides an overview of the metrics that are discussed in this theme and their methodology.

Exhibit 49: Key metrics covered and the methodology for the assessment under theme 7

<table>
<thead>
<tr>
<th>Topics</th>
<th>No. Metric</th>
<th>Metric type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improving access to donor funded procurement markets</td>
<td>7A</td>
<td>Ratio of LMICs to non-LMIC manufacturers participating in donor-funded pooled procurement mechanisms</td>
</tr>
<tr>
<td></td>
<td>7B</td>
<td>Case study of a manufacturer from an LMIC that has recently participated in donor-funded pool-procurement mechanisms (Serum Institute of India)</td>
</tr>
</tbody>
</table>

**C.7.1 Ratio of LMICs to non-LMIC manufacturers participating in donor-funded pooled procurement mechanisms (Metric 7A)**

In order to better understand the access that LMIC manufacturers have to donor-funded procurement mechanisms, the share of LMIC manufacturers participating in the Gavi, UNICEF, and GDF pooled-procurement mechanisms has been examined below.

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\(^{79}\) Source: WHO (https://apps.who.int/iris/bitstream/handle/10665/341901/9789240024670- eng.pdf?sequence=1&isAllowed=y#:~:text=the%20policy%20implemented%3F-,Pooled%20procurement%20increases%20purchasing%20power%20because%20procurement%20costs%20are%20spread%20and%20streamlining%20of%20procurement%20processes.)
The share of LMIC manufacturers participating in donor-funded procurement pools has increased or stayed consistent from 2018 to 2021. This trend holds true even if absolute numbers of LMICs participating in pool-procurement programs are looked at.

Variance is noted for UNICEF particularly: there is a drop in total number of LMIC manufacturers participating in pool procurement programs 2019 (likely driven by COVID-19-related supply-chain disruptions), followed by a significant uptake in 2020 (likely driven by increase in COVID-19-related procurement activities), with numbers stabilizing in 2021. Unfortunately, there was not an opportunity to understand the data more qualitatively through additional interviews with the different agencies.

Interpretation of the procurement volumes and the development of a more nuanced understanding of LMIC participation in these programs are challenging given the lack of more detailed publicly available data on this topic.

**C.7.2 Case study of a manufacturer from an LMIC that has recently participated in donor-funded pool-procurement mechanisms (Serum Institute of India (SIIPL)) (Metric 7B)**

**Context**

In the initial phase of vaccine PQ, only a few multinational companies used the mechanism to register their vaccine. However, given the growing appetite for PQ and the increased scope of vaccines that are covered under PQ, manufacturers from LMICs have taken more than 50% of the market share.

There are a number of vaccines that apply both in HICs and LMICs, such as the pneumococcal conjugate vaccine. PQ team has adopted the LMIC-centric approach, which focuses on the specific needs of the LMIC by considering programmatic suitability and the risks and benefits relevant to the local population, such as the incidence and burden of disease, demographics, and care availability.

A secure supply of quality vaccines against pneumococcal diseases is essential, given that around 15% of all deaths of children under five years, or 808,000 children, are caused by pneumonia (2017). WHO therefore recommends that the pneumococcal conjugate vaccines be included in childhood immunization programs, especially in countries with high childhood mortality.
Given the special requirements for vaccines in LMICs, donor-funded procurers rely exclusively on WHO-prequalified products. As an example, Gavi and UNICEF, which supply about two-thirds of the total donor-funded vaccines for LMIC, only accept prequalified products.

**Approach**

SIIPL approached WHO with a pneumonia vaccine candidate, the pneumococcal conjugate vaccine PNEUMOSIL®. To be granted PQ, SIIPL went through the following five steps:

1. The PQ team offered a helping hand and organized joint meetings/teleconferences with PATH and the Medical Research Council, Gambia, and provided an opportunity to discuss and present the data for the potential vaccine candidate PNEUMOSIL®.
2. The PQ team provided their feedback/guidance and accepted the proposed regulatory pathway that was based on the permission (for export only) from the NRA on record, Drugs Controller General of India (DCGI), to initiate the PQ process.
3. Accordingly, SIIPL submitted application for permission (for export only) from DCGI and obtained approval after the joint inspection of the SIIPL manufacturing premises to verify the cGMP condition and dossier review.
4. After obtaining the export-only permission from DCGI, SIIPL submitted the PQ dossier for pneumococcal conjugate vaccine to WHO in early 2019.
5. The PQ team conducted the GMP inspection to verify the GMP compliance of the SIIPL premises and performed consistency testing of PNEUMOSIL® at WHO-accredited labs. In the following, WHO granted the PQ to PNEUMOSIL® in December 2019.

In total, the PQ team completed the review of the PQ dossier and the GMP audit within around ten months after submission. The PQ team also facilitated the Collaborative Registration Procedure (CRP) to expand the market, with the local NRA supporting the WHO CRP reliance process for registration.

After receiving the PQ, PNEUMOSIL® was distributed using pooled procurement mechanisms from UNICEF and PAHO. Furthermore, any approvals and reviews of post-approval changes or life cycle management procedures were supported by the PQ team, ultimately resulting in an uninterrupted supply of the vaccine.

**Impact and outcome**

After its PQ, up until January 2023, around 12.5 million doses of PNEUMOSIL® were distributed through UNICEF and PAHO pooled procurement processes to 16 LMIC countries, saving millions of lives. Furthermore, as of January 2023, PNEUMOSIL® is registered in more than 35 countries.

**Lessons learned**

Based on their experiences with the PQ of PNEUMOSIL® and the resulting pooled procurement, SIIPL identified the below as lessons learned:

1. PQ is very important and beneficial in terms of product creditability, especially for LMICs in terms of, e.g., harmonization of registrations in emerging countries, predictability and acceleration of registrations, and easier post-registration/life cycle management.
2. The PQ status is well-recognized, and it helps extend the approvals to other emerging market countries.
3. WHO has clear guidelines for vaccine PQ (TRS 978, Annex 6) which have turned out to be a game changer for the industry, procurement agencies, and donors.
4. The industry recommends increasing the budget to hire more staff for the PQ team, which will enhance the efficiency and effectiveness of the PQ process.

5. PQ/EUL specialized TA could encourage the manufacturers in LMICs to submit the PQ/QUL applications, speed up the attainment of PQ/EUL for their products and make them eligible for international, donor-sponsored tenders

C.8 SUPPORTING MEMBER STATES TO BUILD THE ECOSYSTEM AND CAPACITY FOR QUALITY AND SUSTAINABLE LOCAL PRODUCTION (THEME 8)

WHO had been promoting local production and technology transfer and providing support to Member States for many years through its Local Production Program.

After the WHO transformation in 2019, the Local Production Program became the Local Production and Assistance (LPA) unit, with an additional mandate: PQ/EUL-related specialized technical assistance to manufacturers of pharmaceuticals, vaccines, diagnostics, and other health products to speed up the attainment of PQ/EUL. LPA is dedicated to “supporting WHO Member States in strengthening sustainable local production and technology transfer to improve access to safe, effective, quality, and affordable medicines and other health technologies” and is located in the RPQ department as its third unit.

In 2019, the WHO LPA unit led the development and launch of the first interagency statement on promoting local production at the 72nd World Health Assembly. In 2021, the LPA unit was further mandated with the adoption of WHO Resolution WHA74.6 on “Strengthening local production of medicines and other health technologies to improve access” by the World Health Assembly. This WHO Resolution was cosponsored by more than 100 Member States, showcasing global support for local production.

To achieve its objective of sustainable quality local production and technology transfer, the WHO LPA unit has been working together with other teams in the RPQ department as well as governments, industry, partners, and other stakeholders. This work includes:

- Supporting Member States to develop and implement holistic national strategies/roadmaps for sustainable quality local production
- Conducting situational analyses of ecosystems for Member States for sustainable quality local production
- Fostering partnerships and collaborations on local production with UN agencies and international partners as platforms to build synergies, strengthen coordination, and share information
- Building Member State capacity comprehensively and providing specialized technical assistance to achieve quality assurance and sustainability, including for PQ/EUL
- Supporting Member States in promoting long-term high-quality local production and facilitating technology transfer
- Developing global resources for promoting local production and technology transfer, such as guidance documents (including frameworks) and reports analyzing the landscape and latest trends

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80 Source: WHO (https://www.who.int/teams/regulation-prequalification/lpa)
81 Source: Interviews, WHO (https://www.who.int/teams/regulation-prequalification/lpa), interviews
82 “The Local Production & Assistance Unit (LPA) assists governments to conduct holistic situational analyses with a tool to identify gaps in key areas for promoting sustainable and quality local production, such as policy coherence, the business environment, regulations and quality assurance, infrastructure, and the market landscape of the national industry.” Source: WHO (https://www.who.int/teams/regulation-prequalification/lpa/situational-analysis-and-readiness)
Between 2018 and 2022, the RPQ department has:

- Organized training sessions on sustainable local production across WHO regions and stakeholders for more than 5,000 participants (e.g., annual virtual cGMP training marathons, annual training workshop for 60-70 assessors with close to 300 country assessors having attended PQ team/MED’s annual assessment trainings since 2018)
- Provided 3-4-month PQ rotational fellowships for regulators of different countries (9 national experts from LMICs have participated between 2008 and June 2020, after which the program was paused due to COVID-19 pandemic)
- Promoted the adoption of PQ procedures and guidance by NRAs to design and improve their procedures (e.g., of about 70 external assessors that participated in each of PQ teamMED’s assessment sessions, 60% were from LMICs).
- Helped build the capacity of manufacturers, for example, through PQ guidance for manufacturers, pre-submission meetings, scientific advice, and annual manufacturers workshops
- Introduced the ecosystem assessments for quality and sustainable local production to governments and has piloted this with seven countries
- Provided PQ-/EUL-related specialized technical assistance to 18 unique manufacturers of essential pharmaceuticals, vaccines, and diagnostics.
- Updated the “WHO guideline on Technology transfer in pharmaceutical manufacturing”; expected to be published in Q1 2023
- Hosted the first World Local Production Forum (WLPF): Enhancing access to medicines and other health technologies, a new WHO initiative in June 2021. This is expected to be a regular global forum for Member States and the global community to stimulate high-level dialogue and action in addressing the challenges and shaping the global direction of local production. Next forum expected in November 2023
- Organized regional meetings, in collaboration with EMRO, SEARO, and WPRO and technical support from partners, in 2021 and 2022 for addressing the challenges and laying a foundation for developing strategies for regional vaccine production in the respective region.

According to survey results (please see Section B.1.3 for more details), demand for support for building quality and sustainable local production is expected to increase by almost four times with 11% of respondents noting that they have received support from the RPQ department on this topic between 2018 and 2022 and 42% noting that they will need support in the next five years.

Five metrics were identified to measure the impact of the RPQ department in supporting Member States with building an ecosystem and capabilities for quality and sustainable production. Exhibit 51 gives an overview of these metrics and their assessment methodology.

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The WHO LPA unit, as the WLPF Secretariat, organized the first WLPF in June 2021, convening high-level delegates from more than 100 countries, heads of UN agencies and international organizations, civil societies, academia, technology experts and other stakeholders to address key global issues on strengthening local production capacity globally to improve timely access during COVID-19 and beyond.
Exhibit 51: Key metrics covered and the methodology for assessment under Theme 8

<table>
<thead>
<tr>
<th>Topics</th>
<th>No. Metric</th>
<th>Metric type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supporting member states to build the ecosystem and capacities for quality and sustainable local production</td>
<td>8A Number of manufacturers and other stakeholders trained by WHO RPQ in good manufacturing practices (GMP), other regulatory standards, and quality workshops</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>8B Number of manufacturers that received PQ/EUL-related technical assistance</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>8C Number of countries that received ecosystem assessments for quality and sustainable local production</td>
<td>Quantitative</td>
</tr>
<tr>
<td></td>
<td>8D Manufacturer, procurer/donor, and NRA perception of general manufacturing practices</td>
<td>Perception</td>
</tr>
<tr>
<td></td>
<td>8E Case study on supporting a Member State to strengthen local production and the impact of the WHA74.6 resolution on local production</td>
<td>Case study</td>
</tr>
</tbody>
</table>

C.8.1 Quantitative assessment of support for Member States in building sustainable local production (Metrics 8A to 8C)

Metric 8A: Number of manufacturers and other stakeholders trained by the RPQ department in good manufacturing practices (GMP), other regulatory standards, and quality workshops

As part of its capacity building and skills development efforts, the WHO LPA unit has established different types of training related to sustainable local production of high-quality health products. Exhibit 52 below provides an overview of four of the training types and participants between 2018 and 2022.

Exhibit 52: Overview of training sessions related to sustainable quality local production

<table>
<thead>
<tr>
<th>Training name</th>
<th>Breakdown of participants by region</th>
<th>Total no. of participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virtual cGMP training marathons</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30% of 2021 participants continued their learning in 2022</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;200 participants who completed the marathon in 2021 and also completed the CTD in 2022</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Virtual training workshop on CTD requirements of Vx dossiers for WHO PQ/EUL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Virtual training workshop on local production of quality and safe IVDs and WHO PQ, EUL, and ERPD processes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Holistic training workshops on key enabling factors for successful local production</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PQ team quality workshop for manufacturers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PQT workshop for manufacturers of biotherapeutic product manufacturers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>6,500+</td>
</tr>
</tbody>
</table>

In total, between 2018 and 2022 more than 5,000 stakeholders (including manufacturers, regulators, and government officials) participated in these training sessions.
1. Virtual current GMP (cGMP) training marathons
   a. 2020: Training sessions on 12 key GMP topics for pharmaceutical manufacturing were held, which were attended by relevant manufacturers, regulators, government officials, and other stakeholders from more than 60 countries across all six WHO regions.
   b. 2021: Training session on 12 key GMP topics, which focused on vaccine manufacturing was attended by vaccine and biopharmaceutical manufacturers and regulators from more than 60 countries across all six WHO regions.
   c. 2022: In-depth training sessions on 8 GMP topics focused on facility design, technology transfer, and advanced concepts in vaccine manufacturing. This was attended by vaccine and biopharmaceutical manufacturers and regulators from more than 80 countries across all six WHO regions and included an innovative feature of hands-on working group for small groups of attendees to apply the knowledge and skills gained to real-life vaccine manufacturing scenarios.

2. Virtual training workshops on the Common Technical Document (CTD) requirements for vaccine dossiers for PQ/EUL
   a. 2022: Training sessions attended by vaccine and biopharmaceutical manufacturers and regulators from more than 60 countries across all six WHO regions.

3. Virtual training workshop on the local production of quality and safe IVDs and PQ, EUL, and Expert Review Panel for Diagnostics (ERPD) processes
   a. 2021: Training session attended by IVD manufacturers and regulators from more than 60 countries across all six WHO regions.

4. Holistic training workshops on key enabling factors for successful local production were organized by WHO LPA unit with support of partners (such as African Development Bank, The Global Fund, UNICEF, MPP). These workshops deliver a comprehensive range of topics for building capacity in cultivating and leveraging on key enablers for sustainable quality local production, such as: technology transfer, patents/licensing, policy coherence, procurement, quality assurance and regulations, and regulatory affairs
   a. 2018: Training session for AFRO stakeholders, which was attended by manufacturers, regulators, and other relevant government officials and stakeholders.
   b. 2019: Training session for SEARO stakeholders, which was attended by manufacturers, regulators, and other relevant government officials and stakeholders from within the region as well as from Malaysia, Myanmar, and Vietnam.
   c. 2020: Training session for EMRO stakeholders, which was attended by manufacturers, regulators, and government officials.

A proportion of the 2021 virtual cGMP training marathon participants continued their learning journey by attending the virtual cGMP training marathons in 2022 or the 2022 virtual training workshop on the CTD requirements of vaccine dossiers for PQ/EUL.

Metric 8B: Number of manufacturers that received PQ-/EUL-related technical assistance

Since 2020, the LPA unit has supported the “PQ of medicines, vaccines, medical devices, IVD, and blood products, by providing complementary PQ-related technical assistance (TA) to manufacturers and quality control laboratories (QCLs) (in the manufacturing facilities) applying or planning to apply to the PQ or EUL Programmes.”

However, as

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84 Source: WHO (https://www.who.int/teams/regulation-prequalification/lpa/technical-assistance-for-who-prequalification)
of January 2023. the WHO LPA unit has not received requests for TA from such QCLs yet. Exhibit 53 below provides additional details.

Exhibit 53: Number of manufacturers that received PQ-/EUL-related technical assistance

<table>
<thead>
<tr>
<th>Manufacturers that received PQ-EUL-related technical assistance</th>
<th>Number of manufacturers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medicines</strong></td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>1</td>
</tr>
<tr>
<td>2021</td>
<td>1</td>
</tr>
<tr>
<td>2022</td>
<td>3</td>
</tr>
<tr>
<td><strong>Vaccines</strong></td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>0</td>
</tr>
<tr>
<td>2021</td>
<td>0</td>
</tr>
<tr>
<td>2022</td>
<td>5</td>
</tr>
<tr>
<td><strong>Diagnostics</strong></td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>0</td>
</tr>
<tr>
<td>2021</td>
<td>0</td>
</tr>
<tr>
<td>2022</td>
<td>2</td>
</tr>
</tbody>
</table>

Between 2018 and 2022, the WHO LPA unit provided technical assistance related to PQ and EUL submissions to 18 manufacturers across four WHO regions (AFRO, EMRO, SEARO, and WPRO). Currently, TA is provided to manufacturers of medicines, vaccines, and diagnostics with priority given to those located in LMICs. As an outcome of receiving technical assistance, one medicine manufacturer (out of the 18 that received technical assistance) submitted its product for PQ. This was accepted for evaluation in August 2022, and the manufacturer has now requested additional technical assistance for completing the PQ assessment process.

Metric 8C: Number of countries that received ecosystem assessments for quality and sustainable local production

As part of its activities, the WHO LPA unit supports governments by conducting ecosystem analyses to help Member States understand the current landscape and prioritize actions to build a conducive ecosystem for sustainable and quality local production, and to inform the development of a holistic national strategy/roadmap for strengthening local production. The assessment uses tools such as situational assessments to evaluate, e.g., policy coherence, the business environment, and the infrastructure.

Generally, the assessment is conducted according to the following process:

1. Gather intelligence on the country’s ecosystem for an initial desk review.
2. After the review, organize a mission for the country’s ecosystem assessment.
3. At the end of the mission, present and discuss the findings and proposed next steps with the government.

To conduct these ecosystem assessments, the WHO LPA unit has developed a situational analysis tool (currently in the piloting phase), which helps:

- Standardize the approach of the assessments.
- Member States to identify gaps and prioritize actions to build an ecosystem for sustainable and quality local production by providing quantitative and qualitative results from the assessments.
- WHO to provide tailored support and capacity building to Member States to strengthen support for local production.
- Track the progress of Member States through the electronic/digital version of the assessment tool.
As illustrated in Exhibit 54, the assessment tool was piloted between 2018 and 2022 in seven countries within three WHO regions (AFRO, EMRO, and SEARO). In 2022, the WHO LPA unit introduced a target of supporting at least one country a year with its ecosystem assessment. Three pilot assessments were conducted in 2022 and this target was met. The tool is expected to be completed and published by 2025; its impact is discussed in Metric 8E.

Exhibit 54: Number of countries that receive ecosystem assessment for quality and sustainable local production

<table>
<thead>
<tr>
<th>Countries that received ecosystem assessments for quality and sustainable local production</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of countries</td>
</tr>
<tr>
<td>2018</td>
</tr>
<tr>
<td>2019</td>
</tr>
<tr>
<td>2020</td>
</tr>
<tr>
<td>2021</td>
</tr>
<tr>
<td>2022</td>
</tr>
</tbody>
</table>

Source: WHO data (December 5, 2022).

C.8.2 Manufacturer, procurer/donor, and NRA perception of general manufacturing practices (Metric 8D)

Exhibit 55: Manufacturer, procurer/donor, and NRA perceptions on GMP standards

It is noted that the interview question as originally drafted was to ask stakeholders about their perceptions of improvements to manufacturing standards. However, the aspect most stakeholders provided perception on was WHO GMP. Most were not aware of formation of the new LPA unit. As a result, the following perception is specific to GMP (and not more broadly on strengthening of manufacturing).

Overall, stakeholders believe that the WHO GMP guidelines are very helpful and impactful – especially for manufacturers in non-SRA countries (all manufacturers except those based in the US or Europe shared that they rely on WHO manufacturing standards). Feedback was also shared on how these standards could be made even more helpful. The following three topics were most frequently raised in the interviews:
A. Guidelines are perceived as helpful and useful

Stakeholders overall believe that the WHO manufacturing guidelines meet their needs and thus heavily rely on them. They furthermore shared appreciation for the level of detail in the guidelines, which enables them to implement them easily into their processes and improve the quality of their operations accordingly.

- “WHO has the best [manufacturing related] standards and practices by far even compared to EMA and FDA. WHO standards are very detailed and prescriptive, whereas those from the EMA and FDA are very loose in their guidance. WHO is far ahead of any regulator or institution on this.” (Vx manufacturer)
- “The standards are not just written standards on paper; they are really there to help organizations. They are very well written and help us a lot with the implementation and validation of processes.” (Dx manufacturer)

B. Visibility and transparency for manufacturers

In general, stakeholders, especially manufacturers, shared their appreciation of the transparency that is provided in the process of developing and implementing the guidelines. In particular, manufacturers valued the ability to provide comments during the drafting of the guidelines and to participate in GMP seminars. Nevertheless, some manufacturers requested more visibility on feedback opportunities for the final drafts of new guidelines, as well as insights on which guidelines are in the process of being drafted and when they will be published.

- “We appreciate the access to guidance prior to publication, and the ability to comment on guidelines. The template for this is clear and easy to use.” (Vx manufacturer)
- “Sometimes some specific text finds its way into the formal, published version of a new guidance that was never in the draft. Therefore, we did not have the opportunity to comment on it until it was too late.” (Vx manufacturer)

C. Technical assistance and training around manufacturing and building local production capacity

Stakeholders find the technical assistance and training sessions provided around manufacturing and building local production helpful, and they also appreciate the ability to participate in the various workshops and seminars that are being provided by the WHO team. Nevertheless, some stakeholders expressed a wish to have better access to technical assistance and training sessions and believe that WHO could play an important role in terms of capacity building and knowledge transfer.

- “.... technical assistance in local manufacturing has been a lot patchier. There was no continuous agenda. Maybe this is also related to funding.” (Procurer)

C.8.3 Case study on supporting a Member State to strengthen local production and the impact of the WHA74.6 resolution on local production (Metric 8E)

The below case study illustrates how the WHO LPA unit has supported Ethiopia with the transformation of its pharmaceutical sector through the development and implementation of a National Strategy and Plan of Action for the Development of Pharmaceuticals Manufacturing (NSPA-Pharma).

Context

Africa produces about 0.1% of the global supply of vaccines and only 3% of global medicine manufacturing, a challenge the WHO LPA unit is addressing by supporting Member States and local manufacturers in building and expanding their capacity and sustainability. To facilitate building local production in Ethiopia, the WHO LPA unit supported the Government of Ethiopia (GoE) in the development, launch, and implementation of their NSPA-.
Pharma in close collaboration with WHO Country Office in Ethiopia, and with support from WHO Regional Office for Africa and partners. The NSPA-Pharma aims to transform the pharmaceutical sector by assisting local pharmaceutical companies to improve access to medicines through quality local production.

**Approach**

The WHO LPA team has offered various kinds of support in collaboration with WHO Country Office Ethiopia

1. **Provided technical assistance and support**
   - 2015: helped GoE with situational analyses of local production in Ethiopia and the subsequent development of the 10-year NSPA-Pharma
   - During COVID-19: assisted with feasibility studies on the possibility of local manufacturing of cGMP-compliant vaccines in Ethiopia in the context of COVID-19 and beyond.
   - Assisted the GoE in commissioning and developing several study reports and policy briefs for local production development.

2. **Provided operational frameworks and structural analysis**
   - Defined governance structure, working mechanisms, and terms of reference for NSPA-Pharma.
   - Set up and funded a project secretariat for coordination and reporting.
   - 2019: conducted a situational analysis to identify the strengths and gaps in the development of quality-assured Kilinto Pharmaceutical Industrial Park (KPIP).
   - 2020: conducted a study to create a roadmap for the development of quality assured KPIP.

3. **Organized and held supporting activities, such as events, training sessions, and inspections**
   - 2015: assisted the GoE in organizing a high-level launch for NSPA-Pharma.
   - 2018: convened a mid-term review conference to assess progress on the implementation of NSPA-Pharma and the impact of concurrent developments in the country on implementation, resulting in the refinement of NSPA-Pharma to remain relevant within the country’s context.
   - 2016 to 2021: conducted GMP inspections and follow-up assessments to identify gaps and prepare technical and financial support proposals.
   - 2020 to 2022: conducted capacity-building training sessions at the Ethiopian Food and Drug Authority (EFDA), the Food, Beverage, Pharmaceutical Industries Development Institute, and local manufacturer sites.

4. **Supported policy-making initiatives**
   - Developed a draft incentive proposal for the development of local production together with country offices and other partners.
   - Provided technical support to the Ministry of Health in Ethiopia during many intense consultations and negotiations with Member States for the development of Resolution WHA74.6.

**Impact and outcome**

By December 2022, at least four manufacturers had complied with local GMP requirements of the EFDA and obtained GMP certification (compared to 0 at the start of NSPA-Pharma). Furthermore, at least one pharmaceutical manufacturing plant located in KPIP received an EFDA manufacturing license.
**Lessons learned**

The WHO LPA unit had few key takeaways based on the work in Ethiopia, such as:

- Sustained political leadership, commitment, and support are crucial and critical.
- Ecosystem assessment plays an important role in the development of a holistic national strategy.
- Close collaboration among key stakeholders is essential.
- Periodic review and revision of the implementation of a national strategy enables the strategy to remain on-track, agile, and relevant.

**C.8.4 Recommendations**

Based on desk research and interviews, set out below are some options that the RPQ department can consider for actioning the key opportunities for improvement mentioned earlier in this section (referred to as “recommendations” in the table below). It is noted that while there were no specific recommendations for local production in the 2018 assessment, the LPA unit was formed in 2019 (after the period of the 2018 assessment).

<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendations</th>
<th>Example initiatives</th>
</tr>
</thead>
</table>
| 1.  | Revise process or criteria for providing technical assistance to manufacturers such that the team can identify candidates that will most likely submit PQ or EUL applications – critical to ensuring the team’s resources are being used appropriately | a. Understand from manufacturers that have received TA support on why they have not proceeded to submit PQ applications  
b. Understand from other RPQ department teams and WHO teams on screening criteria used to screen applications for TA in different contexts (need not be LPA related)  
c. Using inputs from (a) and (b) above – redesign process for selecting manufacturers for TA to enable identification of candidates more likely to submit PQ. As an e.g., consider introduction of fees for select criteria of manufacturers such as more mature manufacturers and/or manufacturers who are experienced with RPQ department’s activities (e.g., manufacturers who already have prequalified products)  
d. Consider if the TA may be operated on a "pull" system rather than "push" system, i.e., the other two units (and more specifically the PQ teams) have the ability to recommend manufacturers that could benefit from TA support.  
e. Develop more end-impact-oriented KPIs (current KPI is to provide certain number of manufacturers with Technical Assistance, could instead be around ensuring a certain number of DCMs apply for and get accepted for PQ). |
| 2.  | Improve accessibility, user friendliness, and transparency to increase adoption | a. Same as those shared in the broader theme of norms and standards in Theme 11 (in Section C.11.2). |
| 3.  | Strengthen implementation support for NRAs and DCMs to increase adoption and strengthen local production systems | a. Consider evolving the situational analysis tool in a similar direction as the GBT – where there are clear indicators and IDP-like roadmaps that can provide concrete guidance to stakeholders.  
b. Develop clear metrics to be able to track the impact of the ecosystem analysis tool. |
<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendations</th>
<th>Example initiatives</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Consider pathways to support LPA team’s capacity</td>
<td>a. While agenda/strategy setting and coalition building can be done centrally for building local production capabilities within Member States, strategy execution can be coordinated through dedicated LPA resources at regional offices with supervision and expertise from the RPQ departments at HQ</td>
</tr>
<tr>
<td>4.</td>
<td></td>
<td>b. Develop a model similar to CIP (which is used in the formal benchmarking process) – this will allow involvement of many other stakeholders (e.g., donors and development agencies) to support Member States</td>
</tr>
</tbody>
</table>

C.9 **ASSESSING THE ECONOMIC RETURN ON INVESTMENT (ROI): SAVINGS GENERATED BY PQ (THEME 9)**

Exhibit 56 gives an overview of the metric discussed in Theme 9 and its assessment methodology.

**Exhibit 56: Key metrics covered and the methodology for assessment under Theme 9**

**Metric 9A: Economic return on investment: Savings generated by PQ**

The RoI of PQ is a core metric to assess the program’s impact on the global health system and patients in LMICs. It is estimated that the extensive analysis of this impact metric completed in the 2018 assessment is still valid for the period between 2018 and 2022 for three reasons. First, between 2018 and 2022 no major events affected the PQ department’s core treatments, which suggests an updated analysis would show little to no change. Second, PQ participated in the COVID-19 vaccination validation efforts, and therefore any change in RoI would be positive. Third, the 2019 report showed a clear business case for the PQ department, which would not be impacted by any minor change. Consequently, the methodology and results of the 2019 impact assessment are summarized below and the full extract from the 2019 report can be found in Appendix 4.

**a. Methodology**

The economic return of PQ (operating in a broader landscape of global health stakeholders) was analysed as the savings generated per USD that is invested in PQ, given the limited resources available to donors. The RoI was determined in three steps:

1. Savings are calculated on an annual basis for the top products (by donor-funded sales) in each of medicine, vaccine, and diagnostic category.
2. Savings for the main products are summed up and scaled up to the total donor-funded PQ-enabled LMIC market.
3. Savings are aggregated across all product streams and compared to PQ-related costs. The detailed methodology is visually represented in Exhibit 57.

It is recognized that the methodology has some limitations, e.g., it does not quantify the “dollar value” of lives saved (an inherently difficult proposition), and not all savings observed in the market are fully linked to PQ-enabled competition (attributability). More limitations can be found in Appendix 4.

**Exhibit 57: RoI methodology high-level overview**

<table>
<thead>
<tr>
<th>Methodology overview</th>
<th>Detailed method</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROI</td>
<td>For each product/dosage strength, establish price drop between price when 1st major LMIC entered the market and latest price in the database</td>
</tr>
<tr>
<td>Direct economic return</td>
<td>Calculate donor procured volume of top products by disease areas/dosage strength Scale up to total market</td>
</tr>
<tr>
<td>Investment in the PQ program</td>
<td>Calculate PQ related costs</td>
</tr>
<tr>
<td>Calculate PQ related costs</td>
<td></td>
</tr>
</tbody>
</table>

**b. Output**

**Savings**

The estimated total savings range from USD 826 to 1,074 million across medicines, vaccines, and diagnostics, with the following distribution:

1. Medicines: USD 416-592 million
2. Vaccines: USD 407-474 million
3. Diagnostics: USD 3-8 million

Most of the savings are currently generated in medicine and vaccine categories, while savings generated in diagnostics are comparably low. Among others, this is due to the already relatively low cost of diagnostic products (e.g., CHF 0.8 for HIV and CHF 0.19 for malaria).

**Costs**

Costs are calculated in aggregate across all streams, and they reach a total of USD 28.4 million as per FY 2013.

**RoI**

Overall, the analysis shows that for every USD that is invested in PQ, the return in terms of savings (enabled not only by PQ but also by contributions of other global health stakeholders) is approximately USD 30-40.
C.10 CONTRIBUTING TO SAVING LIVES (THEME 10)

The work of the RPQ department has contributed to indirectly saving lives in various ways, including by improving access to medical products globally and by preventing large deployment of and hence access to substandard products. As PQ offers more manufacturers the opportunity to enter global and national markets with their prequalified products, the competition in these markets is likely to increase and prices could fall as a result. If prices are lower, procurers could buy more medical products with the same budget or reallocate the savings to other programs, thereby providing more patients with the medical products they need. This analysis therefore assumes that the increased access to medical products, and hence the RPQ department’s contribution to saving lives, is a direct result of the increased affordability of medical products for patients.

On top of the increased access to more traditional prequalified medicines, vaccines, and diagnostics for medical conditions such as HIV, malaria, and tuberculosis, the impact of the RPQ department’s work increased even further when the COVID-19 pandemic hit in 2020. The pandemic had led to a considerable global demand for COVID-19 vaccines by the end of 2020. Therefore, this report examines both the RPQ department’s contribution to lives saved due to increased access to non-COVID-19-related medical products as well as deaths averted from access to COVID-19 vaccines specifically.

Two metrics were identified to measure how the RPQ department contributed to saving lives. Exhibit 58 gives an overview of these metrics and their assessment methodology.

Exhibit 58: Key metrics covered and the methodology for assessment under Theme 10

<table>
<thead>
<tr>
<th>Metric Description</th>
<th>Metric No.</th>
<th>Metric Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated deaths averted in the first year of COVID-19 vaccinations in LMICs</td>
<td>10A</td>
<td>Quantitative</td>
</tr>
<tr>
<td>Patients accessed/lives saved as a result of increased affordability</td>
<td>10B</td>
<td>Quantitative</td>
</tr>
</tbody>
</table>

Metric 10A: Estimated deaths averted in the first year of COVID-19 vaccinations in LMICs

To estimate the contribution of the RPQ department’s work to lives saved in the context of COVID-19, the analysis conducted by The Lancet has been referenced in this report.

Between 5.1 million and 7.6 million deaths have been averted in LMICs in 2021 thanks to COVID-19 vaccinations (see Exhibit 59). The RPQ department contributed to this positive impact by listing 10 COVID-19 vaccines for emergency use between December 2020 and December 2021. As the large majority of LMICs rely on WHO Emergency Use Listings (EULs), the responsiveness of the RPQ department to list COVID-19 vaccines enabled the delivery of hundreds of millions of doses in 2021 (e.g., COVAX delivered over 842 million doses of COVID-19 vaccines in LMICs in 2021; these doses could not have been delivered without an EUL).

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86 Source: The Lancet [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00320-6/fulltext]
The analysis estimated the averted deaths in LMICs during the first year of COVID-19 vaccinations (2021) using a previously published COVID-19 transmission model and fitting framework. This model was fitted to the various country profiles, using country-level data such as first- and second-dose vaccination rates, vaccination strategies, and vaccine efficacy. Finally, to counter the heterogeneity in death registration and certification worldwide, the model was fitted to two types of mortality data:

1. Officially reported COVID-19 deaths: based on the Johns Hopkins University COVID-19 data repository. These estimates represent the lower bounds of deaths averted, given the worldwide underreporting of COVID-19 deaths.

2. Excess mortality in countries: based on official country reporting and model-based estimates of all-cause excess mortality for countries and/or time periods for which excess mortality was not reported.

As illustrated in Exhibit 59, in both estimates, the LICs account for less than 3% of the total deaths averted in LICs and LMICs. This can be attributed to the fact that the COVID-19 pandemic hit more severely in North America, Europe, and Southeast Asia compared to Africa, and that there are comparatively few people living in LICs (around 718 million in 2021\(^88\)) compared to LMICs (around 3.4 billion in 2021\(^89\)).

**Metric 10B: Patients accessed/lives saved as a result of increased affordability**

An extensive analysis of PQ’s contribution to lives saved was conducted for the 2019 impact assessment of PQ and systems support activities. The calculation was performed in the following three steps:

1. Calculation of the RoI as elaborated in Section C.9; calculation of savings generated by PQ for each disease area based on the RoI

2. Calculation of the freed-up budget by applying the ratio of savings versus the total market to the existing donor spend per disease area and product stream

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3. Calculation of the additional number of patients that could access treatment by comparing the freed-up budget for each disease area with the average cost of treatment per patient per year

Overall, it was estimated that PQ contributed to the access to HIV, malaria, tuberculosis, and rhesus disease medicines, and to vaccines and diagnostics for an additional 400 million people, assuming that the funding was not diverted to other causes. The distribution among medicines, vaccines, and diagnostics is the following:

1. Medicines: an estimated 150-215 million additional patients could get access to treatment based on a freed-up budget of USD 124-145 million and an average treatment cost per patient of USD 0.68. These estimates include
   a. 1.6-2.1 million HIV patients
   b. 183-213 million malaria patients
   c. Less than 1 million tuberculosis patients
   d. Less than 1 million rhesus disease patients.

2. Vaccines: an estimated 154-174 million additional patients could get access to treatment based on a freed-up budget of USD 337-382 million and an average treatment cost per patient of USD 2.19.

3. Diagnostics: an estimated 2.5-5.8 million additional patients could get access to treatment on a freed-up budget of USD 3.4-7.7 million and an average treatment cost per patient of USD 1.33.

C.11 INCREASING ADOPTION OF WHO GUIDELINES AND TECHNICAL STANDARDS (THEME 11)

Member States rely on WHO for expertise and guidance in the regulation, safety, and quality assurance of medicines through the development and promotion of international norms, standards, guidelines, and nomenclature. These guidelines are developed through Expert Committees, which are constituted of Member States, WHO experts, and other intergovernmental representatives.

Norms and standards are developed in collaboration between the RPQ department and the HPS department, implementation and adoption through trainings, etc., are driven by activities in both departments as well.

The impact assessment for this theme was done through two methods:

1. Interviews with manufacturers, donors/procurers, and NRAs to gain their perceptions on the impact and importance of WHO-developed norms and standards.

2. NRA Survey,\textsuperscript{90} which examined NRA’s perceptions of usefulness of a specific set of norms and standards. In this survey, the general perception of overall norms and standards was also tested to supplement the findings from the interviews mentioned in (1) above.

Additionally lack of availability of data on adoption of norms and standards was noted during this assessment. Some data was available for countries that have adopted International Pharmacopeia (44 countries) – however, it is unclear (as the team is relying on an external database that doesn’t contain these details) when this data was last updated.

\textsuperscript{90} The scope, methodology, and participants of the NRA survey are explained in more detail in Section B.1.3 above.
C.11.1 Assessment of value add and adoption of WHO norms and standards (metrics 11A to 11B)

Metric 11A: Manufacturer, procurer/donor, and NRA perception of overall WHO guidelines and technical standards

*Interview results*

Exhibit 61: Manufacturers’, procurers’/donors’, and NRA perceptions on WHO guidelines and technical standards

Almost all stakeholders interviewed shared that WHO’s norms and standards are critical to their day-to-day functioning and operations and that they are developed through a very thorough, technically sound, and collaborative process. Stakeholders rely on and trust WHO’s norms and standards – the involvement of experts and the collaborative nature of the process to develop these norms and standards results in high-quality and technically robust guidelines.

- “WHO has been effective at engaging expertise from around the world, working with academia, regulators, etc. […] They have done a good job pulling together the different stakeholders’ approaches and adapting where and when necessary.” (Industry Association)
- “The creation of standards is a very technical and well-controlled process in which a lot of experts are involved. We therefore trust that they are of very high quality.” (Procurer)

Additionally, manufacturers have been appreciative of the availability and responsiveness of the Norms and Standards (N&S) team when they required clarifications or assistance

- “The team will help and provide guidance if something is not addressed. We sometimes bother the team with a lot of questions, but they always answer really well.” (Rx Manufacturer)
- “Our R&D team needed clarification on the content of a TSS. We reached out to the WHO team, and they immediately came back with response, which was great.” (Vx Manufacturer)
However, most interviewees also acknowledge that there is opportunity to improve adoptions by: (a) strengthening implementation support, (b) and increasing ease of access to specific and up-to-date guidelines. This feedback remains very similar to the feedback shared by stakeholders at the time of the 2018 assessment.

A. **Strengthening implementation support to improve adoption of WHO guidelines**

Stakeholders have noted a lack of support for the implementation of the guidelines. This has particularly been the case since the COVID-19 pandemic. Manufacturers are requiring more technical assistance for the implementation of these technical norms and standards. The training sessions can be more targeted to support individuals higher up in the organizational chart, and with more decision-making power.

- “Implementation is still an issue though. [...] Before the pandemic there was more practical support, but this has fallen away. [...] Many people show up at the training, but these are very often people lower in organizational chart of the organization. [...] At one point before the pandemic the implementation was okay, but it has gotten worse. Since then, it’s gone in the wrong direction.” (Industry Association)
- “More technical assistance is needed on, for instance, how to implement standards, how to update local systems accordingly, etc.” (Vx Manufacturer)

B. **Improving the ease of access to the guidelines**

NRAs and manufacturers have highlighted that they have trouble searching for specific WHO guidelines, notably on the WHO website. These stakeholders note that there is a lack of structure and planning on the website, and that guidelines are moved around different links, making it easy to lose track. Stakeholders also note that life cycle management of the guidelines is difficult to navigate. Manufacturers have no indication as to which is the applicable or most updated guideline available.

- “Sometimes links to guidelines don’t work and information moves around on the website, making it more difficult for us to use the procedure.” (Rx Manufacturer)
- “It is very difficult to find the technical documents on the WHO website, and I have noticed that for many different topics (...) knowledge needs to be made more easily available. We are still using Google to look for guidelines.” (NRA)
- “It is hard to access the different norms and standards if you don’t know specifications like the year they were published. It is also difficult for Member States to understand which norms and standards they should use.” (Rx Manufacturer)

Survey results

The survey results are displayed in Exhibit 62. It shows a higher exposure to N&S across the survey respondents (only 20% with no exposure) compared to interview respondents (70% no exposure). Overall, the perception of survey respondents is similar to what was heard in the interviews – with no stakeholder providing a perception rating of 1 or 2, and 53% of respondents giving a positive to very positive opinion.
Exhibit 62: Survey results on the impact of WHO N&S for NRAs

On a scale from 1 to 5, how would you rate the impact that N&S for health products published by WHO have had for your NRA?

Number of responses, n=39

<table>
<thead>
<tr>
<th>Metric</th>
<th>Perception</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>High/some opportunity for improvement</td>
<td>0</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Mixed perception</td>
<td>10</td>
<td>26%</td>
<td></td>
</tr>
<tr>
<td>Very positive/positive opinion</td>
<td>21</td>
<td>53%</td>
<td></td>
</tr>
<tr>
<td>No exposure</td>
<td>8</td>
<td>21%</td>
<td></td>
</tr>
</tbody>
</table>

1. Excluding N/A
2. 5 being the best

Metric 11B: NRA perception of usefulness of specific guidelines

As part of a survey conducted with NRAs, 39 NRAs were given the opportunity to rate the perceived usefulness of 11 technical guidelines developed by WHO (on a scale from 1 to 5). The 11 guidelines are listed in Exhibit 63 below along with the perception ratings shared by the survey respondents.

Exhibit 63: Survey results on the usefulness of select WHO guidelines for NRAs

On a scale from 1 to 5, to what extent does your organization find the WHO guidelines mentioned below useful?

Number of respondents, n=39

<table>
<thead>
<tr>
<th>Guideline</th>
<th>n=</th>
<th>Survey average perception score</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO GMP guidelines for pharmaceutical products: main principles</td>
<td>32</td>
<td>4.2</td>
</tr>
<tr>
<td>The International Pharmacopoeia</td>
<td>32</td>
<td>4.1</td>
</tr>
<tr>
<td>WHO GMP guidelines for biologicals, including vaccines</td>
<td>32</td>
<td>4.1</td>
</tr>
<tr>
<td>WHO guidelines/recommendations to assure the quality, safety, and efficacy of vaccines</td>
<td>34</td>
<td>4.1</td>
</tr>
<tr>
<td>WHO guidelines for multisource products to demonstrate interchangeability (bioequivalence)</td>
<td>31</td>
<td>4.0</td>
</tr>
<tr>
<td>WHO guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product: quality part</td>
<td>30</td>
<td>4.0</td>
</tr>
<tr>
<td>WHO guidelines on biological (including biotherapeutic products)</td>
<td>33</td>
<td>4.0</td>
</tr>
<tr>
<td>WHO International Measurement Standards for biologicals, including vaccines, biotherapeutic products, blood products, and IVD</td>
<td>28</td>
<td>3.8</td>
</tr>
<tr>
<td>WHO GMP guidelines for blood establishment</td>
<td>21</td>
<td>3.7</td>
</tr>
<tr>
<td>WHO recommendation on the production, control, and regulation of human plasma for fractionation</td>
<td>24</td>
<td>3.7</td>
</tr>
<tr>
<td>WHO guidelines on increasing the supply of PDMPs in LMICs through fractionation of domestic plasma, 2021</td>
<td>21</td>
<td>3.6</td>
</tr>
</tbody>
</table>

1. Excluding N/A
2. 5 being the best

According to the survey results, seven of the eleven guidelines were viewed positively by NRAs. Of the four guidelines that received an average perception score below four, three of them related to blood products and products of human origin.

“WHO GMP guidelines for pharmaceutical products: main principles” also received an average score of 4.2, from 32 respondents, or 82% of the total number of respondents.
C.11.2 Recommendations

Based on desk research and interviews, set out below are some options that the RPQ department can consider for actioning the key opportunities for improvement mentioned earlier in this section (referred to as “recommendations” in the table below). It is noted that the recommendations made in points 2 and 3 below are the same as those highlighted in the 2018 Assessment.

<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendations</th>
<th>Example initiatives</th>
</tr>
</thead>
</table>
| 1.  | Strengthen implementation support for NRAs and DCMs to increase adoption | a. Develop and implement standard guideline release protocols that are used every time a new guideline is released or updated. These release protocols can help make implementation support more systematic and transparent. Guideline release protocols can include:  
   i. Periodic introductory workshops (e.g., weekly, or monthly) for NRAs and manufacturers (for a limited period after the release)  
   ii. Support documentation that includes, e.g., FAQs, examples/case studies, and a summary of changes to the latest version (compared to a previously released version) | b. Strengthen year-round support for stakeholders strategically to tailor implementation support to those who need it the most, e.g., virtual, standardized training and 1-on-1 sessions can be used frequently for large groups. In-person, local, context-focused training for small/new DCMs and NRAs can be provided with lower maturity or fewer staff |
| 2.  | Improve accessibility, user friendliness, and transparency to increase adoption | a. Establish easy-to-navigate platform where all WHO norms and standards are catalogued and accessible by topic, with a major focus on features that will improve access and adoption, e.g.:  
   i. Automate communication about new norms, standards, and revisions (e.g., through newsletters or by allowing stakeholders to ‘follow’ guidelines to receive notifications in case of changes)  
   ii. Remove/archive old or outdated norms and standards (in a publicly available archive)  
   iii. Include guidelines list/table with details on the future outlook, i.e., whether any changes are expected in the next year and if yes, at what stage the update is currently (draft, comments invited, etc.)  
   iv. Establish self-service tool that can allow manufacturers and NRAs to generate a list of all relevant norms and standards by answering a series of short questions/filters.  
   v. Explore linkages to ePQS system being launched in May 2023 | b. Consider alternate pathways (besides working with/relying on the WHO central website/communications development team) to developing a norms and standards microsite that can have the features referenced in (a) above. |
<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendations</th>
<th>Example initiatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.</td>
<td>Develop tracking processes/methodology to monitor implementation levels of different guidelines, thereby allowing targeted structured support for specific regions or on specific guidelines</td>
<td>a. Consider development of systematic processes and methodologies to track and monitor level of adoption by Member States. Some examples pathways could include: the GBT self-benchmarking or formal benchmarking process, submission of a survey as a prerequisite to attending any trainings, annual NRA survey, etc.</td>
</tr>
</tbody>
</table>
D Appendix

APPENDIX 1: ACCESS TO MEDICINES AND HEALTH PRODUCTS AS OF DECEMBER 2022

RPQ department organizational structure

Health product policy and standard (HPS)  |  Regulation and prequalification (RPQ)  |  Local production and assistance (LPA)

Proqualification (PQT)  |  Regulation and safety (REG)  |  Local production and assistance (LPA)

IVD Assessment  |  Regulatory system strengthening  |  Regulatory system strengthening
Inspection services  |  Regulatory convergence and networks  |  Regulatory convergence and networks
Medicines Assessment  |  Facilitated product introduction  |  Facilitated product introduction
Vaccines and immunization devices assessment  |  Laboratory Network and services  |  Laboratory Network and services
Vector control products assessment  |  Incidents and SF medical products  |  Incidents and SF medical products
Medical devices  |  Pharmacovigilance  |  Pharmacovigilance

Note: Out of scope for impact assessment.
APPENDIX 2: OVERVIEW OF RESPONDENTS FROM THE NRA SURVEY

39 responses were obtained out of the 179 NRAs that have received the perception survey on the RPQ department activities. The distribution of the respondents can be found in Exhibit 64. In the case of duplicate answers, an average of the scores for each question was calculated and rounded off if the average was a decimal number.

Exhibit 64: Distribution of the 39 survey respondents

<table>
<thead>
<tr>
<th>Q1 – To which WHO region does your NRA belong?</th>
<th>% of Member States</th>
</tr>
</thead>
<tbody>
<tr>
<td>African region (AFRO)</td>
<td>7%</td>
</tr>
<tr>
<td>Region of the Americas (AMRO)</td>
<td>12%</td>
</tr>
<tr>
<td>South-East Asia region (SEARO)</td>
<td>7%</td>
</tr>
<tr>
<td>European region (EURO)</td>
<td>6%</td>
</tr>
<tr>
<td>Eastern Mediterranean region (EMRO)</td>
<td>10%</td>
</tr>
<tr>
<td>Western Pacific region (WPR0)</td>
<td>2%</td>
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<tr>
<td>Total</td>
<td>39%</td>
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<table>
<thead>
<tr>
<th>Q2 – What is the maturity level (ML) of your NRA?</th>
<th>% of respondents</th>
</tr>
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<tbody>
<tr>
<td>ML1 or ML2</td>
<td>16%</td>
</tr>
<tr>
<td>ML3 or ML4</td>
<td>10%</td>
</tr>
<tr>
<td>Other</td>
<td>13%</td>
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<tr>
<td>Total</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Q3 – To which World Bank income group does your NRA belong?</th>
<th>% of Member States</th>
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</thead>
<tbody>
<tr>
<td>Low-income country (LIC)</td>
<td>4%</td>
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<td>Lower-middle-income country (LMIC)</td>
<td>18%</td>
</tr>
<tr>
<td>Upper-middle-income country (UMIC)</td>
<td>10%</td>
</tr>
<tr>
<td>High-income country (HIC)</td>
<td>5%</td>
</tr>
<tr>
<td>Blank</td>
<td>2%</td>
</tr>
<tr>
<td>Total</td>
<td>100%</td>
</tr>
</tbody>
</table>
APPENDIX 3: CASE STUDY ON IMPACT OF EMERGENCY USE LISTING PROCESS FOR VACCINES

The case study below illustrates the impact of the RPQ department on access to critical tools (i.e., COVID-19 vaccines) to end the acute phase of the pandemic.

WHO officially declared that COVID-19 was a pandemic on March 11, 2020. At that time, there were no authorized COVID-19 product available to treat or prevent the virus as the disease was unknown. There were efforts to develop vaccines on a global scale, but there was no regulatory framework in place to approve vaccines rapidly.

As part of their emergency response, countries adopted various approaches to enable faster distribution of COVID-19 vaccines to their citizens, including:

1. Granting Emergency Use Authorization (EUA) using reliance
   a. Regulatory approach based on PQ EUL (or SRA EAU) reliance
   b. Some countries requested that NRAs’ access to documentation submitted by manufacturers to PQ when applying for EUL, as well as respective assessment reports issued by PQ
   c. A few countries insisted on the submission of an application by a manufacturer

2. “Import authorization” or other authorization for use under exceptional circumstance
   a. Requirement for regulatory authorization is “waived”, relying on referring to WHO EUL
   b. Supply is based on an import authorization without issuance of a national EUA

As a result, 101 countries (out of 145) approved AstraZeneca or Serum Institute of India vaccines within 15 days after WHO EUL and allocated doses in the first COVAX allocation round (see Exhibit 65).

Exhibit 65: Overview of approval of AstraZeneca and Serum Institute of India doses within 15 days following WHO EUL
APPENDIX 4: EXTRACT FROM 2018 ASSESSMENT IN RELATION TO METRIC 9A: “ROI FOR DONOR MONEY INVESTED IN PQ”

It is estimated that the extensive analysis of this impact metric completed in the 2019 impact assessment of the PQ and Systems Supporting Activities report is still valid for the period between 2019 and 2022. Below is an extract from the 2018 Assessment: Quantitative analysis on savings generated by PQ versus investment made.

The assessment has to meet a number of criteria, including the following:

1. A simple methodology that is easy to understand and communicate
2. In line with the overall market and cost analyses
3. Should consider all relevant product streams and alternate regulatory pathways

The analysis conducted as part of this report covers HIV, malaria, TB, and RH for medicines, all vaccines, as well as HIV and malaria for diagnostics. Rather than covering the entire procurement market, it only looks at the donor-procured market for LMICs (excluding government procurement) and the procurement of prequalified products.

It is understood that PQ operates in an environment where its impact can only be achieved in close collaboration with other stakeholders, such as SRAs, procurers, and donors. All of them have made important contributions to increasing access across various product categories. As an example, in malaria and first-line TB, PQ alone has enabled around 90% of market access in terms of total value. For these diseases, SRA plays a minor role as the prevalence is very low in HICs, which makes PQ a natural choice for manufacturers. On the other hand, 51% of HIV-ARVs in value are both WHO-prequalified and SRA-approved while 21% solely rely on PQ. The comparatively small scope of PQ in ARVs is linked to the traditionally important role of PEPFAR, which relies on the USFDA tentative approval (tFDA) for its procurement and provides greater market access than PQ.

The overall philosophy of calculating the RoI is this: it is well recognized that the PQ operates in a reality where donor funding is limited and not sufficient to cover the entire affected population. In the past, donors invested generously in PQ and the economic return was considered to be savings generated per USD invested. The savings generated are a result of increased competition that the PQ has enabled by providing an avenue for DCMs to participate in the market.

In order to estimate the donor-funded PQ-eligible market size, a triangulation of different data sources was conducted. The analysis is based on data from 2014, for which complete data sets are available from all sources used for triangulation. As the donor-funded market size is unlikely to have changed by any significant extent due to a largely fixed donor spend, the estimated range of the RoI calculated for 2014 can be assumed to be representative of the present date.

For medicines, the following sources were used: (i) HIV/ARV: WHO Global Price Reporting Mechanism (GPRM) database, triangulated with Unitaid, UNAIDS, Global Fund, PEPFAR, and CHAI data; (ii) malaria: WHO GPRM database, triangulated with Unitaid, CHAI, IHME, and WHO World Malaria Report data; (iii) TB: Global Fund Price and Quality Reporting (PQR) database, triangulated with IHME, GDF/Stop TB data; (iv) rhesus disease: RH Interchange database. For vaccines, UNICEF Supply Division data was used, complemented by PAHO data, and calibrated to only include sales of prequalified products. Finally, for diagnostics, the data sets used for triangulation were from Global Fund, USAID, UNICEF, and WHO.

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91 WHO Prequalification Annual Report 2016 to Unitaid
92 http://pqr.theglobalfund.org
93 https://www.unfapprocurement.org/ri-home
a. **Methodology**

To calculate the savings generated by the PQ, a three-step approach was followed.

As step one, savings are calculated on an annual basis for the main products (by donor-funded sales) in medicines, vaccines, and diagnostics. Within medicine, savings are separately calculated for the main products in each major disease area covered, i.e., HIV, malaria, TB, and RH. For example, in medicines, the top three drugs analysed for HIV are Efavirenz + Lamivudine + Tenofovir disoproxil fumarate, Lamivudine + Nevirapine + Zidovudine, and Lopinavir + Ritonavir, which together make up about 65% of total donor-funded HIV/ARV sales. Where different presentations or dosage strengths exist, as, e.g., with most ARVs, savings are calculated separately for each.

The methodology for calculating savings for each of the products (or presentations/dosage strengths) is based on a multiplication of units sold and of price drops observed as a result of new manufacturers entering the market due to PQ. To calculate price drops, the price prior to market entry of the first major DCM is generally taken as the starting point (averaged across several years in some cases) and is compared to the latest price point in the data set. In order to focus on PQ-enabled savings, no savings are counted for products where the majority of sales are multinational manufacturers and price drops are unlikely to be enabled by PQ (e.g., pneumococcal conjugate vaccine) as few DCMs have entered, or where prices fluctuate significantly over time.

**Exhibit 66: Step one – Calculate savings for top products**

As step two, savings for the top products are summed up. For the lower-bound scenario, only these savings are considered, and it is assumed that the PQ generated no savings for other products within a stream or disease. For the higher-bound scenario, savings for the top products are scaled up to the full donor-funded PQ-enabled LMIC market size using the ratio of sales of top products versus total market sales of all prequalified products (e.g., excluding PEPFAR procurement based on tentative FDA approval for ARVs).
As step three, savings are aggregated across all product streams and compared to PQ-related costs (FY 2013). The costs taken into account to calculate the RoI for PQ are variable PQ costs, fixed PQ costs, and indirect PQ costs. For details on what the cost items include, refer to the exhibit further below. The RoI is then calculated as the fraction of savings generated per one unit of cost.

**Exhibit 68: Step three – Calculate return on investment**

**b. Output**

The analysis based on the methodology and data sources described above yields an estimated total savings range of USD 826 to 1,074 million across medicines, vaccines, and diagnostics, while acknowledging that PQ operates in the broader ecosystem of global health stakeholders who contribute to these savings as well. Savings are divided into the three streams as follows:

1. Medicines: USD 416 to 592 million
2. Vaccines: USD 407 to 474 million
3. Diagnostics: USD 3 to 8 million

Savings generated for diagnostics as a result of PQ are comparably low at this stage, but it needs to be kept in mind that the situation at the starting point is different between medicines, vaccines, and diagnostics. First, diagnostics only became part of PQ relatively recently (2008); hence, the time frame considered in the analysis is relatively short. Second, prices for many diagnostics were already low when the first diagnostic products were prequalified, partly because they were for use in LMICs (e.g., UN market for HIV RDT has been mature since the early 1990s, with
already low prices – around USD 1.2). Certain products also have a market in HICs (e.g., HIV molecular testing for HIV viral load). However, even though prices dropped in LMICs for these products, volumes were limited initially as this technology requires a specialized laboratory environment and skilled lab technicians.

Overall, it is agreed that quality has a price and that it should not go below a bottom threshold under which quality is impacted.

Costs are calculated in aggregate across all streams, as seen in Exhibit 69. They reach a total of USD 28.4 million as per FY 2013.

**Exhibit 69: Overview of PQ cost components in scope for RoI**

At PQ-enabled savings of USD 826 to 1,074 million and costs of USD 28.4 million across medicines, vaccines, and diagnostics, this leads to an estimated RoI of between 30:1 and 40:1 for the PQ-enabled donor-funded market.

**Exhibit 70: RoI analysis output**

1. Not including PCV and Rotavirus despite price drop, however price drop attribution to PQ is questionable
2. Due to the lack of a reliable dataset, for other products the time interval 2004-2014 is considered
3. Also referred to as pentavalent vaccine
APPENDIX 5: FULL LIST OF NRAS SURVEY QUESTIONS

Introduction

In order to deliver quality-assured medical products for all, WHO has issued in 2019 a 5-year plan (2019-23) to help build effective and efficient regulatory systems with 4 strategic priorities:

1. Strengthen country and regional regulatory systems
2. Improve regulatory preparedness for public health emergencies
3. Reinforce and expand WHO prequalification and product risk-benefit assessment
4. Increase the impact of WHO regulatory support activities

As the end of the 5-year plan approaches and considering the important changes that occurred in the global health ecosystem over the past 4 years, an external assessment of the activities of the Regulation and Prequalification (RPQ) department was commissioned to:

1. Create an understanding of the value that the RPQ department has created in the Global Health ecosystem with a 360-degree view across all stakeholders with a focus on period 2018-22
2. Identify and analyze the main evolutions that have occurred since the publication of the previous assessment in 2018
3. Generate both qualitative and quantitative assessments of the value created by the RPQ department for its main stakeholders with a focus on country impact in line with the 4 strategic priorities for the period 2019-23
4. Develop insights and recommendations that enable both operational quick wins (i.e., allowing for efficiency gains) and long-term improvement opportunities

This survey is a part of the aforementioned 2018-22 assessment and aims to get your perspective on the value that the RPQ department creates for your National Regulatory Authority (NRA).

Confidentiality: All responses remain anonymous and confidential and will not be attributed to you or your organization. From the information received through this survey, quotes might be used without mentioning who said them, besides mentioning the type of stakeholder (i.e., “a national regulatory authority” while ensuring the specific national regulatory authority remains anonymous).

Duration: We expect the survey to take 10 to 15 minutes. You can save your answers along the way and can complete the survey in multiple sessions.

Questions marked with a red asterisk (*) require an answer.

**Question 1:** To which WHO region does your national regulatory authority belong? *

- African Region (AFRO)
- Region of the Americas (AMRO)
- South-East Asia Region (SEARO)
- European Region (EURO)
- Eastern Mediterranean Region (EMRO)
- Western Pacific Region (WPRO)

**Question 2:** What Maturity Level is your national regulatory authority?

- Maturity Level 1 or 2
- Maturity Level 3 or 4
- Other

**Question 3:** To which World Bank income group does your national regulatory authority belong?
- Low-income country (LIC)
- Lower-middle-income country (LMIC)
- Upper-middle-income country (UMIC)
- High-income country (HIC)

**Question 4:** For which of the below topics has your organization received support since 2018 from the World Health Organization’s regulation and prequalification team? Please select all that apply. *
1. Strengthening regulatory systems
2. Improving the management of substandard and falsified medical products
3. Increasing compliance of quality control laboratories with required standards
4. Strengthening pharmacovigilance
5. Enabling faster access to the public to prequalified products (through facilitated product introduction pathways such as Collaborative Registration Procedures (CRP))
6. Improving regulatory preparedness for public health emergencies
7. Improving access to donor-funded procurement markets
8. Building an ecosystem for quality and sustainable local production
9. Norms and standards
10. Other

**Question 5:** For which of the below themes does your organization expect to require support from the World Health Organization’s regulation and prequalification team in the next five years? Please select all that apply. *
1. Strengthening regulatory systems
2. Improving the management of substandard and falsified medical products
3. Increasing compliance of quality control laboratories with required standards
4. Strengthening pharmacovigilance
5. Enabling faster access to the public to prequalified products (through facilitated product introduction pathways such as Collaborative Registration Procedures (CRP))
6. Improving regulatory preparedness for public health emergencies
7. Improving access to donor-funded procurement markets
8. Building an ecosystem for quality and sustainable local production
9. Norms and standards
10. Other

**Question 6:** On a scale from 1 to 5 (5 being the best), how would you rate the impact the Global Benchmarking Tool (GBT) and its applications have had in strengthening and improving maturity levels for your NRA? Please only consider the period of 2018 to 2022 in your response. *
Question 7: Please share the rationale for your rating. Please include some strengths as well as some opportunities for improvement.

Question 8: On a scale from 1 to 5 (5 being the best), how would you rate the impact the WHO’s pharmacovigilance activities have had in your country? Please only consider the period of 2018 to 2022 in your response. *

Question 9: Please share the rationale for your rating. Please include some strengths as well as some opportunities for improvement.

Question 10: On a scale from 1 to 5 (5 being the best), how would you rate the impact that collaborative procedure for accelerated registration (CRP) processes (and other facilitated product introduction processes) have had in streamlining downstream approvals in your country? Please only consider the period of 2018 to 2022 in your response. *

Question 11: Please share the rationale for your rating. Please include some strengths as well as some opportunities for improvement.

Question 12: On a scale from 1 to 5 (5 being the best), how would you rate the impact of (i) the medicines prequalification (PQ) quality assessment training of regulators and (ii) involvement of NRA assessors in medicines PQ assessment activities on your NRA’s regulatory capacity (if applicable). Please only consider the period of 2018 to 2022 in your response. *

Question 13: Please share the rationale for your rating. Please include some strengths as well as some opportunities for improvement.

Question 14: On a scale from 1 to 5 (5 being the best), how would you rate the impact that norms and standards for health products published by WHO have had in your country? Please only consider the period of 2018 to 2022 in your response. *

Question 15: Please share the rationale for your rating. Please include some strengths as well as some opportunities for improvement.

Question 16: On a scale from 1 to 5 (5 being the best), to what extent does your organization find the below mentioned WHO guidelines useful? *
| WHO guidelines for multisource products to demonstrate interchangeability (bioequivalence) (1) | 1 (1) | 2 (2) | 3 (3) | 4 (4) | 5 (5) | Prefer not to answer because this is not a topic my organization has exposure to (6) |
| WHO guidelines/recommendations to assure the quality, safety, and efficacy of vaccines (2) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| WHO guidelines on biological (including biotherapeutic products) (3) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| WHO Recommendation on the production, control, and regulation of human plasma for fractionation (4) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| WHO Guidance on Increasing supply of PDMPs in LMICs through fractionation of domestic plasma, 2021 (5) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| WHO GMP guidelines for biologicals, including vaccines (6) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| WHO GMP guidelines for pharmaceutical products: main principles (7) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| WHO GMP guidelines for blood establishment (8) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| The International Pharmacopoeia (9) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| WHO International Measurement Standards for biologicals, including vaccines, biotherapeutic products, blood products, and in vitro diagnostics (10) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| WHO Guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product: quality part (11) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

Question 17: Do you have any additional feedback you would like to share?
APPENDIX 6: ADDITIONAL DETAILS ON THE ZAIZIBONA JOINT ASSESSMENT PROGRAM

Context

The Southern African Development Community (SADC) is one of the eight regional economic communities of the African Union consisting of 16 countries participating in the AMRH initiative.

The ZaZiBoNa collaborative medicines registration initiative was established in 2013 by four countries (Zambia, Zimbabwe, Botswana, and Namibia) with the support of the PQ team. Currently, there are nine active members.

The initiative was established to address common challenges, such as huge backlogs of product applications, high staff turnover, long registration times, inadequate financial resources, and limited capacity to assess certain types of products such as biologicals and biosimilars.

Approach

Between 2013 and 2022, the initiative has assessed over 360 applications, which is the highest number of products assessed by any regional harmonization initiative on the African continent. Out of these, 176 products have been recommended for registration and the rest has either been rejected or withdrawn.

The WHO RCN team, in collaboration with other WHO teams and AMRH partners, provided technical assistance in different areas, including:

- Developing common technical guidelines, standards, and standard operating procedures, facilitating joint assessment activities since 2014
- Providing basic and advanced training on the assessment of medical product dossiers as well as GMP inspection
- Developing an IT platform (MedNet) for the exchange of documents and reports to facilitate joint assessments
- Granting short-term rotational positions to assessors and inspectors within the PQ team

Impact and outcome

The median time to recommendation is 12 months, which is lower than the registration timelines achieved by some participating countries. These shorter timelines for the approval of medicines have had a positive impact on the increased availability of quality-assured medicines for patients in the SADC region.

Furthermore, following the recommendations, as of March 2022, nine countries have issues market authorizations for various medical products:

- Zimbabwe for 133 medical products
- Botswana for 132
- Zambia for 128
- Namibia for 123
- South Africa for 66
- Tanzania for 20
- Mozambique for 8
- Malawi for 3
- The Democratic Republic of Congo for 1
Finally, work sharing has reduced the workload, and timelines for registration have built confidence and trust between members and provided a platform for capacity building and information sharing.

*Lessons learned from ZaZiBoNa*

- Need for continued commitment of the heads of agencies to ensure the sustainability of the initiative
- Need to maintain technical support by WHO teams and AMRH partners for building the capacity of ZaZiBoNa members and nonmember countries
- Need to develop and adhere to a tracking system