WHO/MPP mRNA Technology Transfer Programme
Cape Town, South Africa, April 17th (2023)

Regulatory Systems Strengthening & Technical Assistance for Prequalification

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Director RPQ
Expand **access to quality assured medicines and health products**

Ensure that quality essential medicines and health products are available in **sufficient quantities and affordable** to the population through functioning regulatory and procurement systems.

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**1 in 10**

observed failure rate of medicines samples in low- and middle-income countries

**This costs**

$US30.5$ billion

*estimated spending on substandard and falsified medicines in low- and middle-income countries, based on wholesale level sales*

**Child deaths**
estimated $72,430$–$169,271$ deaths caused by substandard and falsified antibiotics in children under 5 suffering from pneumonia

**Malaria**
estimated $31,000$–$116,000$ deaths caused by substandard and falsified antimalarials in sub-Saharan Africa

**US$38.5 million**
estimated spending on substandard and falsified antimalarials in sub-Saharan Africa

Source:
- Public health and socioeconomic impact study 2017
  [https://apps.who.int/iris/handle/10665/301199]
- University of Edinburgh
- London School of Hygiene and Tropical Medicine
“End-to-end” health products’ management: shared responsibilities

Legislation, regulation, governance, monitoring

Affordable, timely and equitable access to quality-assured medicines, vaccines & other health products and technologies

- Universal health coverage
- Health emergencies
- Health and well-being
Overall regulatory systems’ maturity level of WHO Member States

ML 1
98 countries
50%

ML 2
39 countries
20%

ML 3, 4
57 countries
30%

* Includes SRAs, NRA (Americas), functional NRAs (vaccines)

Source: WHO RSS database, March 2023
Background to WHO regulatory strengthening activities

• Strong regulatory capacity is an **essential component** of a **well-functioning healthcare system** (Resolution WHA 67.20, 2014)

• Globally, >70% of countries have weak national regulatory systems
  ✓ Only 57 countries (29%) have regulatory systems at GBT maturity level 3/4
    o See: [https://www.who.int/initiatives/who-listed-authority-reg-authorities](https://www.who.int/initiatives/who-listed-authority-reg-authorities)

• WHO regulatory systems strengthening programme responds to this challenge
  ✓ Benchmarking to document strengths and identify gaps
  ✓ Capacity building, including on regulatory preparedness & response
    ❖ In collaboration with partners through the Coalition of Interested Parties (CIP)
  ✓ Promoting smart regulation – good regulatory and reliance practices
    ▪ Implementation of WHO Listed Authorities framework

Four strategic priorities

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

- Guiding WHO regulatory strengthening activities
  - Benchmarking and technical assistance to address regulatory gaps
  - Promoting regulatory convergence, harmonization, work-sharing and reliance mechanisms
  - Improving countries’ ability to carry out risk-based post-marketing surveillance to securing supply chains against substandard and falsified products & safety monitoring of authorized products (vigilance)
    - Includes strengthening national quality laboratories
  - Promote and support sustainable and quality-assured local production through technical assistance

WHO Regulatory Activities
Ensuring normative and technical excellence drives impact at country level

Technical Standards & Specifications
- Set global norms and standards (written & physical) and nomenclatures
- Increase common understanding on regulatory requirements by authority & manufacturer
- Standardize approach used by quality control labs

Prequalification
- Assure safety, efficacy & appropriateness of medical products used in LMICs, including medicines, vaccines, medical devices, cold chain equipment, vector control products & in vitro diagnostics
- Increase competition to shape the market

Regulation & Safety
- Strengthen regulatory systems in countries and regions
- Promote regulatory cooperation, convergence and transparency through networking, work-sharing and reliance
- Mitigate risks and protect against substandard / falsified products

Local production & assistance
- Provide holistic & coordinated support to strengthen local production and technology transfer
- including
  - guidance tools, situational analyses for sustainable quality local production
  - strengthening local production, capacity building and specialized technical assistance

Decreased regulatory burden
Reduced time for regulation
Increased regulatory capacity in LMIC
Decreased cost of regulation
Reduced mortality and morbidity
WHO Five-Step Capacity Building Model for National Regulatory Authorities (NRAs)

As per Resolution WHA 67.20 on Regulatory Systems Strengthening (2014)

- Development of the Global Benchmarking Tool (GBT)
- Benchmarking of the national regulatory system
- Formulation of Institutional Development Plan (IDP)
- Providing technical support, Training/Learning, networking,
- Monitoring progress and impact

Coalition of Interested Parties (CIP)

- Stable, well functioning and integrated regulatory system
- Eligibility for vaccine PQ
- WHO listed authorities (WLA)

[Diagram showing the five steps of the model]
Number of Member States benchmarked by GBT by year

Cumulative bar chart

- 2016: 9
- 2017: 33
- 2018: 44
- 2019: 73
- 2020: 84
- 2021: 86
- 2022: 95
WHO Regulatory System Strengthening Programme
Global status of benchmarking of regulatory systems (2016 – Mar 2023)

95 = 74%

Member-states  World population

Self Benchmarking
1. Algeria  32. Kyrgyzstan
2. Afghanistan  33. Lebanon
3. Albania  34. Liberia
4. Angola  35. Madagascar
5. Benin  36. Malawi
6. Bhutan  37. Malaysia
7. Bolivia  38. Maldives
10. Burkina Faso  41. Mauritius
11. Cameroon  42. Mongolia
12. Cape Verde  43. Montenegro
13. Central African Republic  44. Namibia
14. Chad  45. Nepal
15. Comoros  46. Nicaragua
16. Democratic Republic of the Congo
17. Costa Rica
18. Cote d’Ivoire
19. Djibouti
20. Ecuador
21. Equatorial Guinea
22. Eswatini
23. Gabon
24. Gambia
25. Guatemala
26. Guinea
27. Guinea-Bissau
28. Honduras
29. Iraq
30. Islamic Republic of Iran
31. Jordan

Benchmarking
1. Bangladesh
2. Burundi
3. Cambodia
4. People’s Republic of China
5. El Salvador
6. Egypt
7. Eritrea
8. Ethiopia
9. Ghana
10. India
11. Indonesia
12. Kazakhstan
13. Kenya
14. Lao People’s Dem Rep
15. Mozambique
16. Nigeria
17. Papua new guinea
18. Rwanda
19. Saudi Arabia
20. Serbia
21. Singapore
22. Somalia
23. South Africa
24. South Korea
25. South Sudan
26. Sri Lanka
27. Sudan
28. Türkiye
29. United Republic of Tanzania
30. Thailand
31. Timor-Leste
32. Uganda
33. Viet Nam
34. Zimbabwe
Maturity levels of national regulatory systems

WHO GBT (for medicines and vaccines: as of Mar 2023)

<table>
<thead>
<tr>
<th>ML Level</th>
<th>Description</th>
<th>Oct 2018</th>
<th>Nov 2020</th>
<th>Mar 2023</th>
</tr>
</thead>
<tbody>
<tr>
<td>ML1</td>
<td>With some elements of regulatory system</td>
<td>100 COUNTRIES</td>
<td>100 COUNTRIES</td>
<td>98 COUNTRIES</td>
</tr>
<tr>
<td>ML2</td>
<td>Evolving national regulatory system</td>
<td>44 COUNTRIES</td>
<td>41 COUNTRIES</td>
<td>39 COUNTRIES</td>
</tr>
<tr>
<td>ML3</td>
<td>Stable, well functioning and integrated</td>
<td>50 COUNTRIES</td>
<td>53 COUNTRIES</td>
<td>57 COUNTRIES</td>
</tr>
<tr>
<td>ML4</td>
<td>Advanced level of performance and continuous improvement</td>
<td>73%</td>
<td>70%</td>
<td></td>
</tr>
</tbody>
</table>

In 2022 alone, 6 countries achieved ML 3/M4 in medicines and vaccines reg systems:
- Singapore ML 4 (medicines)
- Republic of Korea ML 4 (medicines & vaccines)
- Egypt, China and South Africa ML 3 (vaccines)
- Nigeria ML 3 (medicines)

Vaccines developed in countries with weak regulatory systems, i.e., ML1/ML2, are not eligible for WHO EUL or Prequalification.
Coalition of Interested Parties (CIP) Network

launched in 2021, now with 20 members

Purpose:
To establish and promote a unified strategic and coordinated approach to strengthening national and regional regulatory systems

Aim:
To increase the effectiveness of collective efforts and desired impact in countries and regions.

Joining the CIP Network

- Eligible entities need to submit an Expression of Interest (EOI) form via the CIP web platform: https://www.cip-network-rss.org/
- Follow the link, click on the "Join Us" tab and then complete and submit the EOI form.
- Following the submission of the EOI form, an application form will be sent to the applicant by the CIP Secretariat.
- The completed application form must be submitted via email to the CIP Secretariat.
- Applications are reviewed against the eligibility criteria set forth in the CIP TOR & the WHO Framework for engagement with Non-State actors (FENSA)

Contact the CIP Secretariat: cip_network@who.int
WHO Listed Authorities (WLA)

- Framework for designating and publicly listing a regulatory authority as a WLA
  - Transparent and evidence-based pathway for regulatory authorities operating at an advanced level of performance
  - Replacing the procurement-oriented concept of stringent regulatory authorities
  - Promote access and supply of safe, effective and quality medical products.
  - Provides for the optimal use of limited resources by facilitating reliance on the work products and decisions of trusted agencies in the decision-making of regulatory authorities, the WHO PQ Programme and procurement agencies
  - Fostering regulatory cooperation, thus contributing to the improvement in good regulatory and reliance practices.
- Launched in March 2022 - 3 pilots advanced and full implementation Q2/2023
- Key resources
  2. Transitional list (tWLA) (2022): https://www.who.int/publications/m/item/list-of-transitional-wlas
Facilitated Regulatory Pathways (FRP) as a solution to NRAs

FRPs are a type of regulatory pathways available to NRAs, which are meant to facilitate and accelerate the regulatory decisions and the introduction of quality-assured products in countries, through the use of the concepts of reliance and collaboration.

When well implemented:
- NRAs leverage on the work performed by others, improving efficiency of the regulatory systems by avoiding duplication of regulatory efforts and work;
- NRAs optimize the use of human and financial resources and increase expertise and build capacities;
- NRAs reduce the time needed to process a product application and reduce workload and backlog at NRAs;
- NRAs perform science-based and transparent regulatory decision-making, while maintaining national independence on their decisions;
- NRAs ensure timely access to quality-assured products in countries.

FRPs, such as the Collaborative Registration Procedure, to be used not only during emergencies but also in the regular and routine regulatory activities of countries to improve efficiency of the regulatory systems and ensure registration of quality-assured products.
WHO efforts to facilitate good quality decisions based on reliance

Internationally, by participation and contribution in regional and sub-regional regulatory networks and initiatives
Facilitation of EUL process

31 December 2020, first WHO EUL for a COVID-19 vaccine (BNT162b2 mRNA vaccine); 10 days after EMA scientific opinion

In-country authorizations for use

- First roll-out in Feb-March 2021 ChAdOx1 vaccine
- Approvals/import permits in 101 out of 145 countries (70%) within 15 days of WHO EUL (15 February 2021)

Reliance in Lifecycle/all reg functions
Authorization, Pharmacovigilance, Batch/Lot Release, Post Authorisation

Overall, over 2 billion vaccines doses allocated in over 160 countries/territories involving close to 5,000 regulatory approvals as of August 2022
WHO’s prevent-detect-response strategy

- WHO supports NRAs
  - Conduct investigations
  - Conduct sampling and testing for market surveillance
- WHO issues risk communications
  - Global Medical Product Alerts
  - Targeted Market Surveillance
  - WHO information notices for IVD users
- WHO develops normative guidance
  - National action plans for SF
  - Selecting technologies to screen/detect SF
  - Handbook for introducing SF into pharmacy school curriculum
LPA Unit’s mandates in strengthening quality and sustainable local production to improve access

Further strengthened by Resolution WHA74.6:

- Global coordination and Partnerships
- Regional & Country support in local production and tech transfer
- PQ/EUL-related specialized technical assistance

World Local Production Forum (WLPF) Interagency statement etc.
Ecosystem assessments for quality and sustainability
Strategy/roadmap setting and implementation
Global resources on local production and technology transfer
Facilitation of technology transfer
Capacity building and technical assistance to achieve quality, sustainability and WHO PQ/EUL

For more information: https://www.who.int/teams/regulation-prequalification/lpa
World Local Production Forum
Enhancing access to medicines and other health technologies

- New WHO initiative to foster global coordination, synergy and partnerships
- Sustainable, global platform for Member States, industry, experts, academia, UN agencies, international organizations, etc.
- High-level collective action to address challenges, harness opportunities and shape strategies and the direction of local production globally

2\textsuperscript{nd} World Local Production Forum (WLPF) will be convened in the Netherlands as the hosting country

https://www.who.int/initiatives/world-local-production-forum
How to proceed from lab to clinic?

Drug (target) discovery

Drug design

Drug development

Nonclinical (preclinical)

Animal studies

Clinical

Industrial partnership

CRO?

GMP of API (NCE/Biotec) QA GLP GMP GCP
Equitable and affordable, timely access to quality medicines and other health products, requires an integrated approach with ALL stakeholders.