

Promoting the Quality of Medicines Plus

What Are Regulatory and Quality Assurance Systems and How Do They Impact Health Programs?

Webinar

Tuesday, November 17, 2020

8:00 – 9:30 a.m. EST



Promoting the Quality of Medicines Plus

Welcome

Jesse Joseph, Alternate Agreement Officer's
Representative and Deputy Director, Office of
Health Systems, USAID



What Are medical product quality Assurance Systems and Why Are They Important?

Beth Yeager, PQM+ Deputy Director

Webinar Overview



- What are medical product quality assurance systems?
- Who is responsible for them?
- What do regulatory agencies do to assure medical product quality?
- What can be done to sustainably strengthen these systems to help ensure the effectiveness of USAID's health programs?

What Do We Mean by 'Medical Products'?

Medical products include medicines, devices, vaccines, other biologics, and commodities used to prevent and treat illness and maintain health.

HIV/AIDS	Malaria	TB	MCH-N	FP/RH	COVID-19	NTDs
<ul style="list-style-type: none">• Antiretrovirals• Rapid diagnostic test (RDT)• Medicines to treat opportunistic infections• Kits for voluntary medical male circumcision	<ul style="list-style-type: none">• Antimalarials• Bednets• RDTs	<ul style="list-style-type: none">• Medicines for prevention and treatment	<ul style="list-style-type: none">• Essential medicines for mothers, newborns and children• Micronutrients• Ready-to-use Therapeutic Supplementary Foods• Vaccines	<ul style="list-style-type: none">• Hormonal contraceptives• Condoms and Intrauterine device	<ul style="list-style-type: none">• Personal protective equipment (PPE)• Medicines• Vaccines	<ul style="list-style-type: none">• Medicines

Is Quality an Issue? YES!

The World Health Organization estimates that **at least 1 in 10** medical products is of poor quality.

This is the **tip of the iceberg.**



Impacts Extend Beyond Health



Health

increased mortality and morbidity, disease spread, antimicrobial resistance



Economic

increased out-of-pocket expenses, lost productivity, wasted health resources



Social

increased poverty, loss of confidence in health systems

Example: MCH

► PLoS One. 2020 Jul 10;15(7):e0236060. doi: 10.1371/journal.pone.0236060. eCollection 2020.

Quality of medicines for life-threatening pregnancy complications in low- and middle-income countries: A systematic review

Maria Regina Torloni ¹, Mercedes Bonet ², Ana Pilar Betrán ², Carolina C Ribeiro-do-Valle ³, Mariana Widmer ²

Affiliations + expand

PMID: 32649710 PMID: PMC7351160 DOI: 10.1371/journal.pone.0236060

[Free PMC article](#)

Findings: We identified 9699 unique citations and included 34 studies (3159 samples from 40 countries) in the review. Most studies (65%) had low quality (scores <6/12). Overall, 48.9% of 1890 uterotonic samples (19 studies) failed quality tests; failures rates were 75% for ergometrine and nearly 40% each for oxytocin and misoprostol. The overall prevalence of failed injectable antibiotics (1090 samples, 18 studies) was 13.4%, ranging from 2.9% for injectable metronidazole (34 samples, 3 studies) to 16.0% for cefazolin (449 samples, 2 studies). The prevalence of low quality magnesium sulphate (179 samples, 2 studies) was 3.4%. We did not find any studies on the quality of carbetocin, tranexamic acid, or clindamycin.



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- 13.4% of 1,090 injectable antibiotics samples
- 48.9% of 1,890 uterotonic samples failed quality tests

Example: Malaria



[JAMA Netw Open](#). 2018 Aug; 1(4): e181662.

Published online 2018 Aug 10. doi: [10.1001/jamanetworkopen.2018.1662](https://doi.org/10.1001/jamanetworkopen.2018.1662)

PMCID: PMC6324280

PMID: [30646106](https://pubmed.ncbi.nlm.nih.gov/30646106/)

Prevalence and Estimated Economic Burden of Substandard and Falsified Medicines in Low- and Middle-Income Countries

A Systematic Review and Meta-analysis

[Sachiko Ozawa](#), PhD, MHS,^{1,2} [Daniel R. Evans](#), MSc,² [Sophia Bessias](#), MPH,³ [Deson G. Haynie](#), MHS,⁴ [Tatenda T. Yemeke](#), MSc,² [Sarah K. Laing](#), MPH,² and [James E. Herrington](#), PhD⁵

Findings

In this systematic review of 265 studies comprising 400 647 drug samples and meta-analysis of 96 studies comprising 67 839 drug samples, the prevalence of substandard and falsified medicines in low- and middle-income countries was 13.6% overall (19.1% for antimalarials and 12.4% for antibiotics). Data on the estimated economic impact were limited primarily to market size and ranged widely from \$10 billion to \$200 billion.



Prevalence of substandard and falsified antimalarials in LMICs – 19.1%

Example: Covid-19

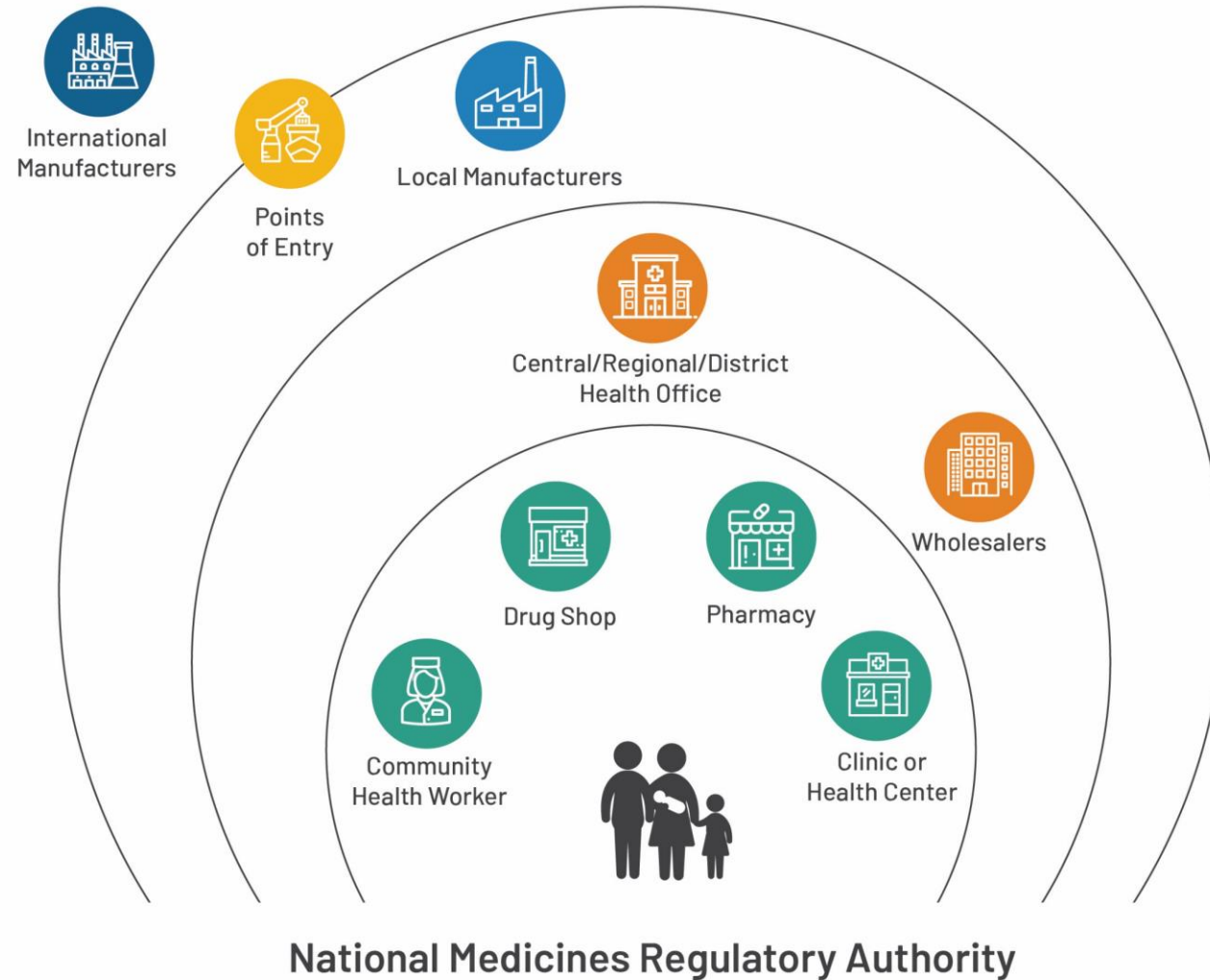
FDA NEWS RELEASE

COVID-19 Update: FDA Warns Consumers About Hand Sanitizer Packaged in Food and Drink Containers

Silver Spring, MD — The U.S. Food and Drug Administration (FDA) is warning consumers about [alcohol-based hand sanitizers](#) that are being packaged in containers that may appear as food or drinks and may put consumers at risk of serious injury or death if ingested. The agency has discovered that some hand sanitizers are being packaged in beer cans, children's food pouches, water bottles, juice bottles and vodka bottles. Additionally, the FDA has found hand sanitizers that contain food flavors, such as chocolate or raspberry.

“I am increasingly concerned about hand sanitizer being packaged to appear to be consumable products, such as baby food or beverages. These products could confuse consumers into accidentally ingesting a potentially deadly product. It's dangerous to add scents with food flavors to hand sanitizers which children could think smells like food, eat and get alcohol poisoning,” said FDA Commissioner Stephen M. Hahn, M.D.

Medical Product Quality SYSTEM



Why Regulate Medical Products?



- **Health and well-being** of patients, families, communities, and populations
- **High market value** makes the pharmaceutical sector especially vulnerable to corruption, waste, and mismanagement
- **Consumers do not have the necessary information** about quality or when, how, or which medicines to use

Source: [Rago et al 2008](#)

Why Regulate Medical Products?



- **The large number of stakeholders** involved increases opportunity for quality to be compromised
- **Premises, practices, and people** must be held to particular standards
- **Supply chains can compromise the quality of medical products** during storage and distribution
- If poor-quality medical products are found, effective **recall, removal, and disposal mechanisms** must be in place

Who Are the Key Actors in Regulatory and Quality Assurance Systems for Medical Products?

Gabriel Kaddu, Technical Advisor Regulatory Systems Strengthening, PQM+

Who Is Responsible for Regulatory and QA Systems? What Institutions Are Included?

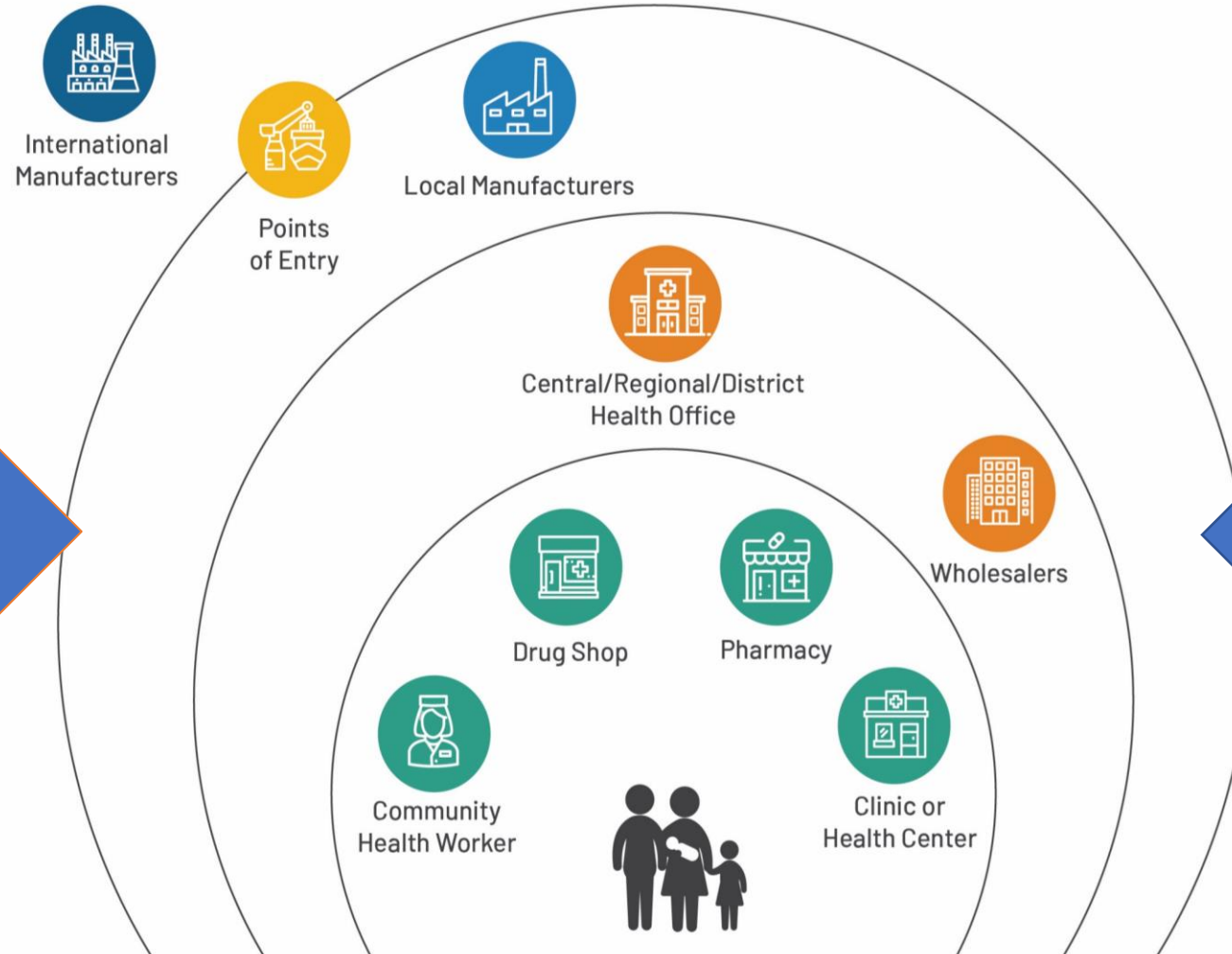
A regulatory system consists of all organizations, people, and actions whose primary intent is to ensure access to essential medicines and other health products of assured quality, safety, and efficacy or performance.



Source: The Global Fund, 2019: Regulatory Systems Strengthening (RSS) Technical Brief – October 2019

GOVERNMENT AGENCIES

Ministry of Health
Customs/Port Authority
Judiciary
Police
Trade



National Medicines Regulatory Authority

NATIONAL DISEASE PROGRAMS

Tuberculosis (TB)
Malaria
Neglected Tropical Diseases (NTDs)
Maternal, Newborn and Child Health (MNCH)

National Medicines Regulatory Authority (NMRA)

Key Regulatory Functions

- Registration and marketing authorization
- Market surveillance and control (includes post-marketing surveillance)
- Licensing establishments
- Regulatory inspection
- Laboratory testing

- Vigilance
- Clinical trials oversight
- Lot release

Other functions

- Price control
- Drug information
- Licensing professionals
- Narcotics / psychotropic control

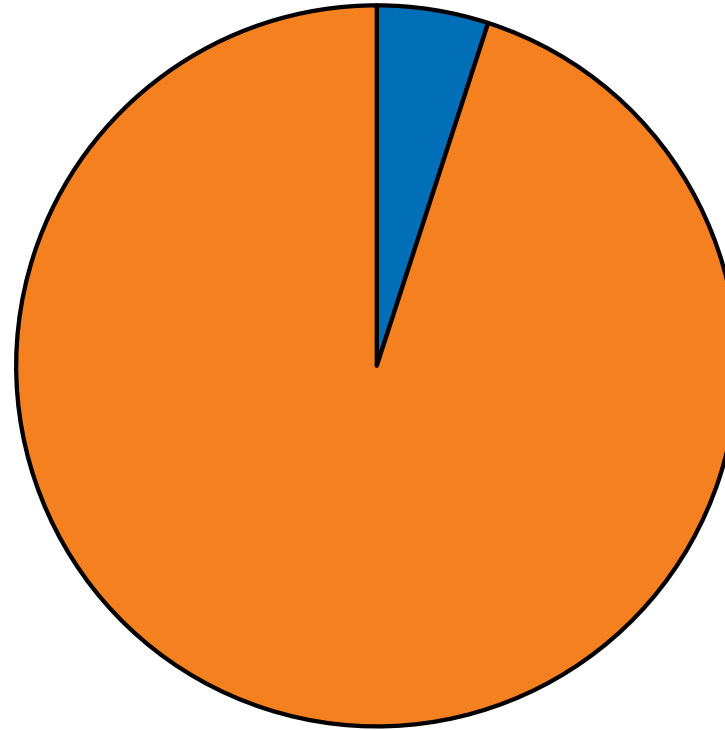
WHO Global Benchmarking Tool (GBT)

The GBT is the primary means by which the WHO objectively evaluates regulatory systems. The tool and benchmarking methodology enable WHO and regulatory authorities to:

- Identify strengths and areas for improvement;
- Facilitate the formulation of an institutional development plan (IDP) to build upon strengths and address the identified gaps;
- Prioritize IDP interventions; and
- Monitor progress and achievements.

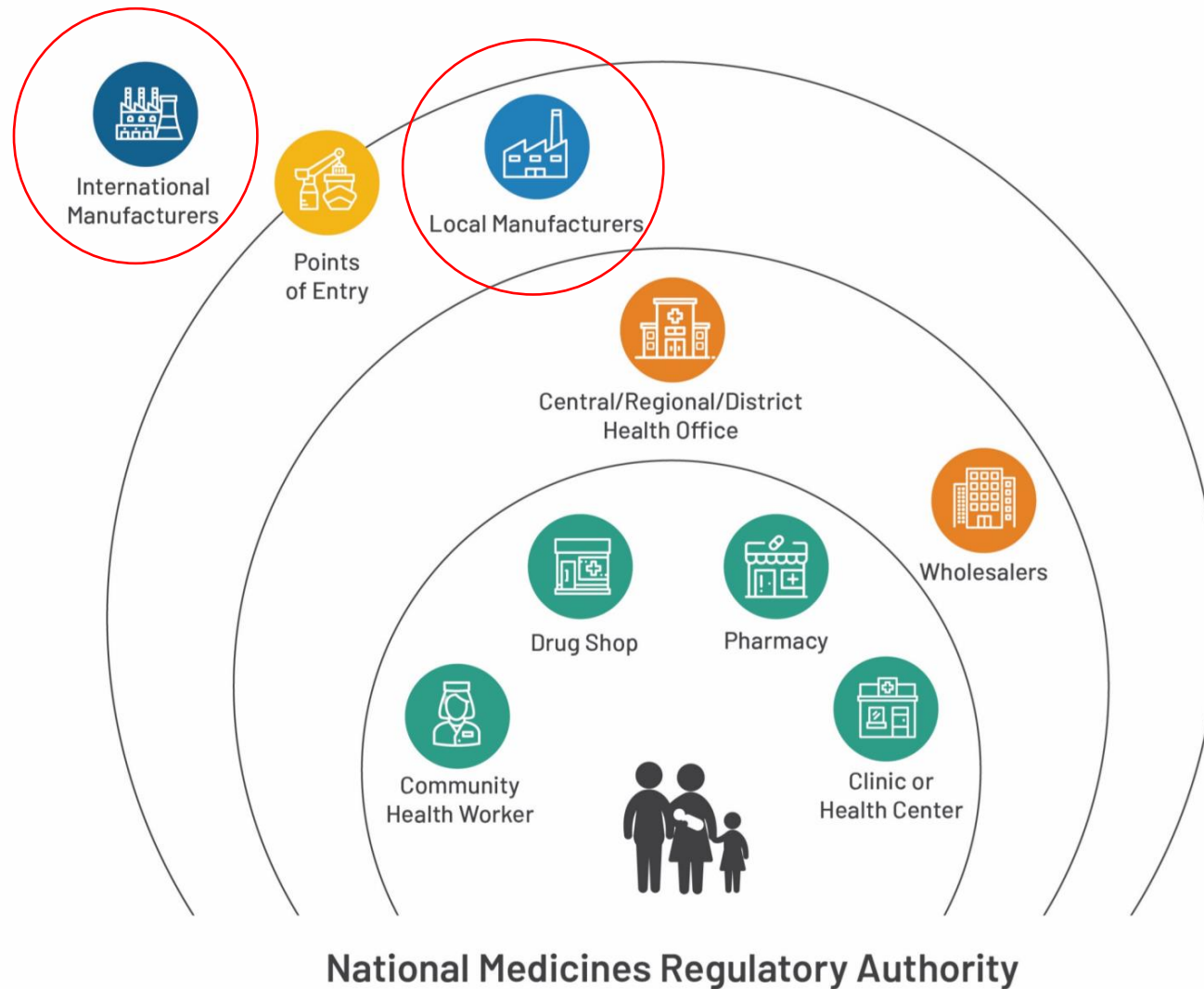
https://www.who.int/medicines/areas/regulation/nras_ml3_ml4/en/

WHO GBT Maturity Level of USAID-Assisted Countries' Regulatory Agencies

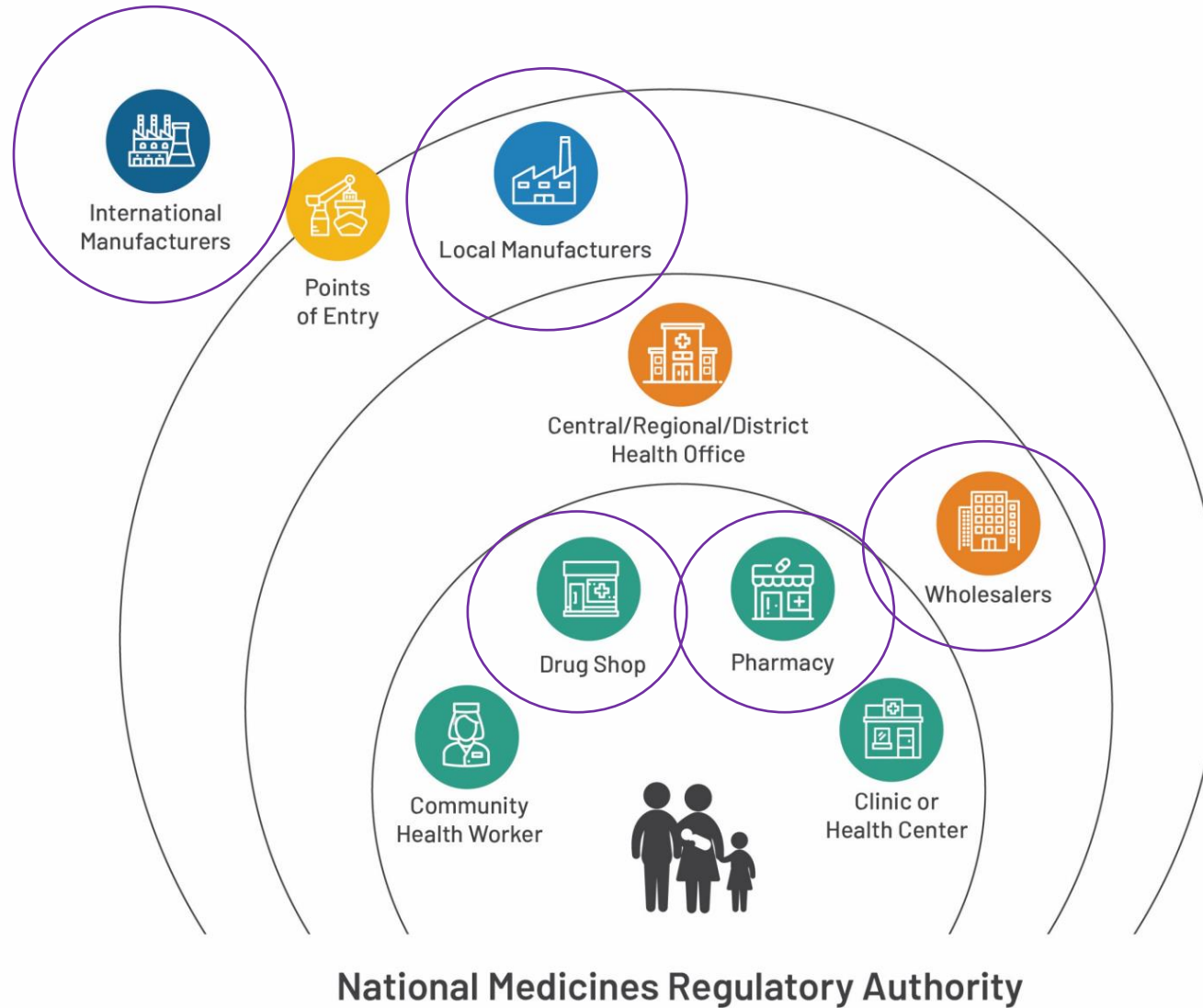


- USAID-assisted countries w/regulatory agencies at Level 3 or 4
- USAID-assisted countries w/regulatory agencies < Level 3

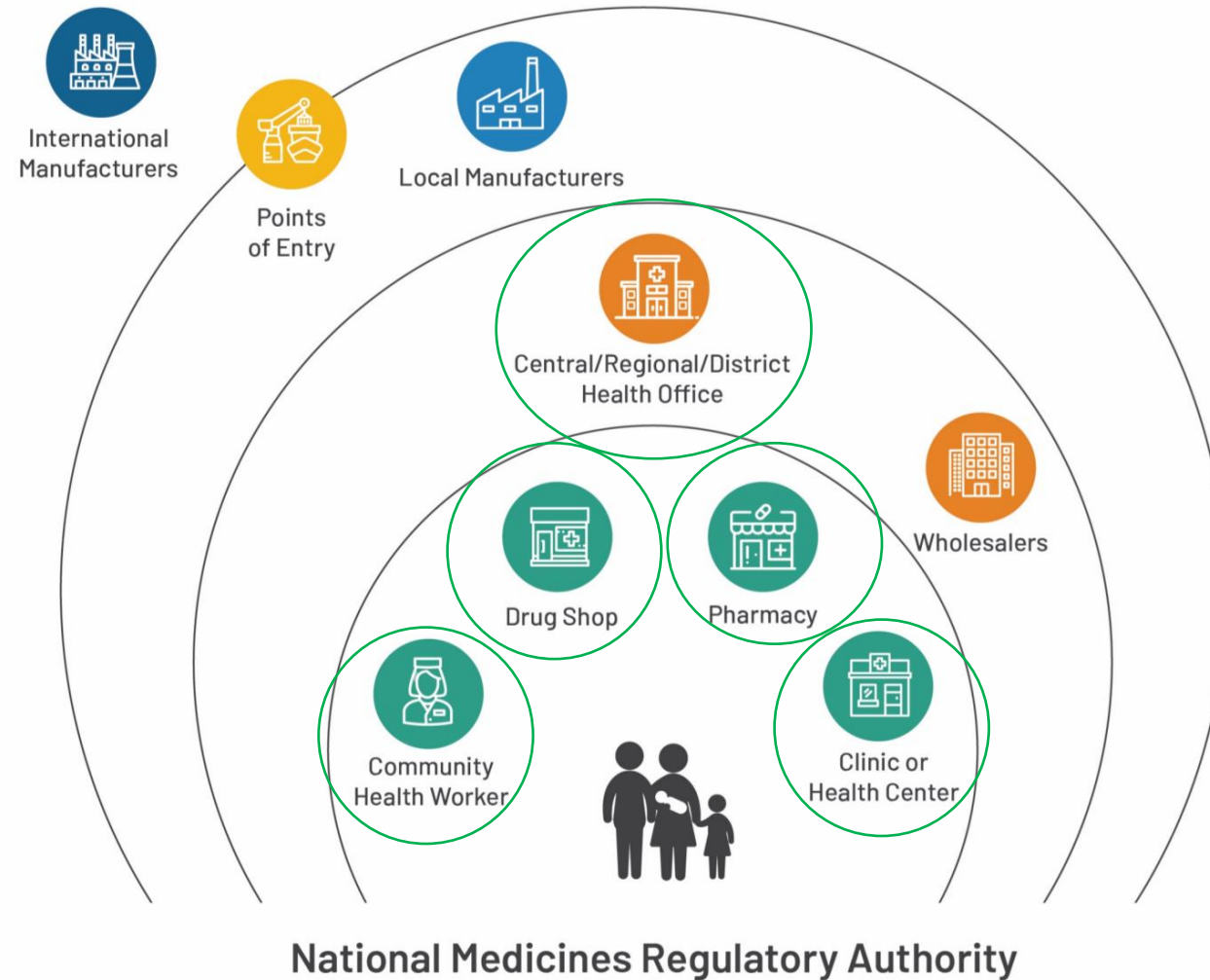
Registration



Licensing and Inspection



Post-marketing Surveillance



Regulatory Functions Supported by the PQM+ Program – Building Capacities

LICENSING

Support licensing of manufacturers, distributors, warehouse, and other pharmaceutical premises

INSPECTION

Build capacity of inspectorates for Good Manufacturing Practices (GMP), Good Storage Practices (GSP), Good Distribution Practices (GDP)

REGISTRATION

Good dossier review practices (GReVP), Collaborative procedures for faster registration (CRP), Bioequivalence

LABORATORY TESTING

Quality Management Systems, Good Laboratory Practices, Testing, Toward WHO Prequalification (PQ) and ISO 17025 certification

RISK-BASED POST-MARKETING SURVEILLANCE (PMS)

Advise PMS technical working groups; RB-PMS protocol design; logistics & planning; sampling and testing methodology

How Does PQM+ Sustainably Strengthen Regulatory and QA Systems?

Evans Sagwa, Chief of Party, PQM+ Kenya

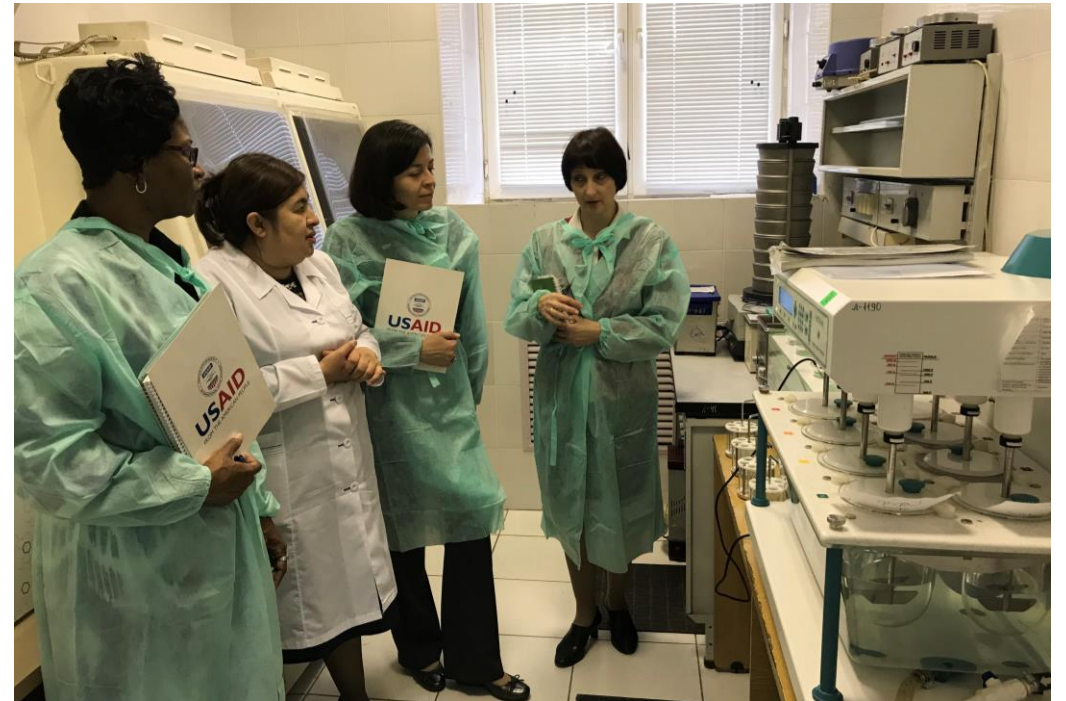
PQM+ Objectives

- Governance for medical product quality assurance systems improved.
- Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved.
- Financial resources for medical product quality assurance optimized and increased.
- Supply of quality-assured essential medical products of public health importance increased.
- Global medical product QA learning and operational agenda advanced.



Sustainability Requires Planning

- **Sustainability** is the ability of a local system to produce desired outcomes over time and to be both resilient and adaptive in the face of changing circumstances. (*Local Systems: A Framework for Supporting Sustained Development. USAID, 2014*)
- **Sustainability** cannot be an afterthought; it is a forethought.



What Makes a Regulatory or QA System Sustainable?



- Resource availability and optimal use
- Process efficiency
- Workforce capacity
- Good governance, leadership and management
- Enabling policy, legal, and regulatory framework

USAID Support for Medical Product QA through PQM or PQM+



AFRICA

Benin+
Burkina Faso+
Ethiopia+
Ghana+
Guinea+
Kenya+
Liberia+
Mali+
Mozambique+
Nigeria+
Senegal+
IGAD+

ASIA

Bangladesh+
Burma+
Cambodia
Indonesia
Nepal+
Pakistan+
Philippines
Asia Regional+

EUROPE & EURASIA

CAR/Kazakhstan+
Serbia+
Uzbekistan+

Lasting Impact in Countries – Illustrative



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- Bangladesh
- Burma
- Ethiopia
- Kazakhstan
- Kenya
- Nigeria
- Pakistan

Product Registration and Marketing Authorization



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- **Ethiopia** – Improved registration processes, increased capacity to review dossiers for new medicines. Time to complete registration reduced by 25 - 40 percent.
- **Kenya** – Medicines registration system upgraded from paper-based to online.

Product Registration and Marketing Authorization

- **Pakistan** - Adopted the Common Technical Document (CTD) for submission of medical product dossiers for marketing authorization, making the process much faster.
- **Pakistan** - NMRA enabled to provide Emergency Use Authorization of specific COVID-19 medical products.



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Quality Control (QC) Laboratories

- In Burma, PQM+ developed the skills of QC lab staff to test Deltamethrin quality in long-lasting insecticidal nets for the national malaria program.
- In-country testing reduced the time needed to test products, saving both money and resources.



QC Laboratories



- In **Nigeria**, supported multiple QC labs to achieve accreditation. Now 100 percent of quality tests for pharmaceuticals are locally performed by these facilities.
- In 2017 alone, QC tests conducted by these labs informed the approval of 11,240 new or generic medical products for the Nigerian market.
- In **Bangladesh** and **Kazakhstan**, QC labs were the first to achieve WHO prequalification, becoming resource labs for their regions as well.

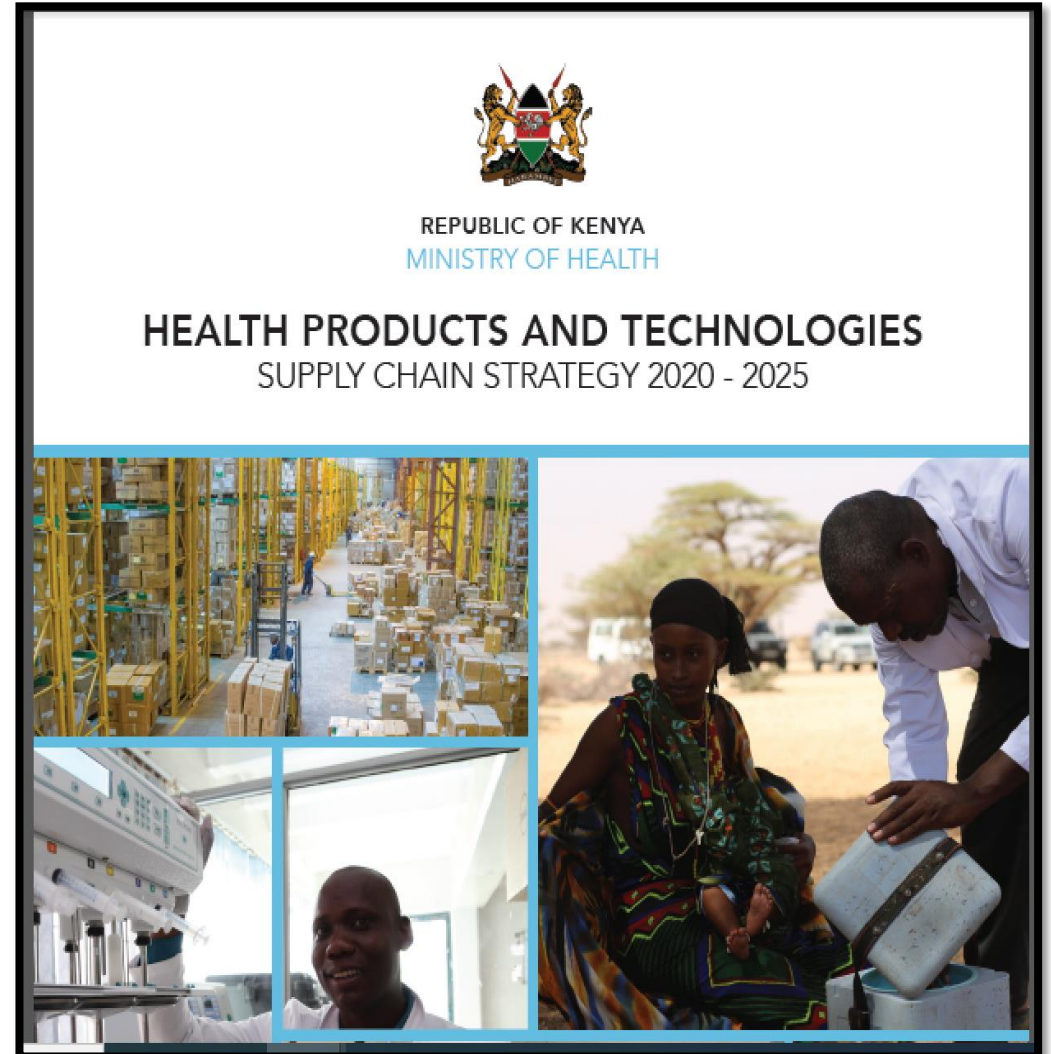
QC Laboratories

- The NQCL Lab in **Kenya** attained ISO/IEC 17025 reaccreditation in October 2020 with minimal donor assistance, showing self-reliance in sustaining reaccreditation.
- In **Ethiopia**, the QC lab achieved ISO/IEC 4074 accreditation for medical devices. With this capacity, Ethiopia was able to test condoms, ultimately recalling or keeping off the market 94 million of poor quality.



Integrated Quality Management Framework – Kenya

- Ministry of Health's Strategy provides a framework for integrating QA into public and private supply chains.
- Public health programs and regulators are included.
- Pharmacovigilance and PMS are integrated.
- National and county levels addressed.



Regulatory Inspection

- **Pakistan** and **Nigeria** are adopting risk-based inspections to focus limited resources on inspecting the manufacturers/facilities that pose the highest risk of poor-quality medical products.
- This approach reduces costs and time in identifying and addressing product quality problems.



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Post-Marketing Surveillance (PMS)

- **Ethiopia** is institutionalizing the capacity of the NMRA to conduct PMS.
- Over a 10-year period, the NMRA has implemented PMS tools and built capacity, testing more than 3,450 medical product samples.



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Post-Marketing Surveillance

- Kenya and the Intergovernmental Authority on Development (IGAD) conducted their first risk-based PMS using a consistent, standardized approach.
- IGAD implemented its first risk-based survey of quality of oxytocin injection and amoxicillin dispersible tablet/suspension circulating in cross-border areas of six countries: Djibouti, Ethiopia, Kenya, Somalia, Sudan and Uganda.



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E-Learning and Building Capacity



- *Strengthening Quality Assurance Systems for Medical Products* available on USAID's Global Health eLearning Center platform.
 - Since September 2019, thousands of visits from 75 countries.
 - <https://globalhealthlearning.org/course/strengthening-quality-assurance-systems-medical-products>
- *Foundations of Good Manufacturing Practices* available on PQM+ website
 - More than 9,000 have registered to take this free course and 4,000 have completed it.
 - <https://www.usp.org/global-public-health/promoting-quality-of-medicines/gmp-online-course>

Conclusions



- Product regulation and QA require a **whole systems approach**.
- QA is spread across an ecosystem of many actors.
- As a result, there are any points of vulnerability and many opportunities to strengthen the system.
- Sustainability can be built into regulatory and QA systems.
- Financial self-reliance, an adequate and competent workforce, good governance, and an enabling policy/legal environment underpin sustainability.

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Questions?



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FROM THE AMERICAN PEOPLE



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Thank you!

<https://www.usp.org/global-public-health/promoting-quality-of-medicines>

