Promoting the Quality of Medicines Plus

Empowering Countries To Pivot and Implement New Regulatory Tactics to Ensure Quality Medical Products During the COVID-19 Pandemic

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Promoting the **Quality** of **Medicines** Plus

Welcome

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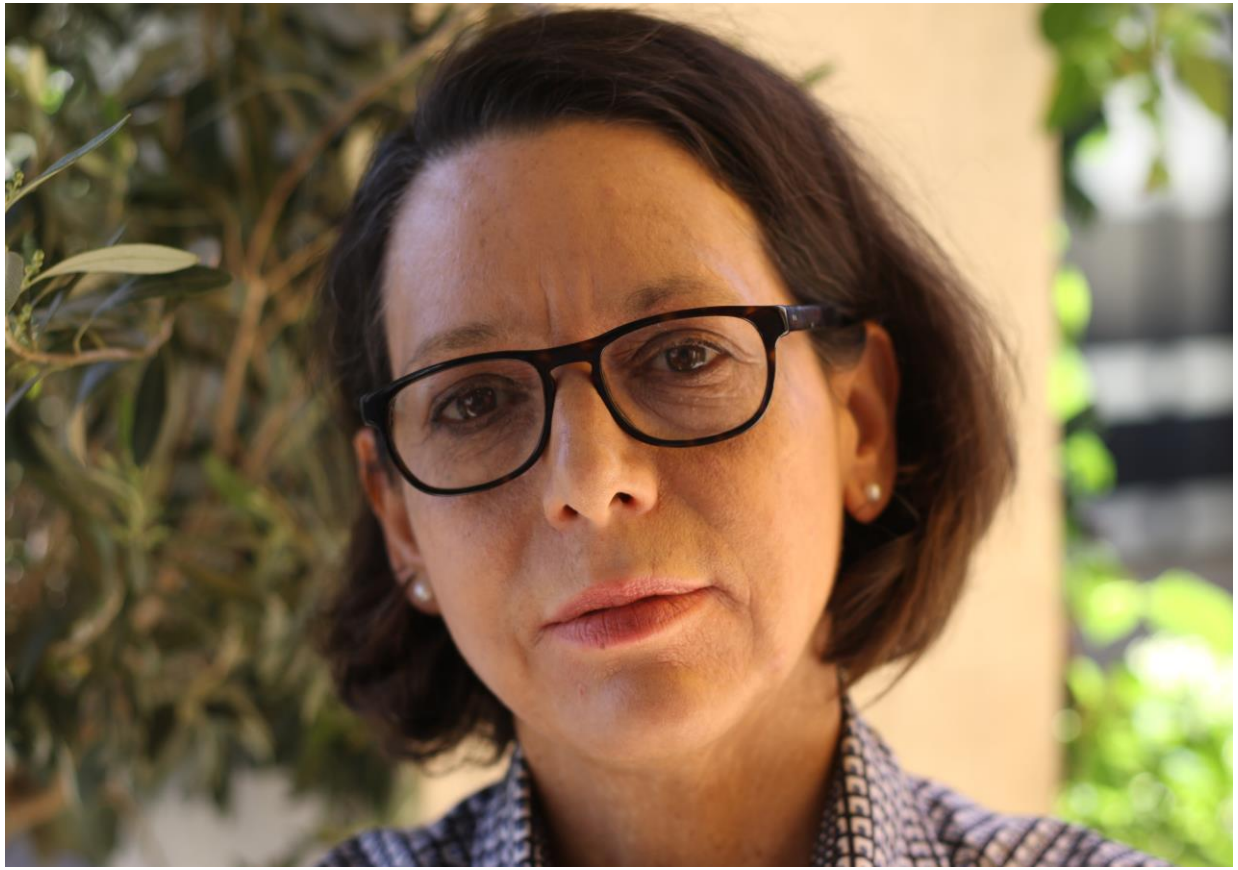
Why is regulation essential during the pandemic?



Yvette Madrid

Vaccines Program Director, US Pharmacopeia

Webinar Overview

- Why are regulatory activities critical during the pandemic?
- What regulatory activities have been critical?
  - Approving use of new medical products
  - Checking the quality of products before they enter the market
  - Monitoring new product safety in patients and the quality of products on the market
- What can we learn from country experiences?

Effective Regulation is Essential – Especially during a Public Health Emergency

Safety, efficacy, and quality matter as much, if not more

- Large numbers of individuals using products expands the risks to health and welfare
- Inability to control the pandemic without the products
- Risk of loss of confidence and spread of misinformation

Extraordinary pressure on regulatory systems

- Range of products
- Unstable supply: disruptions, new suppliers
- Innovative products
- New delivery mechanisms
- Need for speed
- Limited resources

Closer Look at COVID-19 Vaccines

Issue	COVID-19 Vaccine Characteristics that May Differ from Other Vaccines
Vaccine Type	• Different vaccine platforms (i.e., mRNA, adenovirus, protein, inactivated, etc.) from multiple producers may be used in a country.

Storage and Distribution	• New delivery sites
	• Storage temperature, preparation, and use specifications vary across vaccines
	• Select vaccines require ultra-cold chain
	• Manufacturers are collecting real-time stability data concurrent with the rollout leading to
	  ○ Short initial shelf-life
	  ○ Evolving information on expiry dates and storage temperatures

Policies	• Country policies and manufacturer recommendations may be less aligned (e.g., open vial policies).
Data and Labeling	• In some cases, use of manufacturing dates rather than expiry dates • Optional use of QR codes/websites to provide updated information on expiry • Bar codes on secondary packaging with optional use on primary packaging • Vaccine vial monitors (VVMs) not widely used, although they remain a preferred characteristic in UNICEF tenders

Pandemic Challenges Make it Easier for Substandard and Falsified (SF) Products to Spread

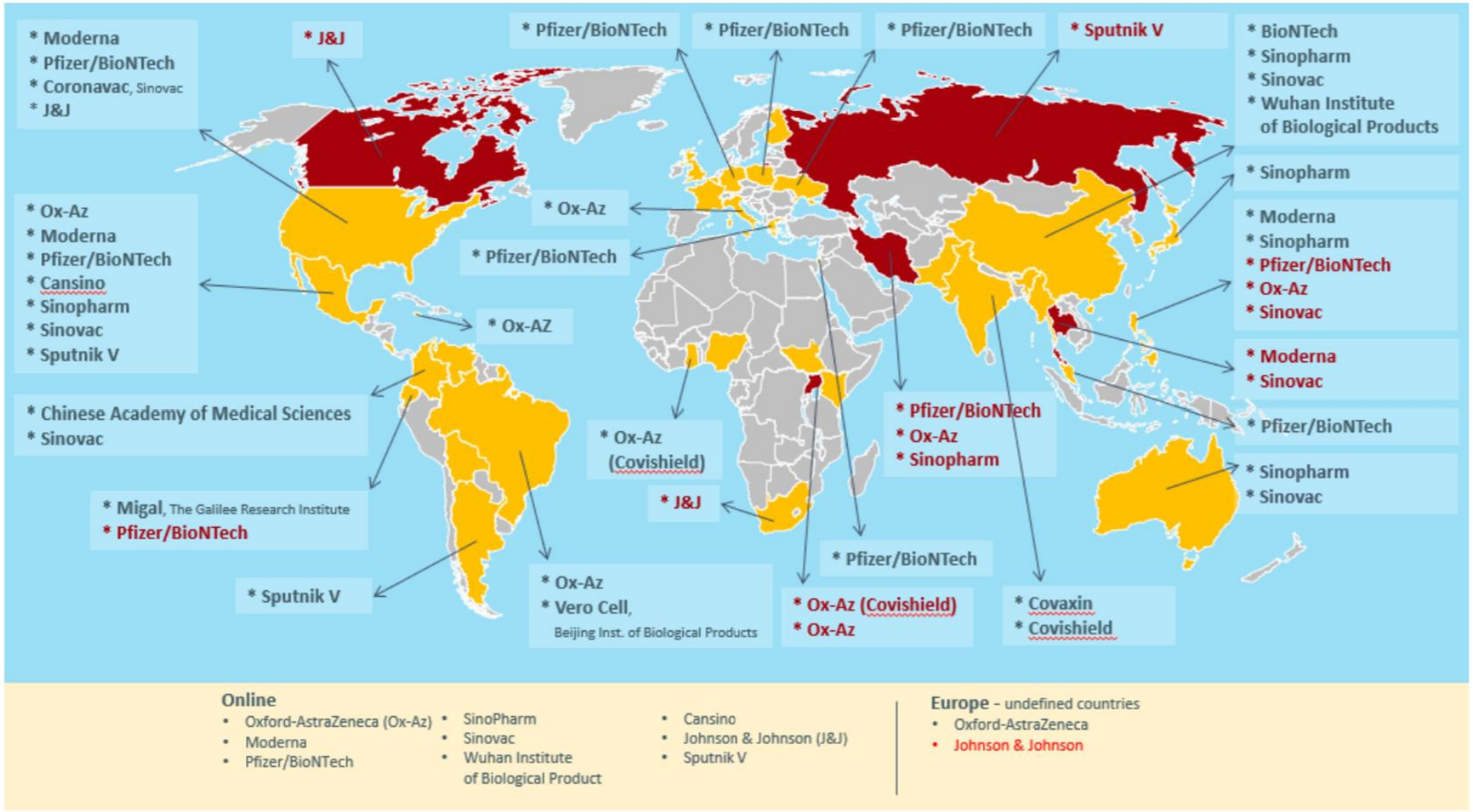
Substandard

Authorized medical products that fail to meet either their quality standards or specifications, or both.

Falsified

Medical products that deliberately/fraudulently misrepresent their identity, composition or source.

SF Public Reports for COVID-19 Vaccines



Source: Medical Product Quality Report - COVID-19 Issues. Issue 12: October 2021
https://www.iddo.org/document/medical-product-quality-report-covid-19-issues-issue-12-october-2021-data-june-july-main

How do regulatory systems respond effectively?

- Planning & preparation
- Intensified selected efforts, including
  - Risk-based approaches
  - Reliance or use of other regulators' decisions
- Applying lessons learned

Emergency Use Authorization: Opening the Door

Waqas Ahmed

Deputy Chief of Party, PQM+
Pakistan

Requirements for Authorizing a Medical Product

- Regulatory authorities require that medicines be registered before they can be used by the population.
- Normal registration of products can take years and requires long-term clinical trial and other study data.
- In an emergency, there is no time to complete these long-term studies. Regulatory authorities make decisions based on short-term safety and efficacy data.
- In lieu of full registration, they provide emergency use authorization of new products.
- Reliance on data and decisions from other regulatory agencies speeds up the process.

Why is EUA critical?

No treatment options are readily available

Conventional registration approval process with full clinical trials takes years

EUA procedures for new medical products help reduce mortality

EUA helps strengthen the nation’s public health protections

CRITERIA FOR EMERGENCY USE AUTHORIZATION

THE PATIENT HAS A **LIFE-THREATENING** CONDITION THAT NEEDS IMMEDIATE TREATMENT

NO GENERALLY ACCEPTABLE **ALTERNATIVE TREATMENT** FOR THE CONDITION EXISTS

BECAUSE OF THE IMMEDIATE NEED TO USE THE PRODUCT, THERE **IS NO TIME TO USE EXISTING PROCEDURES** TO OBTAIN REGULATORY APPROVAL FOR USE

Pakistan's Experience

COVID-19 Pandemic
Regulatory Reforms

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COVID-19 Pandemic: The Regulatory Challenge in Pakistan

- Drug Regulatory Authority of Pakistan (DRAP)-no defined criteria for EUA
- No provision for granting EUA for Medical Devices
- Regulatory Authority lacked expertise to evaluate EUA applications
- No procedure or data requirement for issuance of EUA

- Only govt. laboratory to test biologicals (e.g., vaccines) was under renovation
- Authorities were granting EUA with abbreviated trials
- Limited data to evaluate medical devices safety and efficacy
- Guidelines for clinical trials were under development

Developed New EUA Guidelines

- Describe the conditions for declaring an emergency
- Explain recommendations & procedures for EUA in Pakistan, including criteria and reliance mechanisms
- Include step-by-step procedures for approving devices, fees, and process for terminating authorization

The Routes for EUA of Medical Devices Linked to Risk

Approval by other regulatory authorities	Risk level	Approval pathway in Pakistan
Approved by WHO	Low	Normal route, expedited
Approved by WHO-listed authority (US, EU, Japan, Australia, Canada)	Low	
Approved by other authority (i.e., from other countries)	Medium	Route A
Authorized for emergency (not fully approved)	Medium	
Manufactured locally and not approved by any other regulatory authority	Higher	Route B

Conditions for EUA Approval of Medical Devices

01

Comply with requirements of post-market surveillance & vigilance

02

Ensure labelling, use & storage of medical device are in accordance with manufacturer requirements

03

Establish & implement a system to monitor safety & performance of the medical device

04

Available upon request by the Authority at any time

05

User/healthcare facility responsible if the device continued to be used without registration

Pakistan's EUA for COVID Vaccines

BACKGROUND

There was provision of EUA for pharmaceutical and biologicals in DRAP Act

REVISION OF PROCEDURE

PQM+ supported DRAP to review and revise procedures, term & conditions for EUA

STAKEHOLDERS COLLABORATION

DRAP, WHO, and other major stakeholders collaborated on post-market surveillance and adverse events following immunization (AEFI)

SUPPLY CHAIN INTEGRITY

DRAP monitored cold chain and supply chain integrity of vaccines by inspections and data evaluation after regular intervals

Emergency Authorized Vaccines in Pakistan

Name of Vaccine	Registration Date
Sinopharm	23 Jan 2021
Sputnik V	1 Feb 2021
CanSino	8 Feb 2021
CoronaVac	23 Jan 2021
AstraZeneca	8 Feb 2021
Pfizer	27 Apr 2021

Vaccine statistics

** Last updated:07 Nov, 2021 - 08:52am Islamabad/Pakistan*

First Dose

73,979,036

LAST 24 HOURS: 663,285

Fully Vaccinated

43,849,554

LAST 24 HOURS: 617,684

Total Doses Administered

110,800,576

LAST 24 HOURS: 1,213,592

Pakistan statistics

** Last updated:07 Nov, 2021 - 08:52am Islamabad/Pakistan*

CONFIRMED CASES

1,276,711

Last 24 hours: **471**

DEATHS

28,538

Last 24 hours: **20**

RECOVERED

1,225,363

Last 24 hours: **493**

TOTAL TESTS

21,101,314

Last 24 hours: **43,348**

CRITICAL CASES

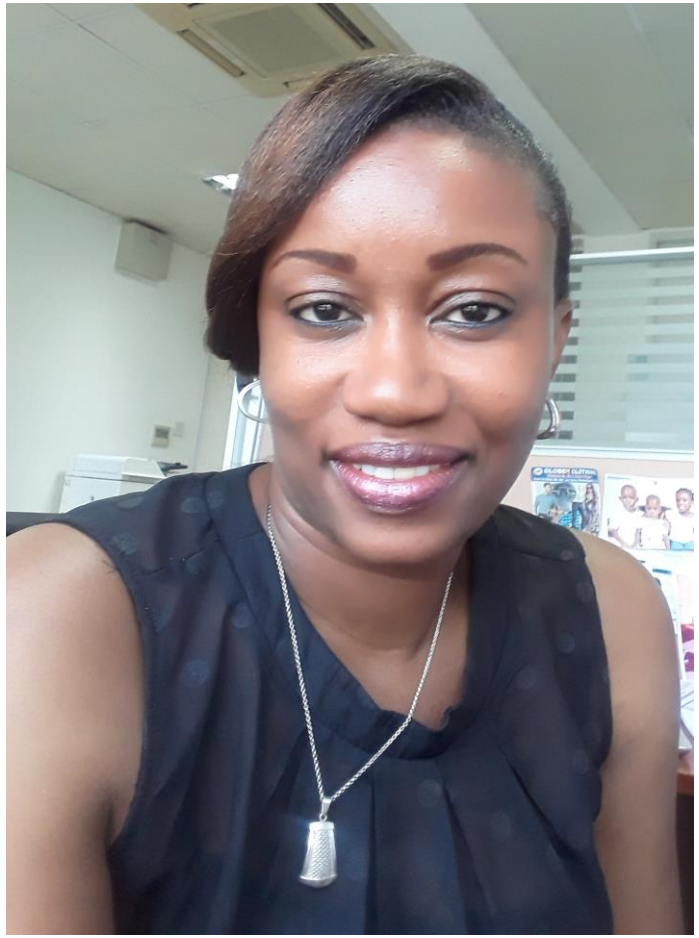
1,233

Last 24 hours: **0**

How can we ensure product safety and quality in the market?

Neimatu Adjabui

Senior Program Manager, West Africa, PQM+



Ensuring Quality and Equity

When the vaccines arrive in country, there needs to be **stringent regulatory oversight** before release for distribution. Procurement agencies need to guarantee the vaccines are **transported** and **stored in recommended conditions**. The regulator **checks along the supply chain** to ensure quality standards are maintained.

How is quality assured after EUA?

Lot Release (for biologics)

- Evaluating each individual lot of a licensed product before giving approval for its release onto the market

Pharmacovigilance

- Looking at safety - detection, assessment, understanding and prevention of adverse effects or any other medical product-related problems

Post-Market Surveillance

- Looking at quality - to ensure compliance of the products placed on the market with established quality criteria

Key Regulatory Functions once Products are in the Supply Chain

Pharmacovigilance (PV)
The detection, assessment, understanding and prevention of adverse effects of medicines after use by patients.

Linked

Post-market surveillance (PMS)
Regular quality inspections of manufacturers, wholesalers, distributors, and retailers and quality control testing.

Pharmacovigilance of COVID-19 Vaccines

New vaccines, new technology, short clinical trials

A lot is still unknown, therefore it is:

- Crucial to **detect** adverse events early
  - Risk management for the right mitigation measures
- **Minimize** adverse events
- **Reduce** negative impact on immunization programs
  - Dispel misinformation
- **Gather** new information
  - To guide our use of the vaccines

Surveillance Approaches for Pharmacovigilance

Surveillance is the detection, assessment, understanding and prevention of **adverse effects of medicines.**

- **Passive surveillance** is when health care providers or patients send spontaneous reports describing an adverse drug reaction to the marketing authorization holder or national regulatory authority
- **Active surveillance** is targeted and seeks to ascertain completely the number of adverse drug reactions through a pre-planned process, such as cohort events monitoring

AEFIs and Surveillance

Routine passive surveillance (spontaneous reporting)

- Vaccine recipients
- Parents of immunized infants and children
- Health care workers
- Immunization staff

Active surveillance

- Cohort event monitoring (e.g., PQM+-supported Ghana study underway)
- Sentinel site surveillance

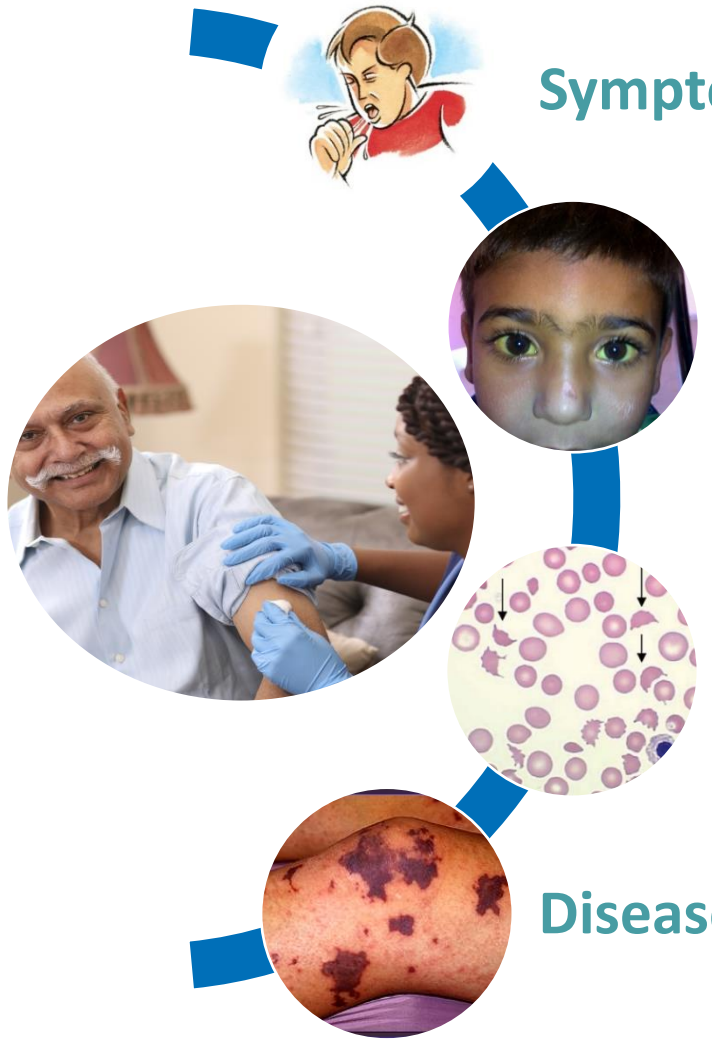
Phase IV clinical studies

- Post-authorization safety study
- Epidemiological studies

Adverse Events Following Immunization

…any untoward medical occurrence which follows immunization and which *does not necessarily have a causal relationship* with the usage of the vaccine

The adverse event may be any *unfavorable or unintended sign, abnormal laboratory finding, symptom or disease.*



Symptom

Sign

Lab Finding

Disease

Generate information to inform decision-making

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Assessing Medical Product Quality

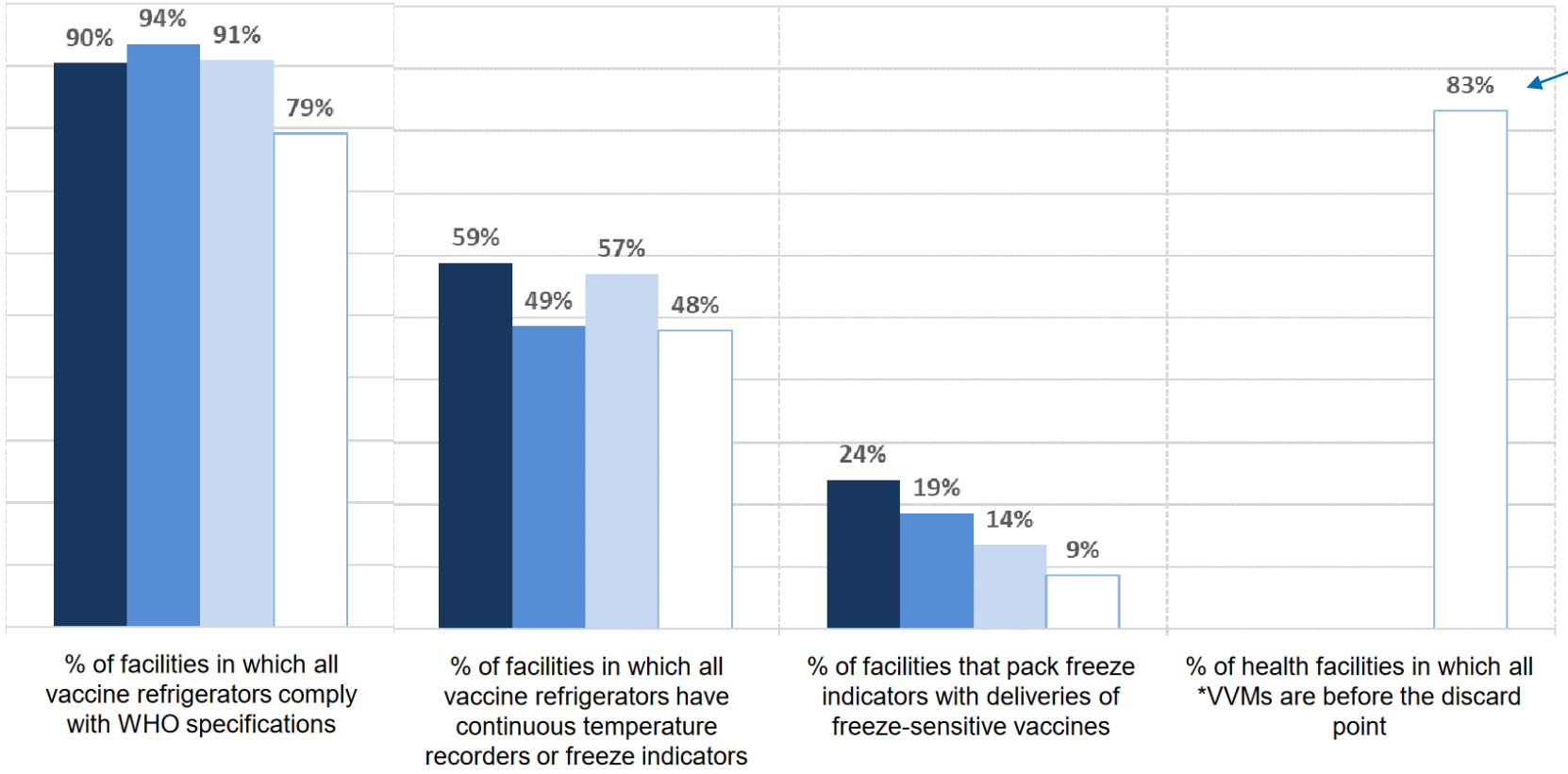
Pharmacovigilance
The detection, assessment, understanding and prevention of adverse effects of medicines

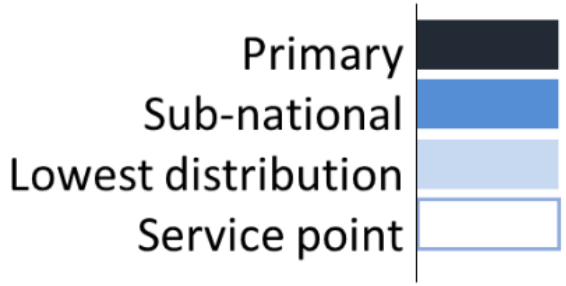
Linked

Post-market surveillance
Includes regular inspections of manufacturers, wholesalers, distributors, and retailers and quality control testing.

Product Quality Linked to Equity

17% of **routine vaccines** at point of distribution (global, 2009-2020) have heat damage = substandard





Source: Effective Vaccine Management (EVM) Global Data Analysis 2009-2020, WHO/UNICEF

After a product enters the supply chain, how can we check for quality issues?

Programmatic assessment: Surveys using randomization in site selection and using key indicators such as undertaken through Effective Vaccine Management (EVM) for vaccines. Highly relevant for vaccines.

Regulatory PMS function: Use randomization in site selection and product sampling to test for quality attributes.

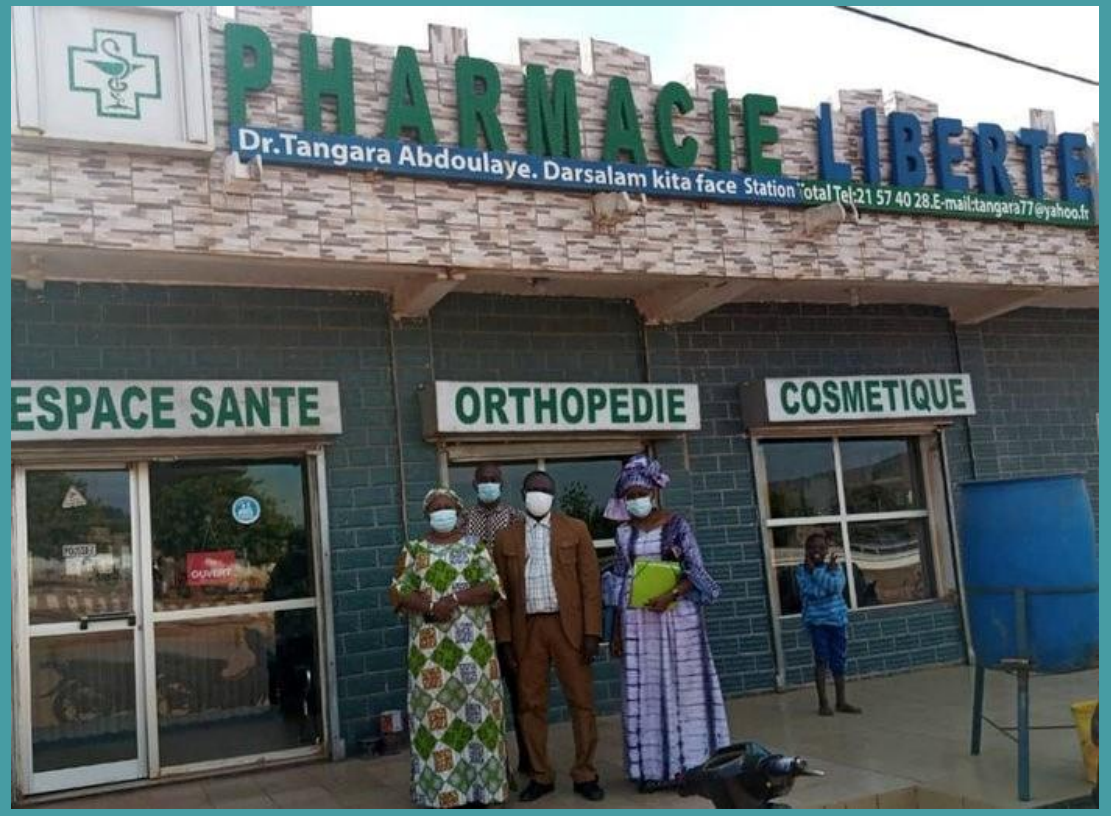
Product sampling & testing can be highly informative

During pandemic conditions:

- **Greater risk for SF**
- **Consequences high**
- **Implementing EVM not practical/as informative**
  - Regular schedule (3-5 years)
  - Delivery mechanisms, supply chain changing
  - Lack of vaccine vial monitors increases risk, decreases ability to monitor

The Risk-based PMS Approach

- PMS is a component of the market surveillance regulatory function.
- Risk-based approaches to PMS channel limited resources toward medicines and locations that present the highest risks to patients.
- The Medicines Risk-based Surveillance (MedRS) tool can be used to identify samples.
- This maximizes the likelihood that higher-risk products will be identified and addressed to protect patient safety.
- RB-PMS can help promote long-term sustainability of financing for PMS activities.



Benefits of Risk-Based PMS

- The RB-PMS approach was deployed fully for the first time in Mali and Senegal with more than 5 more surveys underway.
- Key lessons learned:
  - Smaller sample size
  - Less geographic coverage
  - Fewer facilities needed
  - Less expensive

Representative scientific results

Adapting RB-PMS for COVID-19 Vaccines

- Pilot with PQM+ support in Bangladesh
- Work collaboratively with immunization to
  - Integrate features of EVM
  - Reduce risk of supply disruption
  - Manage reverse logistics
- Sampling and lab testing workflow adjusted for the COVID-19 vaccines with risk-based approach
- Build lab testing capacity in country, but also leverage private sector lab testing networks

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Summary and Conclusions

Jude Nwokike, Vice President, USP

PQM+ Program Director

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Summary

Regulatory authorities have **a critical and very time-sensitive role** to play in a public health emergency:

- Authorizing use of products
- Pharmacovigilance
- Post-marketing surveillance

Successful approaches include:

- Emergency authorization for medical products
- Risk-based approaches
- Reliance on qualified authorities' data and decisions

Conclusions

COVID has highlighted how critical functioning regulatory systems are.

It is important to leave regulatory systems stronger as a legacy of COVID so they are ready for other health crises.

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The next PQM+ webinar will look at manufacturing: **Silver Linings Amidst COVID-19: Tapping into – and Building – the Pharmaceutical Industry in LMICs**

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Questions?

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