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

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Welcome

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Program Management Specialist
USAID Pakistan
Why is regulation essential during the pandemic?

Yvette Madrid
Vaccines Program Director, US Pharmacopeia
Why are regulatory activities critical during the pandemic?

- 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

<table>
<thead>
<tr>
<th>Issue</th>
<th>COVID-19 Vaccine Characteristics that May Differ from Other Vaccines</th>
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<tbody>
<tr>
<td>Vaccine Type</td>
<td>• Different vaccine platforms (i.e., mRNA, adenovirus, protein, inactivated, etc.) from multiple producers may be used in a country.</td>
</tr>
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</table>
| 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  
                          |   o Short initial shelf-life  
                          |   o 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 |
Authorized medical products that fail to meet either their quality standards or specifications, or both.

Medical products that deliberately/fraudulently misrepresent their identity, composition or source.
SF Public Reports for COVID-19 Vaccines

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
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
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

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

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

<table>
<thead>
<tr>
<th>Name of Vaccine</th>
<th>Registration Date</th>
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<tbody>
<tr>
<td>Sinopharm</td>
<td>23 Jan 2021</td>
</tr>
<tr>
<td>Sputnik V</td>
<td>1 Feb 2021</td>
</tr>
<tr>
<td>CanSino</td>
<td>8 Feb 2021</td>
</tr>
<tr>
<td>CoronaVac</td>
<td>23 Jan 2021</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>8 Feb 2021</td>
</tr>
<tr>
<td>Pfizer</td>
<td>27 Apr 2021</td>
</tr>
</tbody>
</table>
Vaccine statistics

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

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

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

Promoting the QUALITY OF MEDICINES Plus

USAID
FROM THE AMERICAN PEOPLE
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.

**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 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.
AEFI 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.

Generate information to inform decision-making
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.
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.

**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

Product sampling & testing can be highly informative
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
Promoting the Quality of Medicines Plus

Summary and Conclusions
Jude Nwokike, Vice President, USP
PQM+ Program Director
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.

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

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