Regulatory Strategies for Assuring Quality of Generic Medicines

Teferi Bedane, Technical Advisor, PQM+
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Outline

• Background
• Strategies to ensure quality of medicines
• Overview of PQM+ objectives to ensure quality
• Local manufacturing
• References
Background: Introduction

- The consequences of poor-quality medicines: on patients and the socio-economical impacts is significant.
  - The worldwide prevalence rate of counterfeited medicine is estimated at 10%.
    - It is estimated that 1% rate of counterfeited medicines accounted to more than 8,000 deaths and 10% counterfeited medicines is accounted to more than 72,000 deaths per year.
    - Based on annual global market size of pharmaceutical product, 300 billion, approximately more than $30 billion is wasted on substandard and falsified medicines.
    - Any percentage reduction of counterfeited medicines saves thousands of lives and billions of dollars!
  - Many organizations and health implementing partners spend billions of dollars for procurement;
    - However, little efforts have been done to promote/improve the quality of generic medicines by working directly with suppliers.
  - Several countries instituted laws and regulation to control medicines;
    - However, many agencies are limited to retroactive regulatory actions to correct failure.
Background: Generic Medicines

• Generic medicines are cross border health commodities: various import and export scenarios related to the product quality need to be addressed strategically by National Medicine Regulatory Agencies (NMRAs).
  • System based regulatory strategies is required to authenticate the source and quality requirements of the product in the international distribution of the product.
  • Through pre-marketing process and post-marketing activities, NMRAs evaluates and monitors product CMC, GMP and other administrative information.
    ▪ In strategic thinking, regulatory action need to be focused on balancing the public health benefit/risks by making objective decision
      ▪ based on scientific information, regulatory standards, and experimental facts
      ▪ by preventing quality failure before it happens
## Background: Generic Medicines

- The basics of generic product regulation is based on establishment of evidence for interchangeability against innovator/comparator.

<table>
<thead>
<tr>
<th>Innovator FPP</th>
<th>Generic FPP</th>
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<tbody>
<tr>
<td>Pharmaceutical product target profile (PPTP) is achieved through clinical studies to ensure the required quality, safety, and efficacy.</td>
<td>PPTP is based on innovators information and achieved through pharmaceutical equivalence and interchangeability demonstration.</td>
</tr>
<tr>
<td>Bioavailability and dosage form regimen are established through clinical study: phase I-III clinical study trails.</td>
<td>Bioavailability and dosage form regimen are known. Interchangeability is demonstrated through BE/BW study.</td>
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<tr>
<td>Formulation and composition is based on extensive experimental trial and error</td>
<td>Formulation and composition is determined based innovator/comparator product information.</td>
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<tr>
<td>Manufacturing process is selected based on extensive experimental study.</td>
<td>Manufacturing process is determined based on innovator product characterization target value and process scale-up study.</td>
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<tr>
<td>Container closure is selected based on experimental study</td>
<td>Container closure is known from innovator product</td>
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<tr>
<td>Specification are developed and contain the user requirements for manufacturability.</td>
<td>Specification targets are typically available; but user requirement should be established experimentally.</td>
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<tr>
<td>Shelf life and storage conditions come from research study.</td>
<td>The target shelf life and storage conditions are known. Stability study is used to confirm.</td>
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Strategies To Ensure Quality

• NMRAs should have strategic tactics for timely review and approval of application for marketing authorization.

• Beyond verification of compliance with requirements, the main purpose of NMRAs is to:
  ▪ evaluate the producers and public health benefit/risk of a product
    ▪ understand and ensure the health benefits of product against its probable risk
  ▪ increase transparency during product review and MA process
  ▪ increase access to innovation and new product
  ▪ create uniform decision and communication system
  ▪ establish full oversight and vigilance for authorized products in the market
  ▪ understand global situation of the product and its manufacturing process
  ▪ ensure access to quality assured medicines
Strategies To Ensure Quality

- The strategic approaches of the NMRAs need to balance producers and public health benefit/risks by making objective decisions based on scientific information.

Figure 1: The regulatory balance between producers and public health benefit/risk to ensure quality.
Strategies to Ensure Quality

• The NMRAs organizational structure is the basis for an effective strategic regulation

  • The structure of NMRA may vary from country to country, the most typical functional framework includes:
    • Marketing authorization
    • Licensing
    • Inspection
    • Quality Control
    • Pharmacovigilance/PMS
    • Clinical trials authorization and monitoring
    • Control of advertising and promotion
      • Plus, Administrative elements

  • The structure of NMRA should be established based on understanding of the country’s situation in response to the public health need.
Strategies to Ensure Quality

• For established NMRA, the core principle of strategic thinking are: sustainability, improvement, and excellence, plays fundamental role to improve supply of quality medicines.

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<thead>
<tr>
<th>System Strengthening</th>
<th>System Understanding</th>
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<tbody>
<tr>
<td>Review</td>
<td>Identify the NRA</td>
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<td>Report</td>
<td>Set Agenda</td>
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<tr>
<td>Evaluate</td>
<td>Identify Existing Document</td>
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<td>Monitor</td>
<td>Document Review</td>
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<tr>
<th>Implementation</th>
<th>Monitoring &amp; Evaluation</th>
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<tr>
<td>Laws, Legislation, and Regulation enforcement</td>
<td>Impact</td>
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<tr>
<td>Procedures and Guidelines Development</td>
<td>Initiation</td>
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<tr>
<td>Hands on technical support</td>
<td>Stage 4</td>
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<tr>
<td>Existing Functional System Analysis</td>
<td>Stage 1</td>
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<tr>
<td>Evaluation of gaps</td>
<td>Stage 2</td>
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<tr>
<td>Develop Strategic Priority Areas</td>
<td>Stage 3</td>
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<tr>
<td>Discussion on Future Plan</td>
<td>Analysis</td>
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<tr>
<td>Identify Intervention Areas</td>
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Figure 2: The strategic approach for RSS
Strategies To Ensure Quality

- The PQM+ objectives are priority areas of USAID in response to the public health need that is available to several NMRAs in LMICs

**Figure 3**—The PQM+ objectives for promoting quality of medicines in low-and-middle income countries

![Figure 3](image-url)
Strategies to Ensure Quality

- PQM+ provides support to NMRAs for gaps identified in the WHO GBT IDP (if available); or conduct gap analysis of a given agency based on the following strategic framework;

Figure 4: Strategic approach for assessment of regulatory system
Local Manufacturing

• Support to local manufacturing is an evolving strategic tactic to increase access to quality assured generic medicines.

• In addition to regulator action, NMRAs should take initiatives to enable local production of essential medicines.
  • For example, the NMRA could collaborate with partners to conduct sectoral analysis to understand and remove barriers to local manufacturing.
    • Financing option of local
    • Creating partnership in gathering and analysis of market information
    • Market intelligence
    • Technology of Transfer
    • Reliance and collaborative registration system
    • Pooled procurement system
    • Non-incentive (indirect) support
    • Discounted price and advance purchase system
    • Removing unnecessary regulatory burden including delay in customs clearance of raw materials.
References


