Three-Level Approach for Ensuring the Quality of Medicines in Resource-Limited Countries

1. ABSTRACT

The availability and use of medicines for the treatment of diseases are basic components of any healthcare system. In order to treat illnesses effectively, medicines must:

- Provide the desired therapeutic effect;
- Have an acceptable safety profile; and
- Be of the appropriate quality.

Compromising any of these three characteristics would lead to ineffective treatment.

Use of poor-quality medicines may:

- Decrease therapeutic effect;
- Jeopardize patient safety;
- Pose a serious threat to consumers; and
- Waste scarce financial resources for healthcare andCountries.

Moreover, the pharmaceutical market, potentially resulting in a rise in the prevalence of poor-quality medicines.

Alternative approaches need to be developed to help health authorities in resource-limited countries ensure proper quality assurance and quality control of medicines in their pharmaceutical markets.

To address this need, the Promoting the Quality of Medicines (PQM) Program designed a three-level testing approach that is cost-effective and efficient for performing QC analysis throughout the supply chain. This is a risk-based approach that may be applied throughout the supply chain and implemented by a variety of stakeholders according to their particular context and needs.

4. COMPONENTS

The three-level approach encompasses the following:

Level 1 (L1) analyses include visual inspection of the package and label and physical inspection of the product.

Level 2 (L2) analyses utilize easy-to-use, simple, rapid, and cost-effective basic analytical methodology that can be implemented in the field to assess medicines quality.

Level 3 (L3) analyses require the assessment of all critical quality attributes of a medicine via complete validated and/or compendial tests.

The following diagram visually represents the characteristics of each level.

5. BASIC TESTS MAY DETECT A LARGE PERCENTAGE OF POOR-QUALITY MEDICINES

Percentage breakdown of data on 325 of total of 771 substandard drugs reported from around the world to WHO database between 1982-1999. This includes antibiotics, antimalarials, and antituberculosis medicines.

6. LEVERAGING USE OF L2 ANALYSIS

Benefits

- Capability to Identify Poor-quality Medicines: Potential to detect most frequent reasons medicines fail quality standards.
- Reliability of Results: L2 analyses are highly reproducible, trustworthy, and validated.
- Large Analysis Throughput: L2 analyses are significantly shorter than validated methods (L3).
- Minimal Infrastructure Requirements: Equipment and tools are minimal, economical, and readily accessible.
- Minimal Need for Specialized Human Resources: Personnel training is rapid and economical.
- Low Acquisition and Maintenance Costs: Costs of procuring and maintaining equipment, tools, and supplies are low.

Capabilities to Test a Wide Range of Therapeutic Treatments: Pre-made, self-contained portable units are available that contain methods and Reference Standards for over 50 medicines for a wide range of therapies (e.g., antimalarial, antiretroviral, anti-tuberculosis, etc.). L2 tests and Reference Standards for other medicines can be developed according to country needs.

Limitations

- Capability to Assess Only a Limited Number of Critical Quality Attributes: Cannot assess all critical quality attributes (e.g., dissolution, uniformity of dosage units, water content, impurities requiring a high level of sensitivity).
- Limited Support for Implementing Corrective Actions: For implementation of corrective actions, country regulations may require testing with validated methods (L3) according to registration specifications.
- Limited Experience of Personnel Performing L2 Analyses: To ensure validity of the results obtained by personnel lacking extensive experience, proper steps need to be implemented to enable other competent institutions (i.e., OMCL) to repeat and verify results.
- Inconclusive Results: The testing conditions or methodology may provide inconclusive results that could require repeating the tests in a lab setting or using other methods.

7. THREE-LEVEL APPROACH IN THE QA FRAMEWORK

8. APPLICATIONS OF THREE-LEVEL APPROACH

Procurement Practical Example

- Source of medicine: Medicines with a history of compliant QC data.
- Current QC practice: National regulations require testing of all incoming materials, including final QC analysis of the product.
- Three-level approach: Combination of L1 and L2 analyses prior to distribution (Path “A” and Path “B”).
- Justification: In cases where a country’s regulations require submitting all pre-manufacturing and/or final QC data, testing, and limited resources or time constraints may make this feasible. In this situation, the medicines would be tested at L1 and L2 levels. L3 testing would be performed at the final QC analysis of the product.
- Benefits: Provides a flexible approach by taking into consideration time and resource limitations and provides added assurance that medicines entering the distribution chain are of adequate quality.