

# Three-Level Approach: A Risk-Based, Cost-Effective Approach to Medicines Quality Monitoring in Low- and Middle-Resource Countries

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Third International Conference for Improving Use of Medicines

November 14–18, 2011 • Antalya, Turkey

www.usp.org/worldwide

## Abstract

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**A Risk-Based, Cost-Effective Approach to Medicines Quality Monitoring in Low- and Middle-Income Countries**  
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**Problem statement:** The use of substandard and counterfeit medicines (SCM) constitutes an increasing public health problem, especially in low- and middle-income countries (LMIC). A USAID-USP program has documented cases where over 40% of sampled medicines were of poor quality. Medicines regulatory authorities (MRAs) in LMIC often cannot assume their medicines quality assurance role, and many do not even monitor the quality of medicines in the supply chain, due to a lack of technical, human, financial, and/or legal capacity.

**Objective:** The study seeks to develop and test a risk-based, three-level approach to medicines quality monitoring (MQM) that enables MRAs in LMIC to exercise better oversight over medicines quality in their countries. The research questions are: (1) Can MQM be achieved on a large scale, to the extent it becomes an effective tool to help reduce the availability of poor-quality medicines in LMIC? (2) What are the requirements for success?

**Design:** This is an operational research case study. It examines the introduction of a risk-based, three-level approach to MQM in two countries: Cambodia and Ghana.

**Setting:** The risk-based approach to MQM can be applied at regional as well as national levels, covering medicines throughout the supply chain, in the private and the public sectors.

**Policy change:** Cambodia introduced MQM in 2003 and Ghana in 2009. Both countries used the three-level approach of visual inspection, basic screening tests, and compendial testing. The sentinel sites were carefully selected and the sampling protocol adjusted to national context, allowing the MRAs to spread the net as wide as possible to catch problem medicines with the given resources. The test results were used to take concrete corrective actions, diagnose quality assurance problems, and/or raise public awareness.

**Outcome measure(s):** (1) Proportion of sampled medicines found to be substandard, (2) number of medicine lots withdrawn, (3) number of operators closed, and (4) other MQM improvement measures.

**Results:** MQM enabled Ghana to identify and take action against specific counterfeiters (including Coartem®) in both years of operation. In Cambodia, 16.9% of antimalarials, sampled in 4 provinces, failed quality testing from 2003 to 2004. The failure rate dropped to 9.4% of 470 samples from 6–10 provinces (2005–07) and to 3.4% of 1,715 samples from 8–12 provinces (2008–09). In 2010, 728 antimalarials were sampled in the same 12 provinces: less than 1% failed quality control tests. Cambodia has closed over 1,000 illegal operators in 2009–11.

**Conclusions:** MQM based on the three-level approach enables an MRA to identify poor-quality medicines in a country's supply chain, without overwhelming scarce financial, human, and laboratory resources. The prerequisites are careful selection of sentinel sites and samples, appropriate use of screening technology, and an operational basic quality control laboratory. To have impact on the ground, timely reporting, political will, and a legal basis for corrective actions are key. To sustainably reduce SCM availability, other MQA activities will likely be required (see also abstract 219).

**Funding source(s):** Promoting the Quality of Medicines (PQM) Program, a USAID cooperative agreement implemented by the United States Pharmacopeia.

## Introduction/Background

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► **Challenge:** Low-resource countries (LRCs) lack financial & technical resources to reduce availability of substandard and counterfeit medicines (SCM)

► **Proposed Tool:** A risk-based, cost-effective, three-level approach to medicines quality monitoring (MQM)

► **Questions:**



- Is it a COST-EFFECTIVE tool for LRCs to help reduce SCM availability?
- What are the requirements for success?

► **Operational Research Studies:** Cambodia and Ghana

## The Three-Level Approach

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► A risk-based, cost-effective approach to monitoring medicines quality throughout the supply chain

LEVEL	TYPE OF ANALYSIS	TYPE OF TEST	PURPOSE	SITE PERSONNEL RESPONSIBLE FOR ANALYSIS
1	Visual & Physical Inspection 	Visual: • Labeling and packaging properties Physical: • Appearance, conditions, and physical characteristics of medicine	Identify expired medicines and/or medicines with insufficient, erroneous, and/or fraudulent information; damage to packaging; damage and/or alterations to the condition of the medicine	Management staff at every stage of the supply chain cycle, from procurement to sale
2	Basic/Screening Tests 	• Disintegration • Colorimetric reactions <sup>1</sup> • Thin Layer Chromatography (TLC)	Identify medicines with deficiencies in four critical quality attributes (identity, content, impurities, and disintegration for solid dosage forms)	Personnel trained in basic tests; OMCL personnel <sup>2</sup>
3	Compendial/Validated Tests	According to registration specifications	Assess all the critical quality attributes of a medicine	OMCL personnel* <small>*Official Medicines Control Laboratory</small>

<sup>1</sup> The use of colorimetric methods is not recommended when a TLC method is available for the same medicine. Field colorimetric tests provide information for only one critical quality attribute (identity); TLC tests provide information on three critical quality attributes (identity, content, and impurities).

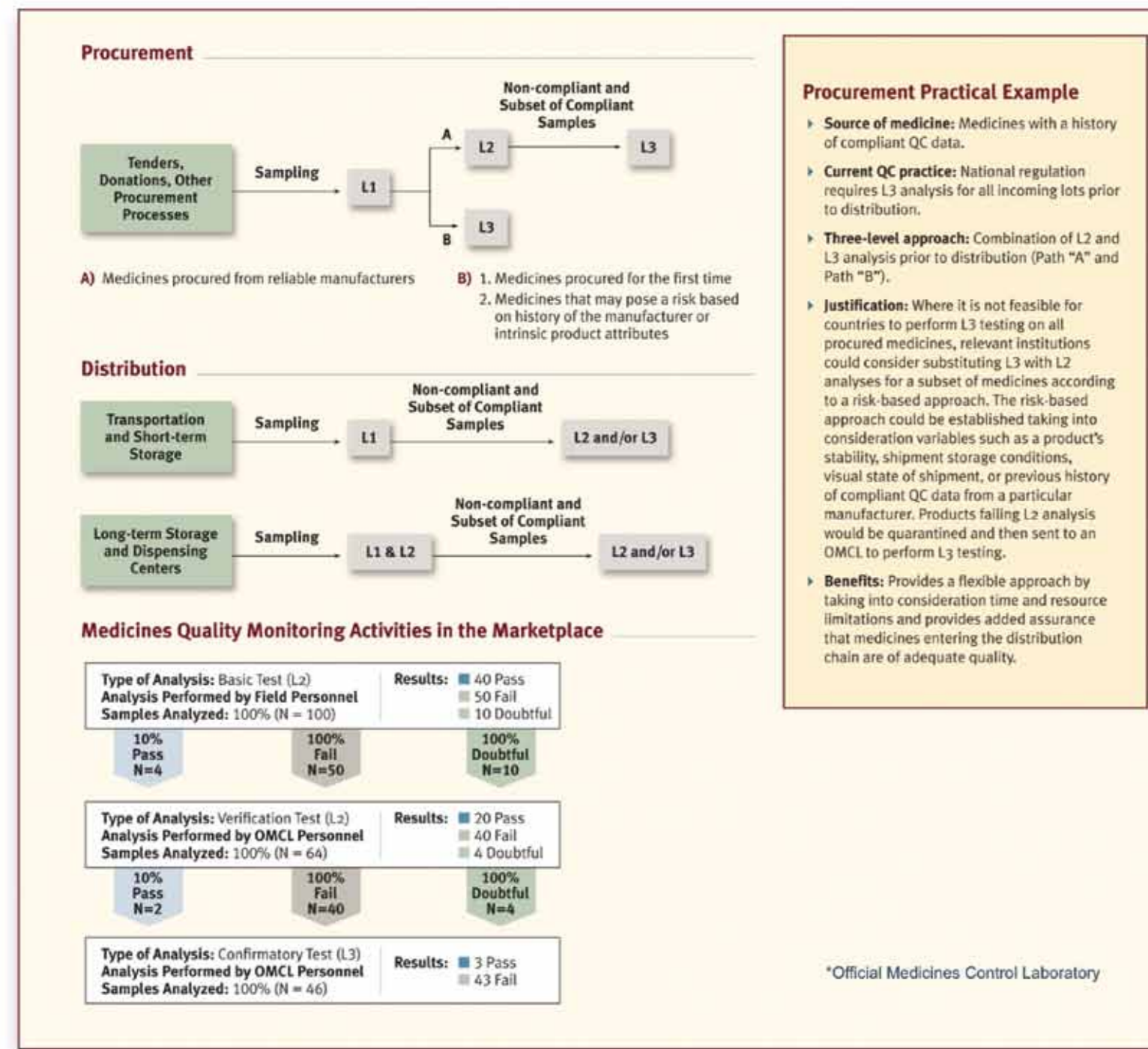
## Three-Level Approach: Pros & Cons

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Advantages	Limitations
Capability to detect poor-quality medicines, in a wide range of therapeutic treatments	Inability to assess all critical quality attributes, e.g., dissolution
Large analysis throughput	Need for verification before enforcement
Minimal infrastructure requirements	Inconclusive results, often due to limited experience of personnel
Minimal need for specialized personnel	
Low acquisition and maintenance costs	

## Three-Level Approach: Application

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## Case Study I: Cambodia

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► In the past seven years, 3,375 antimalarial and other medicines in up to 12 provinces have been sampled through routine MQM. Failure rates have fallen steadily.

Time & Area	Total Sampled	Total Failed	Failure Rate
2003–2004 4 provinces	462	78	16.9%
2005–2007 6–10 provinces	470	44	9.4%
2008–2009 8–12 provinces	1,715	59	3.4%
2010 12 provinces	728	6	< 1%



Cambodia – Sentinel Sites	
1. Battambang	7. Pailin
2. Banteay Meanchey	8. Preah Vihear
3. Kampong	9. Pursat
4. Kratie	10. Svay Rieng
5. Mondulkiri	11. Ratanakiri
6. Odor Meanchey	12. Kampong Cham

## Cambodia (cont.)

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MQM allows regulators to identify and take action against SCMs.

- Inspectors from provincial health departments regularly sample legal/illegal outlets in 12 provinces and test using GPHF Minilabs® (L2).
- Enforcement by Department of Drugs and Food (DDF) includes outlet closings, product recalls, import bans, product blacklisting.
- Pharmacists' Association of Cambodia and DDF launch public awareness campaigns to educate consumers—posters, PSAs, articles.
- Inter-Ministerial Committee and DDF claim government has reduced illegal outlets from 1,081 in Nov. 2009 to 28 in July 2011.



## Case Study II: Ghana

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Sentinel sites are chosen carefully; criteria include:

- epidemiological disease profile
- geography
- administrative factors
- areas known for drug trafficking
- border provinces
- evidence of poor-quality medicines in market



## Ghana (cont.)

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**Three-level approach to MQM yields results in first two years of operation.**

► **2009:** Alert citizen brought suspect Coartem® to MQM site; QC lab confirmed L2 testing—counterfeit. Ghana Food and Drug Board (FDB) promptly seized fakes from pharmacies and levied fines.

► **Note: Importance of informed patients**

► **2010:** SCM versions of 13 key antimalarials discovered in multiple locations across Ghana, including a public hospital. FDB organized a nationwide recall of all 13 medicines and publicly named outlets where they were sold.

► **Note: Need for targeted surveillance and active enforcement of anti-counterfeiting laws**



## Three-Level: Requirements for Success

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- Careful, risk-based selection of sentinel sites and samples
- Appropriate use of L2 analysis, leveraging of benefits and limitations
- Operational quality control laboratory
- Regulatory basis for enforcement/corrective action
- Public education mechanisms
- Collaboration between public and private sectors



## Conclusion

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- MQM, based on the three-level approach, enables a medicines regulatory authority to identify poor-quality medicines in a country's supply chain, without overwhelming scarce financial, human, and technical resources.
- To sustainably reduce SCM availability, other medicines quality assurance activities will likely be required.



## Acknowledgements

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We would like to thank the following people for their contributions to this poster presentation:

- Victor S. Pribluda, Ph.D.
- Laura Krech, M.P.H.
- Siv Lang

Reference

Victor Pribluda et al, *Three-Level Approach for Ensuring the Quality of Medicines in Resource-Limited Countries*, poster presented at ASTMH 59th Annual Meeting, Washington, DC, November 3–7, 2010.

