The State of Antimalarial Drug Quality

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Presentation Outline

◆ Risk factors for counterfeit and substandard medicines in developing countries
◆ Specific country realities that hinder good regulation of medicines and how they are being addressed
◆ The QAMSA Study in 10 African countries
◆ Appropriate, scalable technologies that are helping countries identify bad medicines — Case Study: Ghana
Risk factors for counterfeit and substandard medicines

Unregulated
Business owner diagnoses, prescribes, dispenses

Un-monitored
Informal market

Un-informed
Patient
Quality Assurance of Medicines: Program Objectives

**Build capacity and strengthen QA systems**
- Strengthen medicine quality control labs
- Establish Medicines Quality Monitoring programs

**Help increase supply of QA medicines**
- Improve manufacturer GMP compliance
- Support WHO Prequalification program

**Promoting the Quality of Medicines**
(PQM Program, 2009-2014)

**Combat counterfeit and substandard medicines**
- Collaborate with IMPACT, INTERPOL & other initiatives
- Raise awareness w/PSAs, campaigns

**Provide technical leadership**
- Advocate globally about importance of medicine quality
- Promote new counterfeit/substandard detection technologies
Introduction and Background

Quality of Antimalarial Medicines in Sub-Saharan African Countries (QAMSA) Study

Medicines surveyed:
- Artemisinin Combination Therapy (ACT)
- Sulfadoxine Pyrimethamine (SP)
Countries Surveyed

- Cameroon, Ethiopia, Ghana, Kenya, **Madagascar**, Malawi, Nigeria, **Senegal**, Tanzania, and **Uganda**
Sub-Saharan Africa: QAMSA Study

Findings:
- High failure rate in all three countries with full QC testing
- Consistent across brands
- Indicates quality problem created at source, not in distribution chain

Figure 1. Quality of Antimalarial Medicines Sampled from Madagascar, Uganda, and Senegal
Figure 8. Quality of Antimalarial Medicines Sampled from Different Distribution Sectors in Senegal

Key Findings
Figure 3. Antimalarial Medicines Failure Rate for Assay, Dissolution, and Impurity Tests
Decreasing Effectiveness of Drugs to Treat *P. falciparum* Malaria

**Lessons learned:**
- Lifetime of single drugs limited
- Combination drugs attractive
- Protect newer drugs

Drug Resistance

What is drug resistance

– The ability of a parasite strain to survive and/or multiply despite the administration and adsorption of a drug given in doses equal or higher than those recommended but within tolerance—**WHO definition**

Artemisinin Resistance

– Increase in parasite clearance time as an early warning of artemisinin resistance

Methods of detection

– Ideal method of detection- molecular markers (unavailable)
– Therapeutic efficacy studies- lagging indicator of resistance (immunity and re-infection confounds)
The phenomenon of resistance

- Drug resistance is a natural phenomenon that is bound to occur with time.
- Preventing resistance really means delaying the onset of resistance.

What are those risk behaviors that promote the onset of resistance?

- Use of substandard medicines—Poor Drug Quality
- Irrational Use of medicines
- Lack of surveillance and delay in taking action
Risk Factors for Counterfeit and Substandard Medicines (CSM)

Plethora of Brands

- Limit number of approved brands on market

High Tariffs–Porous Borders

- Limit tariffs on essential medicines
- Greater enforcement across borders
Risk Factors for CSMs — Addressing the Issue

Poor regional cooperation, collaboration

- Form regional networks
- Share information
- Free access drug quality database

PQM Response

- NAMCOL
- MQDB
Heavy reliance on imports (domestic mfg lacks GMP)

- Support local manufacturing of pharmaceuticals

PQM Response

- TA toward WHO prequalification
  - Dossier preparation
  - GMP compliance
Risk Factors for CSMs — Addressing the Issue

High staff turnover, technical constraints

- Use appropriate standards
- Develop regional expertise

PQM Response

- TAP – RS to developing countries
- BREMER with WAHO (WATmMAR)
Limited knowledge of importance of quality in treatment outcomes

- Provide evidence-based data
- Inform public, recommend use of approved vendors

PQM Response

- Raise awareness among leadership
- Communications campaigns
Two classes of techniques

- **Authentication – Product Brand Control**
  - Is the product what it claims to be and made by whom it claims to be made?

- **Quality Control – Product Quality Control**
  - Does the product meet quality specifications?
GPHF Minilab®
Everything needed for drug testing fits into two transportable units, each about the size of a suitcase and weighing about 40 kg
Advantages of the Minilab

- Requires less training- addresses human resource issues and rapid staff turn over
- Task shifting
- Low maintenance cost- address inadequate resources
- Rapid test results—allows quick regulatory action
- Portable- allows the **decentralization** and **ownership** of quality control. Deployed in the provinces and remote places
- Need little infrastructure—battery powered devices
CASE STUDY: GHANA

Sites selected based on specific criteria:

- Epidemiological prevalence of disease
- Geographical, administrative
- Areas known for traffic in counterfeit drugs
- Border provinces

Counterfeit medicines found, verified through Ghana MQM program

Source: USP, 2009
Case Study #3: Cambodia

MQA Improvement since 2003

(i) Lab strengthened

(ii) Postmarketing surveillance (PMS), with enforcement

(iii) Active public awareness campaign, e.g., PSA & videos

PMS Results

932 AML samples collected 2003-08

2003-2004: 23% & 27% failure rates

2006-2007: 11% & 8% failure rates

Source: USP, 2009
PQM Medicines Quality Database (MQDB)

http://www.usp.org/worldwide/medQualityDatabase/

Over 8000 records from Africa, Asia and Latin America
TAKE HOME MESSAGE

◆ Expand product availability paradigm to include focus on pharmaceutical services and quality – need to retool global health funding mechanisms

◆ Product quality remains an overarching concern – strengthen country quality assurance mechanisms

◆ Assuring medicine quality requires use of technology – use appropriate technologies scaled to developing country settings
Regulators need an enabling environment to do your job – empower medicine regulatory agencies to properly enforce laws.

Government need to lead in providing safe, effective medicines – capacitate government to take ownership of health initiatives.
“Dying from a disease is sometimes unavoidable; dying from a medicine is unacceptable.”

– V.K. Lepakhin, Geneva 2005
Questions
Thank You