

# Africa Pharmacovigilance Meeting 2012: Ensuring Quality and Safety of Medicines in Sub-Saharan Africa

Nairobi, Kenya  
April 18-20, 2012

---

## *Trip Report*

Abdelkrim Smine, Ph.D., Consultant

**Promoting the Quality of Medicines**  
Implemented by U.S. Pharmacopeia  
12601 Twinbrook Parkway  
Rockville, MD 20852 USA  
Tel: (+1-301-230-3274)  
Email: [pgm@usp.org](mailto:pgm@usp.org) and [AZS@usp.org](mailto:AZS@usp.org)

**Cooperative Agreement #** GHS-A-00-09-00003-00  
**Funding Source:** Common Agenda  
**Grantee:** Promoting the Quality of Medicines (PQM) Program  
**Author(s) Name:** Abdelkrim Smine, PQM Consultant  
**Language:** English  
**Date of Publication:** May 4, 2012



This report is made possible by the generous support of the American people through the United States Agency for International Development (USAID), under Cooperative Agreement No. GHS-A-00-09-00003-00. The contents are the responsibility of the Promoting the Quality of Medicines Program, implemented by the U. S. Pharmacopeia, and do not necessarily reflect the views of USAID, [PEPFAR], or the United States Government.

PROMOTING THE QUALITY OF MEDICINES

## **Executive Summary**

Dr. Abdelkrim Smine traveled to Kenya to represent PQM at the Africa Pharmacovigilance Meeting and to give a presentation on “The Link between the Quality and the Safety of Medicines.”

The meeting was the first of its kind to address the safety of medicines in Sub-Saharan Africa. The participants and the organizers learned about new and advanced approaches to address medicine safety effectively. Manufacturers, regulators, health program managers, donors, technical partners, and academia were all represented and shared information from different perspectives.

## Table of Contents

<a href="#"><u>Acknowledgements</u></a> .....	4
<a href="#"><u>Acronyms</u></a> .....	5
<a href="#"><u>Background</u></a> .....	6
<a href="#"><u>Purpose of Trip</u></a> .....	6
<a href="#"><u>Source of Funding</u></a> .....	6
<a href="#"><u>Conference Highlights</u></a> .....	6
<a href="#"><u>Additional Meetings</u></a> .....	8
<a href="#"><u>Next Steps</u></a> .....	8
<a href="#"><u>Conclusion</u></a> .....	9
<a href="#"><u>Annex 1: PQM Presentation</u></a> .....	10

### **About PQM**

The Promoting the Quality of Medicines (PQM) program, funded by the U.S. Agency for International Development (USAID), is the successor of the Drug Quality and Information (DQI) program implemented by the United States Pharmacopeia (USP). PQM is USAID’s response to the growing challenge posed by the proliferation of counterfeit and substandard medicines. By providing technical assistance to developing countries, PQM helps build local capacity in medicine quality assurance systems, increase the supply of quality medicines to priority USAID health programs, and ensure the quality and safety of medicines globally. This document does not necessarily represent the views or opinions of USAID or the United States Government. It may be reproduced if credit is given to PQM and USP.

## **ACKNOWLEDGEMENTS**

The author would like to thank:

- Management Sciences for Health– Systems for Improved Access to Pharmaceuticals and Services colleagues for inviting PQM to participate in the pharmacovigilance meeting
- The meeting organizers for their assistance with travel logistics
- PQM colleagues who reviewed the presentation and assisted with editing this report
- Mr. Anthony Boni and Dr. Maria Miralles at USAID/Washington for their support and advice

## ACRONYMS

ADR	Adverse Drug Reaction
AMRH	African Medicines Regulatory Harmonization
CDC	Centers for Disease Control and Prevention
DQI	Drug Quality and Information Program
EMA	European Medicines Agency
FDA	Food and Drug Administration
MOH	Ministry of Health
MSH	Management Sciences for Health
NEPAD	New Partnership for Africa's Development
NGO	Non-Governmental Organization
NMRA	National Medicines Regulatory Authorities
PMS	Post-Marketing Surveillance
PQM	Promoting the Quality of Medicines Program
PV	Pharmacovigilance
QA	Quality Assurance
QC	Quality Control
SIAPS	Systems for Improved Access to Pharmaceuticals and Services
SPS	Strengthening Pharmaceutical Systems
SSA	Sub-Saharan Africa
USAID	United States Agency for International Development
USP	United States Pharmacopeia
WHO	World Health Organization

## Background

Strengthening Pharmaceutical Systems (SPS) and its follow-on program, Systems for Improved Access to Pharmaceuticals and Services (SIAPS) — both implemented by Management Sciences for Health (MSH) — conducted a large assessment of pharmacovigilance (PV) systems in Sub-Saharan Africa (SSA). This study was funded through an interagency agreement between the United States Food and Drug Administration (US FDA) and the United States Agency for International Development (USAID). The study used three methods to assess PV systems and their performance in 46 countries in SSA: literature reviews, mailed surveys, and in-depth assessments in nine priority countries.

The *Africa Pharmacovigilance Meeting 2012: Ensuring Quality and Safety of Medicines in Sub-Saharan Africa* was organized in order to present the findings of the PV assessment and discuss the need for new approaches, tools, and regulations to improve the safety of medicines in SSA.

## Purpose of Trip

Dr. Abdelkrim Smine traveled to Kenya to represent PQM at this meeting and to give a presentation on “The Link between the Quality and the Safety of Medicines.”

## Source of Funding

This trip was funded by USAID core funding for Common Agenda.

## Overview of the PV meeting

Item	Description
Venue and Dates	InterContinental Hotel, Nairobi, Kenya; April 18-20, 2012
Organizers	SIAPS/MSH US and MSH Kenya
Participants	More than 100 participants from over 30 countries representing: <ul style="list-style-type: none"><li>• MSH US and MSH offices in many countries</li><li>• US FDA, CDC, USAID</li><li>• WHO Geneva</li><li>• Pharmaceutical industry, international NGOs, and academia</li><li>• Health Program/MOHs from African and Asian countries</li><li>• Drug regulatory authorities from various countries in Africa</li></ul>
Opening Ceremony	<ul style="list-style-type: none"><li>• Officials from MOH Kenya</li><li>• USAID – Anthony Boni</li><li>• US FDA – Beverly Corey</li><li>• MSH</li></ul>
Agenda	<p><b>First Day:</b> Focused on presenting the findings of the PV assessment in 46 countries, medicines regulatory harmonization initiatives in Africa, WHO PV tool kit, global stakeholders’ perspectives on PV systems, and current PV practices in Africa.</p> <p><b>Second Day:</b> Presentation about PV tools, PV in national health programs, PQM’s presentation, economic evaluation of the impact of PV systems and tools, and workshop on components of PV systems</p>

	<b>Third Day:</b> Summary of priority PV tools, plans for priority tools development, discussion of SIAPS/SPS global active surveillance activities, and workshop on vaccine safety.
Closing Ceremony	<ul style="list-style-type: none"> <li>• SIAPS – David Lee</li> <li>• USAID – Anthony Boni</li> <li>• SIAPS – Sameh Saleeb</li> <li>• Local Organizers – Fred Siyoi</li> </ul>

## Highlights of the PV conference

### Major findings of the PV assessment in SSA

- The pharmaceutical market size of SSA is estimated to be between \$3.7 and 4.7 billion USD
- Pharmaceutical manufacturing capacity exists in 80% of the countries in SSA
- 74% of SSA countries have national medicines regulatory authorities (NMRAs)
- 78% of SSA countries have a national medicines policy
- 5 quality control (QC) labs are WHO prequalified in SSA
- 33 SSA countries are official or associate members of the WHO program for international medicine monitoring
- 74% of SSA countries have PV centers with clear mandates and organizational structures
- 28 out of 46 surveyed countries have legal provisions that requires marketing authorization holders to report serious adverse drug reactions (ADRs) to the NMRA
- Less than 50% of surveyed countries monitor product quality, medication errors, and treatment failures through existing PV systems
- Only 2 out of 46 countries collected more than 100 reports per million population in 2010
- Risk assessment and risk management related to medicines use is still very limited in SSA
- Active surveillance of ADRs is limited and mainly funded by global health initiatives
- Involvement of pharmaceutical manufacturers in reporting ADRs is very limited to absent in most surveyed countries
- Based on the assessment findings, the surveyed countries were split into four groups: 1) Countries with almost no PV capacity; 2) Countries with basic structures in place; 3) Countries with the capacity to collect and analyze safety data on the basis of legal and organizational structures; and 4) Countries with currently performing PV systems to detect, evaluate, and prevent medicine safety issues

### PQM presentation and other workshop activities

The presentation made by Dr. Smine addressed the link between the quality and safety of medicines. The presentation focused on the skills and resources needed to implement effective medicine quality assurance systems of medicines and that the safety of medicines is a key component of overall quality assurances measures. The presentation also demonstrated that ADR reporting alone does not and will not address the lack of adequate medicines safety monitoring in Africa.

Dr. Smine argued that — based on PQM’s medicine quality monitoring (MQM) programs in several countries around the world — medicine quality is the source of the majority of ADRs in

Africa. Dr. Smine suggested that to effectively assure and maintain the quality and safety of medicines in SSA, there is a need for adequate regulations and effective post-marketing surveillance where quality and safety data are monitored, evaluated, and reported through the same systems.

The presentation was well-received, as expressed by many participants, because it put the quality of medicines as equally important to their safety. In SSA, where drug quality is still a major problem impacting all health systems, any new approach to addressing medicines safety will not be successful if it does not consider quality issues at the same time.

In addition to the PQM presentation, Dr. Smine participated in discussing the regulations, laws, and policies needed to start and implement effective PV systems in Africa. Dr. Smine facilitated the discussion and was chosen by the working group to present the group recommendations to all conference participants.

### **Additional Meetings**

During the three day conference, Dr. Smine met with many participants and discussed various issues related to PQM activities. Details of some of these important meetings and discussions are listed below:

#### *Meeting with Dr. Margareth Ndomondo-Sigonda*

Dr. Margareth Ndomondo-Sigonda used to work with the Tanzanian Food and Drug Authority, but she is now the pharmaceutical coordinator of the New Partnership for Africa's Development (NEPAD) of WHO AFRO, based in South Africa. She coordinates the WHO initiatives of African Medicines Regulatory Harmonization (AMRH). Dr. Smine recommended to Dr. Sigonda that AMRH efforts should include focusing on harmonizing QC laboratory standards and practices. He suggested that such an initiative would be easier to achieve if AMRH uses, for example, ISO 17025 as a common standard to achieve. Dr. Smine emphasized that harmonizing technical practices using the same internationally recognized standard is easier and faster to achieve than harmonizing regulations, especially in Africa.

#### Next Steps

Dr. Smine proposed inviting Dr. Sigonda to the next Network of African Medicines Control Laboratories (NAMCOL) meeting, planned to be held in Maputo in June. Dr. Sigonda agreed to participate if her schedule will allow it.

#### *Meeting with representatives from MOH of South Sudan*

Dr. Smine was approached by participants from South Sudan who were interested in receiving technical support from PQM. The meeting was attended by Anthony Boni (USAID), Tesfeye Godana Amare (MSH-South Sudan), Ekoy Bortel Ohisa, (MOH-South Sudan), and Kur Ronjo (Pharmaceutical and Equipment Directorate-South Sudan).

Dr. Smine and Mr. Boni explained how PQM works and how the program is funded. Dr. Smine urged the team to meet with the USAID Mission in Juba to discuss the country's needs and the rationale in requesting technical support from PQM to address medicines quality issues in South Sudan. Dr. Smine explained to the team that the program has a lot of experience in building

country capacity in QC in a step-by-step manner, as it has done in other countries, such as Madagascar, Liberia, and Mozambique.

### Next Steps

Dr. Smine will follow up on this important meeting and work with PQM colleagues to assist this newly-established country as much as possible.

### **Conclusion**

The PV meeting was the first of its kind to address the safety of medicines in SSA. The participants and the organizers learned about new and advanced approaches to address medicine safety effectively. Manufacturers, regulators, health program managers, donors, technical partners, and academia were all represented and shared information from different perspectives.

The assessment of PV systems conducted by MSH showed some important findings. It was the first large assessment of its kind to address medicines safety in so many countries in SSA. Some argued that most of the findings were already known and that the study failed to present solutions to some safety issues. Many PV tools already exist; new initiatives should avoid duplication and adopt all the resources made possible by WHO and its collaborating centers.

PQM's presentation showed the link between the quality and the safety of medicines and gave the participants an idea about the expertise of the PQM program and its activities in Africa.

## AFRICA PHARMACOVIGILANCE MEETING 2012

Ensuring Quality and Safety of Medicines in Sub-Saharan Africa

Nairobi, Kenya | April 18-20, 2012

### SURVEILLANCE OF PHARMACEUTICAL PRODUCT QUALITY AND SAFETY

Abdelkrim Smine, Ph.D.  
Promoting the Quality of Medicines Program



### EXPLORING THE LINK BETWEEN THE QUALITY AND THE SAFETY OF MEDICINES



#### CONTENTS

- Overview of the quality assurance of medicines
- Importance of exploring the link between the safety and the quality of medicines
- USP PQM approach used in medicines quality monitoring
- Challenges with medicines quality assurance in Africa
- Conclusion



#### DEFINITIONS

- **Quality Assurance (QA)** of medicines includes all measures taken to assure its quality from development to use by the patient.

QA = making sure that the medicine is  
**FIT for its intended use** by ensuring its

*Efficacy—Safety—Quality  
Storage—Appropriate Use*



#### DEFINITIONS

- **Pharmacovigilance** is the science and activity relating to the
  - Detection
  - Assessment
  - Understanding, and
  - Prevention
 of adverse effects or any other possible medicine-related problems



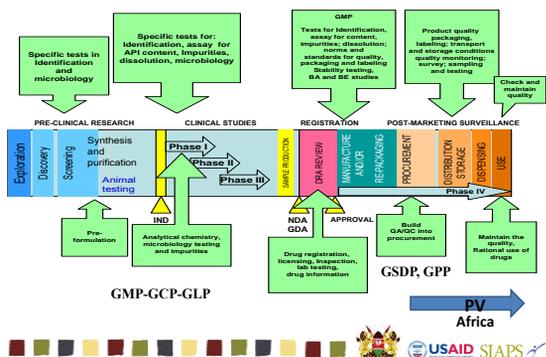
#### PHARMACOVIGILANCE AS PART OF THE QUALITY ASSURANCE OF MEDICINES

##### “The Medicine ”

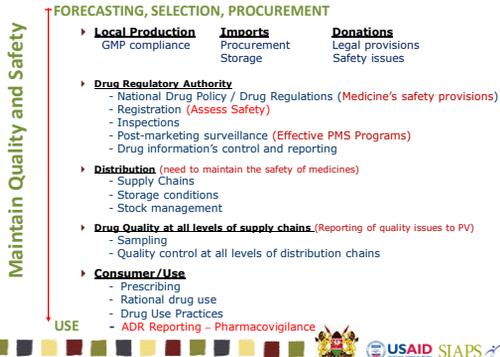
- ▶ Active Pharmaceutical Ingredient (API)
- ▶ Excipients
- ▶ Package
- ▶ Label
- ▶ Storage Conditions
- ▶ Shelf Life
- ▶ Indications for Use



## WHEN DOES SAFETY OF MEDICINES START? END?



## QUALITY ASSURANCE IN AFRICA



## PHARMACOVIGILANCE: OVERVIEW

ICH COUNTRIES	AFRICA
<ul style="list-style-type: none"> <li>PV is under responsibility of sponsor</li> <li>Advanced medicines safety capacities</li> <li>Regulatory provisions, new PV legislation</li> <li>EudraVigilance in EEA</li> <li>Advance mgmt systems for ADR reports</li> <li>Periodic Safety Update Reports (PSUR)</li> <li>EU Network for Center of PV</li> <li>ICH EZE guidelines, E2C guidance FDA</li> <li>Guidelines for good PV practices</li> <li>Pediatric and pregnant women PV</li> </ul>	<ul style="list-style-type: none"> <li>PV not under sponsor's responsibility</li> <li>Weak medicines safety capacity</li> <li>Lack of adequate regulations</li> <li>Safety of medicines is not high priority</li> <li>Increase in PV activities in last 10 years</li> <li>33 African countries have PV</li> <li>Start of active PV activities</li> <li>PV often developed for specific health programs (TB, HIV, malaria, vaccines)</li> <li>Start of pregnant women PV activities</li> </ul>

## LINK BETWEEN QUALITY AND SAFETY OF MEDICINES

### Critical Attributes for Testing Medicines

*Identity, purity, quality, strength, packaging, labeling*

- Identity:** confirmation of API
- Assay / dosage:** amount of active ingredient on the label
- Disintegration:** prerequisite for bioavailability
- Dissolution:** higher level of assurance of bioavailability
- Impurities:** generally related to API toxicity
- Uniformity:** uniformity of content/dosage, GMP
- Sterility:** injectable solutions
- Package & Label:** regulated information
- Others:** specific to type of medicine

## ADVERSE EVENTS RELATED TO QUALITY

Quality Problem	Reported ADR
Identity (API)	No API → 30 reported deaths w/malaria in Cambodia (1999) Same in other countries, but not documented
Dosage	Amodiaquin → reported children deaths in Ghana (2005) FDC (amodiaquine-artesunate) Overdose
Impurities	Heparin → 81 deaths in USA (2008) DEG → hundreds of deaths in USA, Panama, Nigeria, India
Sterility <71>	Koff&Kold, Providone Iodine Pads, Cytarabine Inj → FDA (2012) Lack of Sterility
Particulate Matter <788>	Acetylcysteine, Argatroban, Polymyxin, Vecuronium, Bromide, Treanda HCL → recall, FDA (2012) Visible Particles
Packaging	Norgestimate/Ethinyl Estradiol Tablets → Recall, FDA (2012) Packaging Error (could lead to incorrect dose & toxicity)

## SUMMARY

- Pharmacovigilance** is major part of QA of Medicines
- Medicine's Safety Measures** should be built into overall Quality Assurance Systems of medicines
- Pharmacovigilance/ADR** reporting models assess the safety only at the use level of medicines
- Safety of Medicines** should be key component of QA of Medicines in Africa, as in ICH countries
- Urgent Need** for promoting Safety of Medicines in Africa (quality monitoring, ADRs reporting, medication errors) based on adequate and African specific medicine's regulations and enforcement.

## SUMMARY

- **Majority of ADRs** in Africa are related to medicines quality
- **ADR monitoring and reporting** should integrate with quality monitoring programs as part of PMS activities
- **Strengthening drug safety** in Africa requires MRAs to establish **adequate regulations**, enforce **drug safety assessment** during registration, strengthen **drug-drug interactions** and **medications errors**, and promote the **rational drug use**

*In USA, an estimated 100,000 deaths/year are related to ADRs. What is the case in Africa ?*



## DRUG QUALITY MONITORING

### HOW USP PQM IS ASSISTING COUNTRIES IN AFRICA TO BUILD QUALITY CONTROL CAPACITY



## PQM PROGRAM OBJECTIVES



### Build capacity & strengthen QA systems

- ▶ Provide technical assistance for QA/QC in regulations
- ▶ Establish medicines quality monitoring programs, PMS
- ▶ Train in GLP, analytical methods, quality systems, Minilab<sup>®</sup> testing, registration



### Help increase supply of QA medicines

- ▶ Improve manufacturers' GMP compliance
- ▶ Test procurement agencies' samples



### Combat availability of counterfeit meds

- ▶ Collect evidence-based data for MRA enforcement
- ▶ Raise awareness w/PSAs, campaigns



### Provide technical leadership

- ▶ Advocate and educate regarding medicine quality
- ▶ Promote new detection technologies



## WEST AFRICA SENTINEL SITES (MQM)



<b>SENEGAL</b>
1. Dakar
2. Kaolack
3. Kedougou
4. Louga
5. Matam
6. Richard Toll
7. Touba
8. Vélingara
9. Ziguinchor
<b>GHANA</b>
1. Bolgatanga
2. Kumasi
3. Ho
4. Tema
5. Tarkwa
<b>MALI</b>
1. Gao
2. Kayes
3. Koulikou
4. Mopti
5. Ségou
6. Sikasso
7. Tombouktou



## EAST AFRICA SENTINEL SITES (MQM)



<b>ETHIOPIA</b>
1. East Shoa
2. West Wollega
3. Jimma
4. Borena
5. Hararge
<b>KENYA</b>
1. Eldoret
2. Kakamega
3. Kisumu
4. Mombasa
5. Nairobi
<b>MADAGASCAR</b>
1. Antananarivo
2. Antsirana
3. Fianarantsoa
4. Mahajanga
5. Toamasina
6. Toliara
<b>MOZAMBIQUE</b>
1. Nampula
2. Tete
3. Sofala
4. Maputo

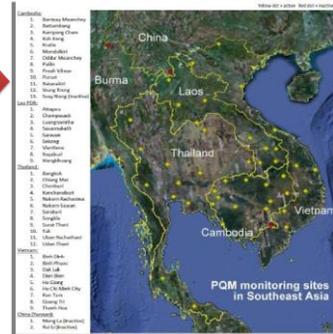


## SOUTHEAST ASIA SENTINEL SITES

Increased # of sites:  
2003: 17  
2006: 28  
2012: 53  
(3 inactive: 2 in Yunnan China and 1 in Cambodia)

Program expanded to include ABT, ATB, ARV, and, AI products

Leveraged support from GFATM in Laos, Cambodia, and Vietnam



## CONSEQUENCES OF POOR QUALITY MEDICINES

- **Health Impact**
  - Increased morbidity and mortality
  - Treatment failure
  - Adverse reaction
  - Antimicrobial resistance
- **Financial Impact**
  - Waste of scarce financial resources
  - Waste of human resources and countries' productivity
  - Increase in health expenditures
- **System Impact**
  - Loss of confidence in conventional medicines
  - Loss of confidence in health care system



## CONSEQUENCES OF POOR QUALITY MEDICINES

### Substandard and counterfeit medicines can kill

- **Substandard: e.g., DEG contamination**
  - Panama 2006-07: 91 died
  - China 2006/2007: 14 died
  - U.S. 2008: 100 died
  - Nigeria 2008-09: 84 children
  - India 2011: 12 pregnant women died
  - Pakistan 2012: 112 died
- **Counterfeit:**
  - Nigeria 1995: ~2500 died – fake vaccine
  - Cambodia 1999: 30 died – fake antimalarial
  - USA 2008: 81 died – counterfeit Heparin
  - China 2009: 2 died – counterfeit diabetes medicine



Source: PQM Media Reports



## PQM EXPERIENCE IN AFRICA

### Medicines Quality Monitoring & Building QC Capacity

- ▶ Benin, Ethiopia, Ghana, Kenya, Madagascar, Mali, Mozambique, Senegal, Liberia

### Building Regulatory Functions – Accreditation

- ▶ PQAD QC lab in Ethiopia awarded ISO 17025 accreditation, Nov. 2011, QC labs of Ghana & Mali on the way!
- ▶ Strengthening regulatory functions of MRAs, registration, PMS (Ethiopia and Liberia)

### Regional Initiatives

- ▶ Collaborative QC studies (PQM-WHO in 10 African countries)
- ▶ QC labs network (6 countries)



## FINDINGS

- **Quality Assurance** of medicines is still weak in most USAID supported countries
  - Weak medicines regulations
  - Lack or absence of post-marketing surveillance program
  - Quality, safety, and efficacy poorly assessed in registration
  - Access and affordability of medicines still highest priorities of MOHs in Many African countries
  - Weak or complete enforcement
  - Lack of resources



Ghana 2010



## MAJOR CHALLENGES IN AFRICA

- Lack of human and financial resources
- Weak medicines policies and regulations
- Political instability
- High turnover of trained staff and Ministers of Health
- Weak enforcement of existing laws and regulations
- Lack of or inadequate technical assistance from donors
- Lack of governance and conflict of interest in pharmaceutical sectors



## CONCLUSION

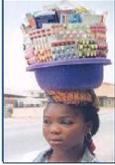
- ▶ There is an urgent need to build effective **Quality Assurance** systems for medicines in Africa
- ▶ Because of the strong links between **quality, safety, and efficacy** of medicines, model ADR reporting alone will not be sufficient to address all safety risks
- ▶ **Establishing appropriate policies and regulations** should be the starting point to building quality assurance systems
- ▶ **Close and effective collaboration** between donors and all stakeholders is key to success



## MEDICINES QA CHALLENGE IN AFRICA & ELSEWHERE

### Unregulated

Business owner  
diagnoses,  
prescribes,  
dispenses



### Un-monitored Informal market



### Un-informed Patient



*THANK YOU*

Abelkrim Smine, Ph.D.  
PQM Program Consultant  
The United States Pharmacopeia Convention  
[AZS@usp.org](mailto:AZS@usp.org)  
[www.usppqm.org](http://www.usppqm.org)

