HNP DISCUSSION PAPER

# Assuring the Quality of Essential Medicines Procured with Donor Funds

Thomas Moore, David Lee, Niranjan Konduri, Lombe Kasonde

April 2012


# ASSURING THE QUALITY OF ESSENTIAL MEDICINES PROCURED WITH DONOR FUNDS

**Thomas Moore**
**David Lee**
**Niranjan Konduri**
**Lombe Kasonde**

**April 2012**

## Health, Nutrition and Population (HNP) Discussion Paper

This series is produced by the Health, Nutrition, and Population (HNP) Family of the World Bank's Human Development Network (HDN). The papers in this series aim to provide a vehicle for publishing preliminary and unpolished results on HNP topics to encourage discussion and debate. The findings, interpretations, and conclusions expressed in this paper are entirely those of the author(s) and should not be attributed in any manner to the World Bank, to its affiliated organizations or to members of its Board of Executive Directors or the countries they represent. Citation and the use of material presented in this series should take into account this provisional character.

Enquiries about the series and submissions should be made directly to the Editor, Martin Lutalo (mlutalo@worldbank.org). Submissions undergo informal peer review by selected internal reviewers and have to be cleared by the Task Team Leader's Sector Manager. The sponsoring department and author(s) bear full responsibility for the quality of the technical contents and presentation of material in the series.

Since the material will be published as presented, authors should submit an electronic copy in the predefined template (available at www.worldbank.org/hnppublications on the Guide for Authors page). Drafts that do not meet minimum presentational standards may be returned to authors for more work before being accepted.

For information regarding the HNP Discussion Paper Series, please contact Martin Lutalo at mlutalo@worldbank.org or 202-522-3234 (fax).

# Health, Nutrition and Population (HNP) Discussion Paper

## Assuring the Quality of Essential Medicines Procured with Donor Funds

Thomas Moore,[a] David Lee,[b] Niranjan Konduri,[c] Lombe Kasonde[d]

[a] Center for Pharmaceutical Management, Management Sciences for Health, Arlington, VA, USA
[b] Center for Pharmaceutical Management, Management Sciences for Health, Arlington, VA, USA
[c] Center for Pharmaceutical Management, Management Sciences for Health, Arlington, VA, USA
[d] Operations Analyst, HNP, The World Bank, Washington, DC., USA

Paper commissioned as part of an ongoing workstream on medicines procurement harmonization under the Interagency Pharmaceutical Coordination group (IPC), April 2012

**Abstract:** The donor community spends millions of dollars annually on procuring essential medicines as part of development assistance for health. Defining and enforcing quality standards for these medicines continues to prove challenging as this involves complex regulatory processes. While developed countries with stringent regulatory authorities in place have the capacity to comply with strict regulatory requirements, the essential medicines procured for developing countries are either not available in developed country markets, or are not the most competitively priced medicines internationally. Donors have therefore been forced to independently develop systems to purchase at lowest feasible cost, essential medicines for the developing world without compromising quality. Through a desk review and consultation with key stakeholders, this paper compiles data on various approaches used by international agencies and donor bodies to improve the quality of essential medicines they procure, beyond the WHO Prequalification of Medicines Programme and the Global Fund Expert Review Panel, which focus only on medicines for treating HIV/AIDS, tuberculosis, and malaria. This paper additionally explores pragmatic options for a harmonized approach to ensuring the quality of medicines procured with donor funds. Based on the observed limitations of existing approaches, this paper considers a risk-based approach initiated by WHO, through which medicines in the WHO Model List of Essential Medicines are classified according to risk categories (high, medium, and low). In the long run, the goal of international donor aid is to build the capacity of developing countries to take the lead in assuring the health of their citizens. Effective harmonization, coordination, and optimal leveraging of existing approaches may help national regulatory authorities to strengthen their own capacity to better control their markets, including registering products according to stringent standards, improving domestic manufacturing where applicable, and enhancing postmarketing surveillance.

**Keywords:** Quality assurance, essential medicines, (stringent) regulatory authorities, prequalification, procurement, donors, international organizations

**Disclaimer:** The findings, interpretations, and conclusions expressed in the paper are entirely those of the authors, and do not represent the views of the World Bank, its Executive Directors, or the countries they represent.

**Correspondence details:** Andreas Seiter, Senior Health Specialist, the World Bank, 1818 H Street, NW, Washington, DC 20433; Tel: +202-473-3629; e-mail: aseiter@worldbank.org.

# TABLE OF CONTENTS

# FOREWORD

Assuring the quality of medicines procured with public or donor funds is a challenge for government procurement agencies and financing institutions alike. On the one hand, there is pressure to buy the lowest cost medicines available; on the other, the risks of buying low-quality medicines for health outcomes and for the reputation of institutions involved are significant. In an ideal world, one would be able to rely on regulatory agencies to ensure that only quality medicines are available in the market. In reality, however, many developing country regulators have limited capacity and are not able to monitor their markets in a way that gives buyers confidence. As a result, government procurement agencies and many financing institutions have developed their own quality assurance guidelines and procedures. Some of these are public, others remain undisclosed. This issue is particularly relevant for medicines not covered by WHO's Prequalification of Medicines Programme. For recipients of development financing, the experience has been that each agency has its own demands, making a coordinated and pooled procurement process for medicines difficult and increasing turnaround time. Development partners have different constituencies and technical focus, which influences the level of detail to which quality assurance policies are set as conditions for recipients. The International Health Partnership (IHP+) is an attempt to reduce the diversity of rules and processes imposed on recipients of development funding. This paper is an attempt to capture the ongoing discussion on how to work towards convergence of the various policies and strategies applied by the Global Fund, UNICEF, the World Bank, not-for-profit private procurement agencies, and NGOs to their own procurement. If successful, the result would be a more streamlined national procurement process capable of pooling funding from different sources, which could have a positive effect on prices, timelines, and ultimately access to essential medicines.

Andreas Seiter, the World Bank, May 2012

# ACKNOWLEDGMENTS

This publication was made possible through a grant from the International Health Partnership (IHP+) and funding provided by the US government through USAID's Strengthening Pharmaceutical Systems (SPS) Program. The paper is part of an ongoing workstream on medicines procurement harmonization under the Interagency Pharmaceutical Coordination group (IPC). The concept note for the paper was developed in close collaboration with WHO (Clive Ondari and Lembit Rago), the Global Fund (Joelle Daviaud and Sophie Logez), and UNICEF (Ian Pett). Peer reviewers for the draft paper were Karina Mostipan and Timothy A. Johnston (both from the World Bank) and Alastair West (UNIDO).

The authors are grateful to the World Bank for publishing this report as an HNP Discussion Paper.

# ACRONYMS

| | |
|---|---|
| API | Active pharmaceutical ingredient |
| ARV | Antiretroviral |
| ATM | AIDS, tuberculosis and malaria |
| DG ECHO | Directorate-General of European Commission's Humanitarian Aid |
| EFTA | European Free Trade Association |
| EMA | European Medicines Agency |
| EML | Essential medicines list |
| EOI | Expressions of interest |
| ERP | Expert Review Panel |
| FPP | Finished pharmaceutical product |
| GCP | Good clinical practice |
| GDP | Good distribution practice |
| GDF | Stop TB Partnership/Global Drug Facility |
| GLP | Good laboratory practice |
| GIZ (formerly GTZ) | Deutsche Gesellschaft für Internationale Zusammenarbeit (German agency for international cooperation) |
| GMP | Good manufacturing practices |
| GSP | Good storage practice |
| HPC | Humanitarian Procurement Centre |
| ICH | International Conference on Harmonisation |
| ICRC | International Committee of the Red Cross |
| IMS | IMS Health (Intercontinental Marketing Services) |
| ISO | International Organization for Standardization |
| IPC | International Pharmaceutical Coordination group |
| JSI | John Snow, Inc. |
| MQAS | Model Quality Assurance System for Procurement Agencies |
| MSF | Médecins sans Frontières (Doctors without Borders) |
| MSH | Management Sciences for Health |
| NGO | Nongovernmental organization |
| NMRA | National medicines regulatory authority |
| NPC | National procurement center |
| OFDA | Office of Foreign Disaster Assistance |
| PAHO | Pan American Health Organization |
| PEPFAR | US President's Emergency Plan for AIDS Relief |
| PFSCM | Partnership for Supply Chain Management |
| PIC/S | Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme |
| PQ | Prequalification |
| PQM | Promoting the quality of medicines |

| | |
|---|---|
| PSA | Procurement service agency |
| QA | Quality assurance |
| QUAMED | Quality Medicines for All |
| RH | Reproductive Health |
| SCMS | Supply Chain Management System |
| SOP | Standard Operating Procedure |
| SPS | Strengthening Pharmaceutical Systems Program |
| SRA | Stringent Regulatory Authority |
| TB | Tuberculosis |
| UN | United Nations |
| UNFPA | United Nations Population Fund |
| UNICEF | United Nations Children's Emergency Fund |
| UNION | International Union Against Tuberculosis and Lung Disease |
| UNITAID | International Drug Purchasing Facility |
| UNOPS | United Nations Office for Project Services |
| USAID | United States Agency for International Development |
| USP | United States Pharmacopeia |
| VPP | Voluntary Pooled Procurement |
| WB | World Bank |
| WHO | World Health Organization |
| WHO-PQ | World Health Organization Prequalification |
| WHO-PQP | World Health Organization Prequalification of Medicines Programme |

# EXECUTIVE SUMMARY

Defining and enforcing quality standards for medicines, diagnostics, and devices involves complex regulatory processes. Many low- and middle-income countries have either weak or absent regulatory systems. As a result, a significant percentage of medicines in circulation in these markets does not meet internationally accepted quality standards and may harm patients. The World Health Organization (WHO) established the Prequalification of Medicines Programme, but it covers only a limited number of products. Unfortunately, for a wide range of essential medicines, no centralized, internationally accepted certification process is in place that could be used as a basis for product prequalification.

This report describes an analysis of options for a pragmatic approach to assure the quality of essential medicines that are procured with donor funding. The analysis is based on a review of surveys and practices in quality assurance (QA) of medicines, interviews of international stakeholders, and recommendations from a stakeholder consensus meeting.

**Toward a Harmonized and Coordinated Pragmatic Approach**

The interviews and document review suggest that—

- Most stakeholders believe that the quality of all products should be evaluated against a standard level of stringency; however, the many barriers to this mean it will not happen for a long time.
- Many organizations do not rely on medicine quality evaluations conducted by others.
- A process must be developed to share QA documents and results, which are generally considered proprietary. Dossiers submitted for registration are not standardized, which makes it difficult to strengthen capacity to evaluate the dossiers.
- The international community must make a more concerted effort to strengthen national medicines regulatory authorities (NMRAs) and country-based (national) procurement centers.
- Leveraging and sharing resources help address limitations in the quantity and quality of technical resources available for pharmaceutical evaluation.
- Decision-making authority for the QA function must be separated from that of the procurement or purchasing function to avoid conflict of interest.
- Interest exists in harmonizing donor policies and approaches to QA of essential medicines and using improved tools to assess manufacturers and wholesalers.

Given the limitations of current approaches (WHO Prequalification of Medicines Programme, WHO-Global Fund Expert Review Panel, stringent and nonstringent NMRA approvals, and reliance on procurement service agencies), considering a pragmatic approach that enhances and optimizes the use of existing mechanisms and resources while building country ownership and regulatory capacity may be most realistic.

Thirty-three participants from seventeen organizations participated in the Joint Stakeholder Meeting on Quality Assurance of Essential Medicines, organized by WHO and the Global Fund

in August 2011.[1] Participants agreed that harmonized, risk-based approaches are being introduced to maximize QA measures; resources and independent technical expertise for pharmaceutical QA are becoming increasingly scarce worldwide; and the WHO Model Quality Assurance System for Procurement Agencies (MQAS) can serve as a basis for an independent qualification system.

Meeting participants recommended the following:
- Continuing to develop a risk-based categorization of essential medicines
- Harmonizing tools to assess procurement agencies' capacities and risks
- Harmonizing quality assurance approaches
- Developing a mechanism to share information

**Toward a Five-year Road Map**

The following initiatives can be developed over the next five years to develop this pragmatic approach:
- Development of risk-based categorization of essential medicines that do not include those related to AIDS, tuberculosis, or malaria
- Harmonization of quality assurance policies
- Harmonization of MQAS-based assessment tools and development of procurement services agencies and a prequalification body for wholesalers
- Phased strengthening of NMRAs' QA capacities
- Information sharing through a website that includes information on manufacturing site inspections planned and completed by WHO and its partners
- Development of a "Common Technical Document" to facilitate and to lower the cost of the registration process, both for NMRAs and for submitting manufacturers

Illustrative overarching activities for each initiative or project include the following:
- Defining the lead organization (champion), which in most cases will be WHO, and key partners from the Interagency Pharmaceutical Coordination group as well as others
- Engaging potential collaborators and establishing working groups
- Preparing a budget and proposals for funding activities
- Identifying potential funding sources
- Preparing and implementing respective work plans
- Conducting broader stakeholder consultations

**Conclusion**

Nongovernmental agencies and procurement services agencies will continue to prequalify the medicines they need that are not already approved through the WHO Prequalification Programme or through stringent regulatory authorities. Assuming increased stringency of

1. World Health Organization and the Global Fund, "Report of Joint Stakeholder Meeting on Quality Assurance of Essential Medicines" (Geneva: the Global Fund, August 30–31, 2011).

product and manufacturer prequalifications, more quality-assured essential medicines will be available for procurement using donor funding.

There is consensus that NMRAs should be doing quality assurance assessments and registering products according to stringent standards and methods; however, with a risk-based approach, capacity building can be achieved while donors gradually decrease dependence on prequalifications conducted by the international community.

If the cost (to donors or to those benefiting economically from improved quality) for implementing the proposed pragmatic, coordinated activities is not fundable, then product quality will only improve at a pace dictated by market dynamics.

# INTRODUCTION

## Problem to be Addressed

Procurement of medicines and medical supplies is one of the most important steps in the implementation of donor-financed health projects. The volume of medical goods procurement has grown significantly over the last decade with the availability of major donor funding and increasing demand associated with prevention and treatment programs for HIV, tuberculosis, and malaria.

Defining and enforcing quality standards for medicines is not trivial. The quality of a pharmaceutical product is assessed against explicit standards and specifications for all characteristics—including purity, strength, packaging, and labeling—which allow the pharmaceutical product to deliver its intended treatment. Manufacturers must ensure that each of their pharmaceutical products complies with quality assurance standards and specifications, at release and throughout its shelf life, according to the requirements of the country of use. Pharmaceutical products that fail to meet required standards and specifications are known as substandard medicines. Counterfeit medicines are pharmaceutical products that are deliberately and fraudulently mislabeled with respect to identity or source; this may apply to both branded and generic products and may designate products with correct ingredients but fake packaging, with wrong ingredients, without active ingredients, or with sufficient active ingredients.[2]

Elaborate regulatory systems protect consumers in developed countries. In contrast, many low- and middle-income countries have weak or no regulatory systems. Rapid assessments performed at national medicines regulatory authorities of 26 African countries over an eight-year period revealed that structures and main functions for medicines regulation existed but were often inadequate and did not form a coherent regulatory system. Common weaknesses included a fragmented legal basis in need of consolidation, weak management structures and processes, and a severe lack of staff and resources. Countries did not have the capacity to control the quality, safety, and efficacy of the medicines circulating in their markets or passing through their territories.[3]

A significant percentage of medicines in circulation in these markets is not meeting internationally accepted quality standards and may harm patients. There are estimates that counterfeit medicines may total more than 30 percent of all medicines sold in Africa.[4] Effects on patients and the economy are difficult to quantify and not cited in public health statistics. Dramatic cases such as diethylene glycol poisoning deaths of children, and vaccination of 60,000

2. World Health Organization, “Substandard and Counterfeit Medicines,” Fact sheet no. 275 (November 2003), http://www.who.int/mediacentre/factsheets/2003/fs275/en/print.html, accessed April 2, 2012.
3. World Health Organization, “Assessment of Medicines Regulatory Systems in sub-Saharan African Countries: An Overview of Findings from 26 Assessment Reports” (Geneva: WHO, 2010).
4. However it is difficult to determine this with certainty, including the relative risks of counterfeits between the public and the private sectors. Most of the literature on counterfeit medicines is the result of investigative journalism, and published product quality surveys refer to detection of counterfeit products from samples obtained in the marketplace; although some surveys include public sector facilities.

people with fake meningitis vaccines during a meningitis epidemic in Niger have been reported.[5] Investigations revealed that the donated meningitis vaccines, which originated in Nigeria, had been substituted with counterfeit product containing no active ingredients. In Togo, over a quarter of donated antimalarial medicines were stolen from the government central medical stores, and then sold in their original packaging in street markets across the country, but under conditions that damaged the quality of the medicines.[6]

Available studies published in scientific journals and project reports have documented product quality problems in as many as 20 Sub-Saharan countries. Problems have been detected with antiretroviral medicines, antimalarials, antibiotics, antidiabetics, antihypertensive medicines, and analgesics.[7][8] Substandard medicines are products whose composition and ingredients do not meet the correct scientific specifications and are consequently ineffective and often dangerous to the patients.[9] Since the financial assistance provided by donors is normally to poor or developing countries, a significant proportion of the funds used for medicines may be creating a public health risk in the ineffective and unsafe treatment of patients as well as being wasted. It is for both these reasons that appropriate QA procedures must be implemented, and organizations involved in medicines procurement using donor funds must establish effective medicines quality assurance programs.

The World Health Organization (WHO) established the Prequalification of Medicines Programme (PQP) to assist resource-limited countries in procuring quality-assured pharmaceuticals, but this program covers only a limited range of products. Unfortunately, for a wide range of essential medicines, there is no centralized, internationally accepted certification process in place to be used as a basis for prequalification of products. Country-level procurement agencies have three basic options to qualify bidders:

- Relying on the capacity of national regulatory agencies, which is not always a good option since most developing country regulatory agencies have difficulty controlling their markets;

- Relying on evaluations done by "stringent" regulatory authorities (basically those in the developed markets) and buying only products approved by those agencies; or

- Setting up their own quality assurance procedures in line with international standards, which requires a level of resources and capacity that is unlikely to be available in low-income countries.

---

5. R. Cockburn, et al., "The Global Threat of Counterfeit Drugs: Why Industry and Governments Must Communicate the Dangers," *PLoS Med* 2 no. 4 (2005), e100,doi:10.1371/journal.pmed.0020100.
6. R. Bate, Africa's Epidemic of Disappearing Medicines, http://www.foreignpolicy.com/articles/2011/01/11/africas_epidemic_of_disappearing_medicine?page=0,1, accessed January 11, 2011.
7. A. A. Amin and G. O. Kokwaro, "Antimalarial Drug Quality in Africa," *J Clin Pharm Ther* 32, no. 5 (2007): 429–40, doi:10.1111/j.1365-2710.2007.00847.x.
8. J. Primo-Carpenter and M. McGinnis, "Matrix of Drug Quality Reports in USAID-assisted Countries," prepared by the U,S, Pharmacopeia Drug Quality and Information Program, Rockville, MD (2006).
9. http://www.who.int/mediacentre/factsheets/2003/fs275/en/

Donor technical support has primarily been focused on assuring quality of medicines for prevention and treatment of HIV/AIDS (including some medicines to treat opportunistic infections associated with HIV/AIDS), tuberculosis, and malaria (ATM), but donors are now increasingly financing procurement of other essential medicines.

## Objectives and Methodology

### *Objectives*

The World Bank, in collaboration with the USAID-funded Strengthening Pharmaceutical Systems Program (SPS), commissioned an analysis of options for a pragmatic approach to assure the quality of essential medicines procured with donor funding. The specific objectives were the following:

- Analyze options for approaches to assure the quality of essential medicines not addressed by existing donor agencies' requirements;

- Propose a harmonized pragmatic interagency approach that resource-limited countries can use when procuring with donor funds; and

- Describe a five-year roadmap to design, adopt, and implement the recommended harmonized interagency approach.

### *Methodology*

This report is based on a desktop review of publicly available and accessible reports on surveys and current practices in quality assurance of medicines conducted by key international organizations; interviews of key international stakeholders; and the discussion and recommendations of the World Health Organization and the Global Fund Joint Stakeholder meeting in Geneva in August 2011.

The consultants conducted an online search and retrieved study reports and slide presentations; obtained electronic or hard copies of available documents from key interviewees; and reviewed relevant studies on quality assurance of pharmaceuticals other than antiretroviral, antituberculosis, and antimalarial medicines that were commissioned by the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund), the Stop TB Partnership/Global Drug Facility, the United Nations Population Fund (UNFPA), WHO, the Directorate-General of the European Commission's Humanitarian Aid (DG ECHO), the World Bank, and the United States Agency for International Development (USAID) (see references).

The consultants conducted telephone and e-mail interviews with representatives of key stakeholder organizations during the month of July 2011. Of the 19 requests for interviews, 15 organizations participated, and 4 were not available (annex 1). Annex 2 provides the list of questions that guided the key informant interviews.

On behalf of the World Bank and the Strengthening Pharmaceutical Systems Program, the consultants presented a summary of key findings and a pragmatic approach integrating the various existing strategies to assuring quality of medicines for procurement with donor funds, at the WHO and Global Fund Joint Stakeholder Meeting on Quality Assurance for Essential Medicines, held at the Chateau de Penthes in Geneva on August 30 and 31, 2011.[10]

10. "WHO and the Global Fund Joint Stakeholder Meeting Report, Geneva," August 30–31, 2011.

# CURRENTLY AVAILABLE SOLUTIONS

## Quality Assurance Policies and Quality Assurance Systems

Donor policies requiring compliance with stringent standards for assuring the quality of medicines procured with their funds have predominantly focused on medicines for treating HIV/AIDS, tuberculosis, and malaria. The Global Fund is a major donor organization with an effective policy for assuring the quality of these priority medicines as well as in-house technical and pharmaceutical competency. Given the importance of medicines to treat opportunistic infections (OIs), there is strong interest in extending the Global Fund's stringent policy on quality of antiretroviral, antituberculosis and antimalarial ("ATM medicines") to cover these and other "non-ATM medicines".

Some donors delegate quality assurance responsibility and expertise to their recipients or to contractors. For example, while the U.S. Agency for International Development (USAID) has a policy based on U.S. Food and Drug Administration (FDA) approval, quality assurance is largely delegated to contractors that implement USAID's supply chain projects, for example, USAID/Deliver and Supply Chain Management System. The Directorate-General of the European Commission for Humanitarian Aid (DG ECHO), the UK Department for International Development (DFID), and Danida, on the other hand, appear to hold the fund recipients responsible for assuring the quality of medicines that are procured with donated funds.[11]

Table 1 provides a summary of five basic approaches for assuring quality of medicines procured with donor funds.

11. J-M. Caudron and C. Pouget, "Analysis of Quality Assurance Policies of Global Fund Partners for the Procurement of Pharmaceutical Products Other than ARVs, Anti-TB, and Antimalarial Medicines ("non-ATM Medicines"), submitted to the Global Fund, Geneva, 2009.

**Table 1.Summary of Types of Essential Medicines Covered by Five Basic Approaches and the Donors and Implementing Organizations Relying on Each Approach**

| Quality Assurance approach | WHO Prequalification Programme (PQP) | Global Fund-WHO Expert Review Panel (ERP) | Stringent regulatory authority (SRA) approval | National medicines regulatory authority approval | Procurement service agency quality assurance system |
|---|---|---|---|---|---|
| Products covered and number of approved products | HIV/AIDS<br>TB<br>Malaria<br>Influenza<br>Reproductive health<br><br>WHO-prequalified<br>253 total:<br>190 HIV/AIDS<br>7 influenza<br>17 malaria<br>8 repro health<br>31 TB | HIV/AIDS<br>TB<br>Malaria<br><br>ERP-approved products:<br>10 HIV/AIDS<br>11 TB<br>1 Malaria<br><br>UNFPA technical committee approved:<br>16 reproductive health | HIV/AIDS<br>TB<br>Malaria<br>Other essential medicines<br>Global Fund–listed:<br>192 HIV/AIDS<br>25 TB<br>12 Malaria | All WHO-listed essential medicines | Medicines approved through WHO-PQP, SRA, and ERP for all Voluntary Pooled Procurement (VPP) agencies; and WHO-listed essential medicines approved through internal QA procedures |
| Donors and procurement service agencies using approach | Global Fund<br>Stop TB GDF<br>PFSCM/SCMS<br>JSI/Deliver (PMI)<br>UNFPA<br>UNICEF<br>MSF | Global Fund<br>Stop TB GDF<br>WHO-PQP<br>UNFPA and UNICEF have designated “internal technical review committee”<br>MSF | Global Fund<br>Stop TB GDF<br>PFSCM (PEPFAR/ SCMS)<br>JSI/Deliver (PMI)<br>UNFPA<br>UNICEF<br>MSF | Global Fund no longer allows this mechanism (formerly called “category C items”) | PFSCM (for Global Fund VPP)<br>GTZ<br>UNICEF<br>IDA<br>Mission-pharma<br>Action Medeor<br>MSF (internal technical committee)<br>ECHO humanitarian procurement centres |

*Source: Authors.*
*Note:* ECHO: European Commission Humanitarian Organization; GDF: Global Drug Facility; GTZ: Deutsche Gessellschaft fur Technische Zusammenarbeit (German Technical Cooperation); IDA = International Dispensary Association; John Snow, Inc.; MSF: Medécins sans Frontières; PEPFAR: US President’s Emergency Plan for AIDS Relief; PFSCM: Partnership for Supply Chain Management; PMI: US President’s Malaria Initiative; PQP: Prequalification Programme; SCMS: Supply Chain Management System; UNICEF: United Nations Children’s Fund; UNFPA: United Nations Population Fund; WHO: World Health Organization.
*Note:* As of May 31, 2011, for HIV and TB products; as of November 5, 2010, for malaria products. Only “B” products were counted, http://www.theglobal fund.org. As of May 31, 2011, for HIV and TB products; as of November 5, 2010. for malaria products, http://www.theglobalfund.org.

### *National medicines regulatory authority approvals for quality assurance*

Some national medicines regulatory authorities are regarded as stringent for their capacity to assess and control the quality of medicinal products in their respective markets. The Global Fund, supported by WHO, has identified a number of regulatory agencies as stringent, based on their participation in the International Conference on Harmonisation (ICH), and on formal agreements of non-ICH participating countries with ICH members.[12] The US Agency for International Development (USAID) defines a stringent regulatory agency as one that has standards and procedures similar to those of the FDA.[13] The USAID definition includes only those European regulatory agencies whose home countries were members of the European Union prior to 1995, as well as the European Medicines Agency (EMA) in its role as evaluation agency for the European Union. This definition is similar to the Global Fund's definition of a stringent regulatory agency.

Although other NMRAs may consider themselves to be stringent regulatory agencies, they have not been included in the above definitions. According to WHO, only 20 percent of the 193 member states of the United Nations are recognized as having mature medicines regulatory systems.[14] As indicated previously, many low- and middle-income countries have weak regulatory systems, and in some cases, none at all. Although structures and main functions for medicines regulation exist, they are often inadequate. Common weaknesses include a fragmented legal basis in need of updating and consolidation, weak management structures and processes, and a severe lack of staff and resources.[15]

### *World Health Organization Prequalification of Medicines Programme*

The WHO Prequalification Programme (PQP) was established in 2001 to ensure that medicines procured by procurement agencies meet acceptable standards of safety, efficacy, and quality. Originally focused on antiretroviral, antituberculosis, and antimalarial medicines, it has been extended to cover medicines for influenza and reproductive health, as well as zinc for management of acute diarrhea in children. As of March 2011, WHO had prequalified 253 products (190 for HIV/AIDS, 31 for tuberculosis, 17 for malaria, 8 for reproductive health, and 7 for influenza).

The PQP process includes five components: (1) invitation to manufacturers to submit an expression of interest (EOI) for product evaluation; (2) manufacturer dossier submission of a comprehensive set of data about the quality, safety, and efficacy of the product for evaluation; (3) assessment of submitted data by WHO staff and experts from national medicines regulatory

12. http://www.stoptb.org/assets/documents/gdf/drugsupply/List_of_Countries_SRA.pdf.
13. USAID.ADS 312, "Additional Help Document.GH/OHA/SCMS 'Restricted Commodity' Approval of Pharmaceuticals," available at http://www.usaid.gov/our_work/global_health/aids/TechAreas/treatment/info_approval.pdf
14. Aedes Foundation, "Medicine Themes Day Report," Brussels, September 21–23, 2010.
15.WHO, "Assessment of Medicines," 2010.

authorities worldwide; (4) inspection by a team of inspectors to verify manufacturing site compliance with good manufacturing practices (GMPs) for both finished pharmaceutical product and its active pharmaceutical ingredients (APIs), and to verify that contract research organizations involved in clinical studies of the submitted product comply with good clinical practice (GCP) and good laboratory practice (GLP); and (5) decision to add the product to the WHO list of prequalified medicinal products if the specified product requirements are met, and the associated manufacturing sites and contract research organizations are compliant with WHO standards. Studies suggest that WHO prequalification is an effective quality assurance system for applicable medicines: sampling and testing of selected antimalarial medicines collected in six African countries showed that less than 4 percent of total samples of WHO-prequalified products failed quality control tests (a ten-fold lower failure rate compared with other products).[16] An earlier study on the quality of antiretroviral medicines did not reflect this; it reported an overall failure rate of 1.8 percent of 395 samples collected (three of the failed samples were WHO-prequalified and four were non–WHO-prequalified); over one-half of all sampled products were WHO-prequalified, most of the products were registered by the corresponding national medicines regulatory authority.[17]

### *The Global Fund's Expert Review Panel mechanism*

To facilitate procurement of priority medicines that have fewer than three WHO-prequalified or SRA-authorized suppliers, the Global Fund established the Expert Review Panel (ERP) mechanism as a temporary measure while the manufacturer or supplier is awaiting prequalification or product marketing approval.[18] The ERP is an independent technical body established and administered with WHO guidance. It is composed of external technical experts in the pharmaceutical and medical fields, including members with SRA work experience. The ERP reviews potential risks and benefits associated with the use of finished pharmaceutical products that are not yet WHO-prequalified or SRA-authorized and advises the Global Fund on its decision on whether or not to allow grant funds to be used to procure finished pharmaceutical products. The two key prerequisites for ERP review eligibility are the following: (1) the supplier's application for WHO prequalification or application for SRA assessment and marketing approval has been accepted, and (2) the manufacturing site is GMP-compliant with SRA, WHO, or PIC/S standards. Eligibility was recently expanded to include finished pharmaceutical products that are included in standard treatment guidelines but not listed in a WHO-PQP invitation for an expression of interest to prequalify a specific product.[19]

16. World Health Organization, "Survey of the Quality of Selected Antimalarial Medicines Circulating in Six Countries of sub-Saharan Africa" (Geneva: WHO, 2011), WHO/EMP/QSM/2011.1.
17. World Health Organization, "Survey of the Quality of Antiretroviral Medicines in Selected African Countries" (Geneva: WHO, 2007), WHO/PSM/QSM/2007.9.
18. The Global Fund, "Quality Assurance Policy for Pharmaceutical Products: The Expert Review Panel Mechanism," PowerPoint presentation, July 2010, http://www.theglobalfund.org.
19. The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme, jointly known as PIC/S, are two international cooperation instruments for member countries and pharmaceutical inspection authorities to collaborate on good manufacturing practice standards and their compliance. There are about 40 countries participating in PIC/S; http://www.picscheme.org.

ERP-endorsed product eligibility for procurement with grant funds is limited to a maximum of 12 months or until the product is WHO-prequalified or SRA authorized, whichever is earlier. It is possible to extend this period of eligibility up to an additional 12 months if the product is still pending WHO prequalification or SRA authorization.

The ERP categorizes the reviewed products into four categories, on the basis of the following: (1) GMP status of the manufacturing site, (2) finished pharmaceutical product (FPP) manufacturing process and FPP specification, (3) stability data, (4) evidence of therapeutic equivalence, and (5) API source and API quality. Categories 1 and 2 may be considered for time-limited procurement. Products classified in category 3 may be considered for procurement only if there is no other option and the risk of not treating the disease is higher than the risk of using the product. Products classified under category 4 may not be considered for procurement under any circumstances. The ERP has assessed 210 products as of mid-2011, and approved at least 22 products (10 antiretrovirals, 11 antituberculosis and 1 antimalarial). The high level of expertise assembled in the ERP panel is neither readily available nor easily replicated by other organizations; the cost of the reviews is moderate for one-off, abbreviated assessments.

### *International and national procurement service agencies and wholesalers*

Table 2 lists selected United Nations organizations that operate procurement operations and services for low- and middle-income countries. It also identifies selected major international for-profit and not-for-profit agencies that supply developing countries. Details on their operations may be obtained from their corresponding websites.

**Table 2. Selected International Organizations that Conduct Pharmaceutical Procurement Operations and Provide Services to Low- and Middle-income Countries**

| United Nations organizations | Selected private procurement and wholesalers |
|---|---|
| Pan American Health Organization (PAHO)<br>United Nations Children's Fund (UNICEF)<br>United Nations Office for Project Services (UNOPS)<br>United Nations Population Fund (UNFPA)<br>World Health Organization (WHO—houses and administers the Stop TB Partnership/Global Drug Facility) | Action Medeor [www.medeor.de]<br>Imres [www.imres.nl]<br>International Dispensary Association [www.ida.nl]<br>Missionpharma [www.missionpharma.com]<br>GIZ (formerly GTZ) [www.giz.de]<br>Donors supply project implementation:<br>JSI [USAID/Deliver Project] [www.deliver.jsi.com]<br>Partnership for Supply Chain Management (PFSCM; two major projects are SCMS and VPP) [www.pfscm.org]<br>Medécins sans Frontières (MSF) for its country programs [www.msf.org] |

*Source: Authors.*

The US President's Malaria Initiative (PMI) and the President's Emergency Plan for AIDS Relief (PEPFAR) rely on their contractors' systems to support procurement of quality-assured pharmaceuticals. They also require that HIV/AIDS medicines be approved by the U.S. Food and Drug Administration. USAID has recently issued guidance on requirements for pharmaceuticals to be procured for programs including malaria, tuberculosis, neglected tropical diseases,

emerging pandemic threats, and maternal and child health, as well as for diagnostic test kits. For situations that may require procurement of non–FDA–approved products, a waiver process is followed, requiring documentation of safety, efficacy, and quality under standards similar to those of the FDA.

### *John Snow, Inc.*

The USAID/Deliver Project, implemented by John Snow, Inc., assists health supply chains in the development of a range of essential health commodities for family planning, malaria, avian influenza, HIV and AIDS–related medicines and supplies, laboratory reagents and supplies, and essential medicines. It supplies products procured through the project's own procurement system for USAID or through USAID's central procurement system. Quality assurance of oral contraceptives and intrauterine devices (IUDs) are managed by Family Health International (FHI).

### *Partnership for Supply Chain Management*

The Partnership for Supply Chain Management (PFSCM) is a nonprofit organization established in 2005 by JSI Research & Training Institute, Inc., and Management Sciences for Health (MSH).[20] It implements USAID's Supply Chain Management System (SCMS) project and the Global Fund's Voluntary Pooled Procurement (VPP) mechanism. SCMS was established to ensure a reliable, cost-effective, and secure supply of high-quality medicines and health products for HIV and AIDS prevention, care, and treatment. SCMS procures and distributes essential medicines, HIV test kits, laboratory supplies, and other products for HIV/AIDS programs; provides technical assistance to transform existing supply chains; and collaborates with in-country and global partners to coordinate efforts [www.pfscm.org].

The Voluntary Pooled Procurement was established by the Global Fund as a procurement support service (along with capacity-building services) for its principal recipients to ensure a cost-effective and efficient procurement process. VPP manages and coordinates procurement for antiretroviral medicines, rapid diagnostic kits for HIV, artemisinin-based combination therapies, long-lasting insecticide treated nets, rapid diagnostic tests for malaria, and noncore VPP products such as medicines that treat opportunistic infections or sexually transmitted infections, diagnostic laboratory supplies, postexposure prophylaxis kits, condoms, and tablets for retreatment of insecticide-treated mosquito nets. In the first 18 months of operation, more than 74 grants from 40 countries placed orders through the VPP.[21]

---

20. The team is composed of 13 organizations, including Booz Allen Hamilton (USA), Crown Agents (USA and UK), i+solutions (Netherlands), JSI Research & Training Institute, Inc. (USA), Management Sciences for Health (USA), the Manoff Group (USA), MAP International (USA), North-West University (South Africa), Northrop Grumman (USA), RTT (South Africa), UPS Supply Chain Solutions (USA), Voxiva (USA), 3i Infotech (USA and India).

21. The Global Fund, "Procurement Support Services Progress Report: June 2009 – Dec. 2010" (Geneva: the Global Fund, March 2011).

PFSCM assures the quality of the SCMS products that it procures through prequalification of its suppliers and tests products for compliance with specifications. PFSCM also helps host country organizations create standards and systems that help ensure quality. North-West University in South Africa is a WHO-prequalified laboratory accredited by International Organization for Standardization (ISO) 17025 standards, which provides laboratory testing support to PFSCM. The university offers risk-based quality assurance analysis, physical examination, sampling and testing to ensure pharmaceutical quality. In addition, SCMS works with the Pharm R&D Lab at the Muhimbili University of Health and Allied Sciences in Tanzania to perform product quality screening assessments. For VPP, PFSCM uses the appropriate quality assurance standards recommended by WHO and applied by the Global Fund.

### *ECHO humanitarian procurement centers*

The European Community Humanitarian Office (ECHO) is the largest humanitarian aid donor.[22] ECHO provides assistance by financing United Nations and other international organizations, and nongovernmental organizations (NGOs) that possess administrative and logistical capacities. In most countries receiving ECHO support, health may comprise between 30 to 50 percent of the spending budget; between 20 to 30 percent of this amount goes to purchase and management of medicines and medical supplies, equivalent to between 40 and 90 million euros.

Medicines and medical supplies are obtained through international and local procurement, and through a Humanitarian Procurement Centre (HPC), as well as combinations of these methods. ECHO has a program that prequalifies wholesalers, largely based on financial criteria including internal control systems, and accounting and procurement rules to assist its partners. Procurement organizations that apply for HPC status and meet ECHO criteria are designated as Humanitarian Procurement Centres.[23] ECHO recognizes the importance of quality of medicines and supplies but lacks the resources to assure quality; consequently it relies on partners to assume responsibility for quality assurance of the procured pharmaceuticals. To build quality assurance capacity of its partners, ECHO commissioned a review of quality assurance mechanisms[24] and the publication of guidelines[25] for quality assurance of medicines and supplies in humanitarian aid. Prequalification and use of the WHO Model Quality Assurance System (MQAS) are major elements in these guidelines (see Principles of Prequalification listed in annex 3 and in the ECHO guidelines).

---

22. V. Pommato and C. Schuftan, "Review of Quality Assurance (QA) Mechanisms for Medicines and Medical Supplies in Humanitarian Aid," concept paper submitted to the European Commission's Directorate –General for Humanitarian Aid (DG ECHO), Aachen, Germany: GFE Consulting Worldwide, June 2006.
23. ECHO HPCs include Medécins sans Frontières (MSF Logistique), France; Ex-Transfer Relief Supplies and Services (formerly known as Transfer, now called MSF Supply), Belgium; Centrale Humanitaire Medico-Pharmaceutique (CHMP), France; International Dispensary Association (IDA Foundation), Netherlands; Association Regionaled'Approvisionnement en Medicaments Essentiels (ASRAMES), Democratic Republic of Congo; Logistics and Resource Mobilisation Department of the International Federation of Red Cross and Red Crescent Societies (LRMD), Switzerland; United Nations Children's Fund, Supply Division (UNICEF Supply Division), Denmark; Inter-Agency Procurement Services Office of the United Nations Development Programme (IAPSO), Denmark; Deutsches Medikamenten-Hilfswerk Action Medeor (Action Medeor), Germany; and Operational NGO Food Security Network Euron Aid (EuronAid), Netherlands.
24. V. Pommato and C. Schuftan, "Review of Quality Assurance," June 2006.
25. Ibid.

### *Assessment tools for quality assurance in procurement agencies and wholesalers*

A procurement service agency is an organization that purchases pharmaceutical products, vaccines, or other health sector goods. A procurement service agency (PSAs) may be a nonprofit, nongovernmental, or UN organization. A PSA usually purchases from manufacturers—the companies that produce, package, repackage, label, or relabel pharmaceutical products. Wholesalers are dealers that purchase supplies from a manufacturer and may store the goods before reselling and delivering them to the final buyers. Some procurement service agencies may also be wholesalers.

#### *WHO Model Quality Assurance System (MQAS)*

Recognizing the need to assist procurement agencies and wholesalers in developing and implementing quality assurance systems for prequalification, purchasing, storage, and distribution of pharmaceuticals, WHO published a model quality assurance system (MQAS) in 2007.[26] This included guidelines to harmonize evaluation of data and information on products as part of the prequalification procedure, and unified standards for inspection of manufacturers and suppliers to assess compliance with GMP.

The MQAS consists of six modules covering general requirements for procurement agencies; prequalification; purchasing; receipt and storage of purchased products; distribution; and reassessment. Specifically, module II on prequalification of products provides recommendations that procurement agencies should implement when evaluating their product needs and assessing both the products offered as well as the manufacturing and supply arrangements. The MQAS publication also provides illustrative forms, including a pharmaceutical product questionnaire (box 1), an example of a standard operating procedure for screening and assessing product information, a technical questionnaire for pharmaceutical manufacturers, and examples of standard operating procedures for planning and preparation of inspections.

26. World Health Organization. "Interagency Guidelines: A Model Quality Assurance System for Procurement Agencies. Recommendations for Quality Assurance Systems Focusing on Prequalification of Products and Manufacturers, Purchasing, Storage and Distribution of Pharmaceutical Products," (2007), previously published as annex 6 of the 40th report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations (Technical Report Series no. 937).

**Box 1. Sections in the Model Pharmaceutical Product Questionnaire**

Product identification
Manufacturer of the product
Supplier identification
Regulatory situation (licensing status) in the country of manufacture
Regulatory situation (licensing status) in other countries
Finished product specifications
Stability
Label and insert information
Samples
Therapeutic equivalence
Active pharmaceutical ingredient(s) (APIs)
Commitment

*Source: WHO 2007*

The MQAS is widely recognized as the basis for qualification of procurement services. Various agencies (such as UNICEF, International Committee of the Red Cross [ICRC], and MSF) have agreed to use a standardized Interagency Pharmaceutical Product Questionnaire, which is a first step to harmonization of quality assurance procedures. Usage of this questionnaire, however, is not standardized but rather left to each agency based on its own internal capacity, policies, and procedures. Over the past five years, several organizations have independently developed procurement service agency assessment tools that are also based on the MQAS.

### *USAID Office for Disaster Assistance (OFDA) Wholesaler Precertification Project assessment tool*

The USAID Office of U.S. Foreign Disaster Assistance (OFDA), through the Rational Pharmaceutical Management Plus Program (RPM Plus), requested that Management Sciences for Health (MSH) develop a framework and process for precertification of pharmaceutical wholesalers. The goal was to develop criteria, justification, and draft procedures that OFDA could use to precertify pharmaceutical wholesalers as a source for off-patent (FDA-approved and non-FDA–approved) essential medicines and supplies for emergency purchase by USAID-funded private voluntary organizations in developing countries.

With assistance from WHO, ECHO, and several international and country-based wholesaler organizations,[27] RPM Plus developed, tested, and refined draft wholesaler precertification screening and site inspection tools. Because of the need to obtain supplies quickly in disaster situations, the report suggested implementation of a pragmatic and risk-based system whereby wholesalers are rated according to ability to meet transparent criteria and international prequalification standards,[28] and where selection is based on rating. For example, if three rating levels were established, the highest ranked wholesaler would be contacted first (highest rated for

27. N. Heltzer, "USAID Office of Disaster Assistance Wholesaler Precertification Project," submitted to the U.S. Agency for International Development by the Rational Pharmaceutical Management Plus Program. (Arlington, VA: Management Sciences for Health, 2007).
28. World Health Organization, "A Model Quality Assurance System for Procurement Agencies," WHO Technical Report Series no. 937, annex 6 (2006).

criteria associated with lowest risk of substandard medicine quality), then the next level–ranked wholesaler, and finally the lowest level–ranked supplier.

### *The World Bank Procurement Service Capacity and risk assessment tool*

In 2008, the World Bank contracted MSH to develop a tool to assess government procurement agency capacity for potential certification to conduct donor-supported procurement of medicines and other health goods.[29] The tool was designed to allow for a systematic assessment of the physical premises and all activities specific to a full-service procurement office. Its format includes eight modules with two of the modules further divided into submodules.

The procurement capacity tool assesses compliance with 160 standards based on the WHO MQAS plus 3 standards exclusive to World Bank procurement. Of the 160 standards, 30 including the 3 World Bank standards are considered mandatory; this means that full compliance of these standards (either during the assessment or subsequently based on a capacity-building action plan) is required for a PSA to undertake procurement for national or international tendering from advertisement up to evaluation and contract award. For the remaining standards, a variable scoring system was proposed that allows for flexibility in determining PSA eligibility to undertake procurements. The tool was applied to assess the Tamil Nadu Medical Services Corporation in Chennai, India.

The World Bank–commissioned tool was subsequently expanded to include a module to assess distribution capacity and service contracting capacity in order to assess procurement service capacity in 10 states in India in 2009.[30] The UK Department for International Development in India planned to address the identified procurement service capacity deficits under a bilateral capacity-building project.

### *The PFSCM wholesaler assessment tool*

PFSCM modified the original MSH checklist document for prequalification of wholesalers. The current version includes a point or grading system that informs PFSCM re-audit frequency as well as its sampling strategy (see annex 4). PFSCM is using the revised tool to assign a grade to all wholesalers as they undergo a periodic staggered two-year re-evaluation. To date, USAID has approved six procurement service agencies and wholesalers assessed by PFSCM: Action Medeor, Amstelfarma, Imres, International Dispensary Association (IDA) Foundation, Medical Export Group (MEG), and Missionpharma.[31] Most recently the tool has been adapted to assess and prequalify wholesalers based in developing countries.

29. N. Heltzer, A. Shrivastav, and M. Clark. 2008. "Developing a Certification System for Procurement Agencies in India," submitted to the World Bank by the Center for Pharmaceutical Management (Arlington, VA: Management Sciences for Health, 2008).
30. M. Clark and A. Shrivastav, "Assessment of Procurement Capacity in 10 States in India," submitted to the UK Department for International Development by the Center for Pharmaceutical Management (Arlington, VA: Management Sciences for Health, 2009).
31. USAID.ADS 312, "Additional Help Document.GH/OHA/SCMS."

### *The Belgian Institute of Tropical Medicine QUAMED assessment tool*

The Institute of Tropical Medicine in Belgium is implementing the QUAMED initiative, funded by the Belgian Directorate General for Development Cooperation. QUAMED aims to improve the technical capacity of organizations involved in the procurement of essential medicines for low- and middle-income countries. Its ultimate objective is to improve access to quality medicines by supporting partner organizations in strengthening their respective product quality–assurance procedures. It has set up a network of Northern and Southern actors active in procurement of essential medicines in or for developing countries, aimed at sharing and rationalizing the use of information and resources. QUAMED supports its partners in developing and using tools and data analyses for the evaluation of pharmaceutical products and suppliers.

QUAMED activities include the organization and facilitation of training sessions on topics related to pharmaceutical quality, the preparation or support (coaching) of audits at pharmaceutical manufacturer or supplier levels, support in assessment of specific pharmaceutical dossiers, the development of standardized procedures and tools for the evaluation of pharmaceutical sources and suppliers, the facilitation of access to international standards (pharmacopoeias, WHO technical report series, and ICH and EU guidelines) and to sources of official information (stringent regulatory authorities' websites). QUAMED has also set up a database where validated information (sources of essential medicines) is available to the platform on an ongoing basis [http://www.quamed.org].

Based on the MQAS, QUAMED conducts its assessments with a rating system comprising 350 questions to identify gaps in five major areas, including regulatory information, quality assurance system, qualification of sources, good distribution practices, and monitoring. Specialized expertise in pharmaceutical quality assurance is needed for proper use of the QUAMED assessment tool.[32]

### *The United States Pharmacopeia Promoting Quality of Medicines (PQM) Program*

The United States Pharmacopeia (USP) Promoting the Quality of Medicines (PQM) Program[33] is a USAID-funded mechanism to help ensure the quality, safety, and efficacy of medicines essential to USAID priority diseases, particularly malaria, HIV/AIDS, and tuberculosis. Since 2009, building on previous cooperative agreements with USAID,[34] USP/PQM works to (1) strengthen quality assurance (QA) and quality control systems, (2) increase the supply of quality-assured medicines, (3) combat the availability of substandard and counterfeit medicines, and provide technical leadership and global advocacy. PQM develops regional capacity by establishing regional QA centers of excellence, strengthening regional networks among national laboratories, and developing web-based communications.

---

32. "WHO and the Global Fund Joint Stakeholder Meeting Report," Geneva, August 30–31, 2011.
33. USAID, "Growing Threat of Substandard and Counterfeit Medicines in Developing Countries," press release addressed by New USAID-USP Cooperative Agreement. October 26, 2009, http://www.usaid.gov/press/releases/2009/pr091026_1.html.
34. United States Pharmacopeia Drug Quality and Information Program and Collaborators. "Ensuring the Quality of Medicines in Resource-limited Countries: An Operational Guide." Rockville, Md: the United States Pharmacopeial Convention, 2007; www.usp.org/worldwide/dqi/resources/technicalReports.

A key activity involves developing sustainable Medicines Quality Monitoring (MQM) programs in Africa, Asia, Eastern Europe, and Latin America and the Caribbean. PQM provides guidelines for countries to use in designing protocol for collecting and testing samples of essential medicines in their markets. Its online Medicines Quality Database currently contains the results of MQM activities coordinated by PQM and local stakeholders and national authorities in 11 countries of Africa (Ghana and Kenya), Asia (Cambodia, Lao People's Democratic Republic, Philippines. Thailand, and Vietnam), and South America (Colombia, Ecuador, Guyana, and Peru).

### *Comparison of QA policies of selected organizations*

Table 3 provides a comparative listing of QA policies, standards, and assessment tools implemented by selected organizations, including WHO, donors, procurement service agencies, and quality assurance technical support providers.

**Table 3. Comparison of Selected Donors', Procurement Service Agencies', and Quality Assurance Organizations' QA Policy, Standards, and Assessment Tools**

| Organization | Policy | Standards | Assessment Tool |
|---|---|---|---|
| WHO | WHO prequalification | MQAS-based | Illustrative forms |
| Global Fund | WHO prequalification; stringent regulatory authority approval; Expert Review Panel recommendation | MQAS-based (WHO Prequalification of Medicines Programme) | n.a. |
| ECHO | QA guidelines based on prequalification and MQAS have been developed, but 10 humanitarian procurement centres selected on basis of financial and organizational sustainability | Quality assurance method not assessed | None |
| World Bank | Prequalification of bidders (not products) | Health goods procurement guidelines | MQAS-based (developed for use in India) |
| USAID | U.S. FDA or other stringent regulatory authority approval; WHO manufacturer and product prequalification; UNICEF; PFSCM/SCMS procurement service agency prequalification. Approval of source, origin, and nationality waiver requires information attesting to safety and quality of product, or that it meets the standards of U.S. FDA or other controlling US authority. | U.S. FDA approval-based<br>US source and origin GMP<br>Good storage and distribution practices | PFSCM/SCMS MQAS-based tool<br>USAID/OFDA MQAS-based draft tools |
| DFID | Not known | MQAS-based | World Bank MQAS-based |
| Procurement service agencies (including UN agencies, nonprofits, and commercial operations) | Source of funding (donor) requirements | Many agencies using a modified MQAS-based on their company policies | Proprietary, most considered consistent with MQAS |
| Institute for Tropical Medicine, Antwerp, Belgium QUAMED Project | n.a. | MQAS-based | QUAMED MQAS-based |
| United States Pharmacopeial Convention USAID/Promoting Quality of Medicines (PQM) Program | n.a. | Official standard-setting organization in the United States for medicines and other health care goods MQAS-based | Sample forms and questionnaires in an operational guide for ensuring medicines' quality in resource-limited countries |

*Source: Authors. Note:* ECHO = European Commission's Humanitarian Aid Department; DFID = Department for International Development; MQAS = Model Quality Assurance System; PFSCM = Partnership for Supply Chain Management; SCMS = Supply Chain Management System; USAID = U.S. Agency for International Development; WHO = World Health Organization; n.a. = not applicable.

# OPTIONS FOR THE WAY FORWARD

## Advantages and Limitations of Current Approaches

Table 4 summarizes advantages and limitations of the existing quality assurance approaches. It compares length of time taken for review of documentation, including technical dossiers; acceptance by stakeholders; degree of country ownership; and cost or technical resource requirements, among others. Annex 5 provides a detailed summary of findings from interviews and selected document reviews.

To assure the quality of non-ATM and other essential medicines, one might consider increased use of selected or individual mechanisms or develop an approach that optimizes the use of existing mechanisms and country ownership for medicines' quality assurance. Options might include:

1. Expanding the WHO Prequalification of Medicines Programme

2. Expanding the use of the ERP mechanism

3. Continuing to rely on NMRA approval, both SRA and non-SRA

4. Relying on (international or national) PSAs

However, given the limitations identified for each of these approaches, it may be more feasible to consider an approach that enhances and optimizes the use of all existing mechanisms and resources while building country ownership and regulatory capacity (as the aspirational and long-term goal).

**Table 4. Length of Time for Evaluation, Advantages and Limitations of Current Medicines' Quality Assurance Approaches**

| Quality Assurance approach | WHO Prequalification Programme (PQP) | Global Fund-WHO Expert Review Panel (ERP) | Stringent regulatory authority (SRA) approval | National medicines regulatory authority | Procurement service agency quality assurance system |
|---|---|---|---|---|---|
| Length of time for review | Median times (2010): 4.3 months (innovator products); 31.6 months (generic products)[35] | 6–8 weeks | 6 months (priority review) to 16 months (standard)[36] | Variable, usually long overall time frames (3 months to 5 years) [37] | Not reported; continuous process |
| Features | Evaluation of antiretroviral (ARV) and antimalarial products | Temporary measure to fill gaps when fewer than three WHO-prequalified suppliers.<br>Other organizations expressed interest in participating in harmonized ERP procedure, due to limited number of very specialized technical expertise. | Quality assurance approach accepted by all.<br>Some SRAs already contributing with accelerated or conditional approvals (U.S. FDA) or European Union "Article 58 opinions" (EMA).[38] | Some PSAs would accept NMRA approvals if product is needed and if there are no approvals by WHO-PQP, SRA, or ERP, but if also based on own procedures.<br>Moving to SRA status is a desirable long-term goal for all NMRAs. | All PSAs indicated they follow internal quality assurance guidelines before procuring.<br>All accept WHO-PQP, SRA, and ERP mechanisms.<br>Informal group of PSAs already share some QA materials when prequalifying a supplier's product.<br>Method allows country national procurement centers and NMRAs to focus on QC until they are strengthened. |

35. World Health Organization, "The WHO Prequalification Programme and the Medicines Patent Pool: A Primer," http://apps.who.int/prequal/info_general/documents/FAQ/PQ_PatentPool.pdf.
36. Illustrative, based on U.S. FDA data at http://www.fda.gov/forconsumers/byaudience/forpatientadvocates/speedingaccesstoimportantnewtherapies/ucm128291.htm#compare, accessed November 28, 2011.
37. World Health Organization. "Assessment of Medicines Regulatory Systems" (Geneva: WHO, 2010).
38. The European Commission established Article 58 as a mechanism to assist developing country registration authorities with assessment of a dossier for pharmaceutical product used outside the European Union.

| Quality Assurance approach | WHO Prequalification Programme (PQP) | Global Fund-WHO Expert Review Panel (ERP) | Stringent regulatory authority (SRA) approval | National medicines regulatory authority | Procurement service agency quality assurance system |
|---|---|---|---|---|---|
| Limitations and needs | Long time to prequalify a product.<br>WHO-PQP could be reserved for prequalifying active pharmaceutical ingredients (APIs).[39]<br>There is little country ownership.<br>Few suppliers are prequalified, causing supply concerns when problems occur.<br>Expensive (costs a minimum US$40,000 to prequalify one product [to WHO-PQP]; medium to small suppliers will probably not be able to prequalify.<br>Could cause global shortages until enough prequalified suppliers.<br>Need many more technical experts and financial resources to support the program. | Period of validity is too short for supplier to meet remaining requirements for WHO prequalification.<br>Little advantage for expansion of QA of essential medicines.<br>Some country authorities do not accept ERP unless procuring with Global Fund grants.<br>Little country ownership.<br>Need many more technical experts and financial resources.<br>ERP review costs considered moderate for one-off evaluations. | All SRAs are not equal; therefore some PSAs still do a level of QA for medicine sources.<br>SRA mechanism not well understood at local level. Need to provide website listing all SRA countries and all products approved by an SRA.<br>Would limit the number of suppliers. | NMRA staff are inadequate, manufacturing sites are not inspected, or inspections are done with inconsistent standards.<br>Many African NMRAs lack technical capacity to improve to international quality standards.<br>Too difficult to rate NMRAs (e.g., by WHO) [too many (193member states) and too few medicine producers in some countries].<br>Depending on their mandate, some PSAs cannot accept (not yet stringent) NMRA approvals.<br>Need to develop a stepwise approach for NMRAs to reach SRA status.<br>Need to develop regional efforts for countries to share QA resources and QA of supplier results.<br>Need technical experts and financial resources. | QA systems with variable level of stringency.<br>Need harmonization of QA criteria by donors.<br>There should be a body to accredit PSAs, but must be transparent and without conflict of interest among agencies.<br>Need to develop trust of other PSA's QA procedures for more sharing of QA approvals.<br>Among accredited agencies, most would still do a certain level of QA themselves.<br>Provides little country ownership.<br>Need many more resources to support the accreditation body for PSAs. |

*Source: Authors.*

39. WHO has been conducting API site inspections, starting in 2002; on average, about 8 sites are inspected per year since 2005.

## Toward a Harmonized and Coordinated Pragmatic Approach

The interviews and documents reviews suggest the following:

1. There is consensus that QA of all product quality evaluations should be conducted at the same stringency level, but that this is not realistic worldwide and cannot happen given the world's array of sovereign states and their various economic interests. Therefore other mechanisms must be used for prequalification of essential medicines. It is also unlikely that the WHO-PQP can be extended to cover all essential medicines, given the level (quantity and cost) of technical and financial resources needed to expand services. There would also have to be sufficient incentive for manufacturers to increase their participation in the scheme.

2. Because of due diligence and liability considerations, organizations do not rely on medicine quality evaluations conducted by each other. Even though most interviewees agreed that harmonization of QA criteria by donors, a risk-based analysis of medicines on the WHO Model List of Essential Medicines List (EML), and transparency of prequalification methods by other organizations would be a big step in the right direction, they said they would still need to conduct some form of QA assessment for products they procure. However, they concluded that the amount of time spent on their own prequalification activities would likely decrease, compared to current levels of effort.

3. A process must be developed to allow sharing of QA documents and results, which also takes into account the proprietary concerns of the different PSAs and manufacturers. Harmonization of policies, criteria, standards, and procedures and access to quality assessment is expected to increase both stringency and transparency in QA and will help build trust among the stakeholders. This will require active collaboration among donors, regulators, and procurement services agencies.

4. There was consistent agreement among interviewees that the international community must exert more concerted effort to strengthen national medicines regulatory authorities (NMRAs) and country-based (national) procurement centers. Interviewees pointed out that it is because of NMRA weaknesses that many donors and others involved in procurement have established their own QA systems. This can be addressed through increased active participation of NMRAs in the WHO-PQP (dossier evaluation and GMP inspections). NMRAs could also be involved in a multicountry team approach to evaluations at the regional or subregional level, as there are ongoing registration harmonization initiatives in Sub-Saharan Africa, with WHO assistance. A pragmatic and more efficient approach to address dossier evaluation through shared efforts or use of evaluations by SRAs should also allow countries to focus on more effective management of the quality of their domestic pharmaceutical manufacturing, where applicable, as well as on postapproval measures to control the market.

5. There has been much international discussion about the need for a Common Technical Document that would standardize the requirements for dossiers submitted for registration. This would facilitate building capacity of NMRAs and should speed up and lower the cost of registration for both NMRAs and for manufacturers.

6. Leveraging and sharing resources addresses limitations in available quantity and quality of technical resources for pharmaceutical evaluation (dossier review and GMP inspections). This should facilitate more efficient use of limited resources and reduce costs associated with evaluation and supplier and product prequalification.

7. Avoidance of conflict of interest through separation of the decision-making authority for quality assurance function from the authority for procurement or purchasing decisions is another critical concern.

8. There is genuine interest in harmonizing donor policies and approaches to quality assurance of essential medicines and use of improved tools, such as the MQAS, to effectively assess manufacturers and wholesalers.

### *Risk categorization of essential medicines*

The WHO Prequalification of Medicines Programme has developed a risk-based approach to classifying manufacturers, and determining frequency and scheduling of inspections as well as risks of active pharmaceutical ingredients.[40] For example, inspections are scheduled on a risk basis, considering factors such as results of previous WHO inspections or inspections by other national regulators, type of active pharmaceutical ingredients (APIs), products and dosage form manufactured, activities performed, recalls or complaints since last inspection, results of product testing, significant changes within the manufacturer (such as changes in key personnel, buildings, equipment, products), and other relevant information.

WHO has now begun to explore an approach to categorize essential medicines as high, medium and low risk based on criteria such as (1) difficulty to manufacture a bioequivalent or bioavailable product; (2) the risk to patients if they receive a substandard product; and (3) inclusion of important products by therapeutic use (for example, reproductive health or family planning). Definitive criteria and their application are still under development. Some preliminary findings in identifying clinical consequences and risks associated with medicines' manufacturing defects were presented at the recent joint stakeholder meeting[41] and are summarized in annex 6. Table 5 is a very basic illustration for initiating discussion and work toward defining risk criteria, which would be carried out by relevant experts.

40. L. Rago. "Quality Risk Management in the WHO Prequalification Programme;" http://www.apec-ahc.org/files/tp201105/Lembit_Rago_April_27_Parallel_Track_Track_2.pdf.
41."WHO and the Global Fund Joint Stakeholder Meeting Report," annex 2, Geneva, August 30–31, 2011.

**Table 5. Selected Illustrative Criteria for Categorizing Essential Medicines' Product Quality Risk**

| Risk category | Therapeutic use | Pharmacologic characteristics or manufacturing processes | Formulation/dosage form |
|---|---|---|---|
| High | Anti-infectives for systemic use (ARVs, antituberculosis, antibiotics)<br><br>Antimalarials<br><br>Cardiovascular medicines<br><br>Cancer medicines<br><br>Hormonal medicines (systemic use)<br><br>Other critical or life-saving medicines | Active ingredient is of biological origin<br><br>Polymorphs of active pharmaceutical ingredients that may affect bioequivalence<br><br>Excipients (inactive ingredients) that may affect bioequivalence<br><br>Pharmaceutical processes used in manufacturing that may affect bioequivalence<br><br>Steep dose-response curve or narrow therapeutic index<br><br>Toxic impurities | Injections (intravenous, intramuscular)<br><br>Oral solids (tablets, capsules) for medicines with documented bioavailability problems<br><br>Oral solids with low content (e.g. digoxin) |
| Medium | Analgesics (parenteral)<br><br>Anti-inflammatory medicines (oral and parenteral)<br><br>Hormonal medicines (nonsystemic use)<br><br>Psychoactive medicines (oral and parenteral) | High solubility in water<br><br>Manufacturing process not complex | Oral solids of medicines with low potential for bioavailability problems<br><br>Oral liquids of medicines for "nonsymptomatic" treatment<br><br>Ophthalmic preparations |
| Low | Anti-infectives (nonsystemic use)<br><br>Analgesics (oral)<br><br>Antacids<br><br>Disinfectants<br><br>Symptomatic remedies<br><br>Vitamins | | Ear preparations<br><br>Nasal preparations<br><br>Oral liquids (syrups)<br><br>Topical (skin) creams and solutions |

*Source: Authors.*

A quality assurance risk categorization would be the basis for establishing a pragmatic and progressively harmonized and coordinated approach to assuring the quality of essential medicines procured with donor funds. As the level of risk or consequence determines the level of

effort required to assure the quality of the product, such a classification would allow a rational approach to optimize the use of limited technical resources (of varying levels of expertise) that are available in the existing international and national mechanisms. WHO plans to engage additional experts and SRAs (for example, U.S. FDA) to further develop the risk-based classification of medicines in the Model List of Essential Medicines. NMRAs would also have a role to play in this process: their acceptance of the approach is critical as their engagement would provide an important capacity-building platform.

### *Framework for a pragmatic (and coordinated) approach*

The proposed pragmatic approach creates a system out of the various "parallel" initiatives to optimize overall yield of existing mechanisms (PQP, ERP, SRA approval, NMRA approvals, PSA-QA). Table 6 provides an overview of how the various existing mechanisms can be leveraged to support quality assurance of essential medicines procured with donor funds. It classifies the types of medicines according to risk level: "high," "medium," and "low."

Medicines designated as "high risk" because of therapeutic importance, combined with critical pharmacologic characteristics, high complexity of manufacturing procedures, and requirements associated with their formulation or dosage form would require evaluation and approval by SRAs and PQP (to supplement those not SRA-approved). This is currently in place for HIV/AIDS, TB, and malaria medicines and expanding to other medicines.

The WHO-PQP would cover HIV/AIDS, TB, and malaria medicines as well as other essential medicines classified as high risk for manufacture-related quality problems. It is likely that additional criteria will need to further discriminate high-risk products, as it is unlikely that the WHO-PQP will be able to cover all possible high-risk essential medicines. The WHO-PQP will have to strategically focus on those that have critical impact. Therefore, given the technical and financial resources needed, further discussion is required to determine if the WHO-PQP should also cover medicines categorized as "medium risk." Expanding WHO-PQP to address products classified as "low risk" is not going to be cost-effective.

The ERP can only grant a time-limited approval, which is linked to eventual approval by PQP or SRA. It is very helpful as a temporary measure to increase the number of potential reliable suppliers, but it is also unlikely that this will be a cost-effective stand-alone mechanism to address medium- and low-risk medicines.

SRAs currently cover all medicines approved for their respective markets, regardless of risk category. The U.S. FDA and EMA also support access to public health priority medicines through "tentative approval" and the mechanisms of the European Commission's Article 58 to support developing country registration authorities with assessment of dossiers for medicines used only in the developing countries. Medium- and low-risk medicines that are not assessed by SRAs would be addressed through evaluation and approval for prequalification by other mechanisms, including NMRAs and qualified procurement service agencies.

NMRA capacity varies among countries, but they can play an important role in QA while further developing their capacity and moving toward the long-term goal of achieving SRA status. NMRAs can increase their capacity to assess high-risk medicines through active participation in WHO-PQP[42] and regional initiatives, such as the African Medicines Registration Harmonization, and PIC/S. Regional collaboration would formally leverage specific expertise in different technical areas to optimize and support collaborative technical assessment of registration applications for medium-risk medicines. This enhances country ownership of stringent QA for essential medicines, including ATM and non-ATM medicines. NMRA assessment and approval of low-risk medicines should be acceptable for product procurement with donor funds under predefined minimum technical requirements, such as evidence of bioavailability and certificate of analysis for each batch of product, as appropriate.

Procurement service agencies and wholesalers can also have an important role in this pragmatic system. Currently, there is variation in their QA systems, policies, assessment tools, and practices. Although many of the QA systems are MQAS-based, there is need to harmonize and standardize them and to establish a mechanism to independently and rigorously assess and qualify PSAs or wholesalers based on a standard MQAS assessment tool. Such qualified or certified PSAs and wholesalers can share technical evaluations, complementing or supplementing the database of prequalified manufacturers and suppliers for procurement of essential medicines using donor funds. It is likely that the greatest contribution would be in the assessment of medicines categorized as medium risk.

This coordinated pragmatic approach intends to expand coverage of essential medicines beyond those for HIV/AIDS, TB, and malaria, in a way that optimizes the use of limited technical expertise through harmonization and standardization, reducing duplication of efforts and leveraging complementary contributions. All current stakeholders have an important role to play, and NMRAs can systematically and progressively develop stringent regulatory QA capacity.

42. Technical staff of selected African countries currently participate in the WHO-PQP process.

**Table 6. Quality Assurance Approaches Coverage of Essential Medicines, Based on Risk Category**

| | Assessing Entity | | | | |
|---|---|---|---|---|---|
| | WHO Prequalification Programme (PQP) | WHO-hosted Expert Review Panel (ERP) | Stringent regulatory authority (SRA) approval | National medicines regulatory authority (NMRA) approval | Procurement service agency MQAS-based qualification by an independent body |
| Risk level | | *(Time-limited approval)* | | *(Capacity building/ cooperation* | |
| High | HIV/AIDS, TB, malaria (ATM) medicines<br>Non-ATM medicines on WHO-EOI list (opportunistic infections & others) | HIV/AIDS, TB, malaria (ATM) medicines<br>Non-ATM medicines | HIV/AIDS, TB, malaria (ATM) medicines<br>Non-ATM medicines | High-risk medicines to be defined *(through participation in WHO-PQP and regional initiatives)* | HIV/AIDS, TB, malaria (ATM) medicines<br>Non-ATM medicines |
| Medium | Further discussion may be required to determine if this group should be covered | Further discussion may be required to determine if this group should be covered | Non-ATM medicines | Medium-risk non-ATM medicines to be defined *(through participation in regional initiatives)* | Non-ATM medicines |
| Low | Probably not cost-effective | Probably not cost-effective | Non-ATM medicines | Non-ATM medicines | Non-ATM medicines |
| Rationale | Prioritizes use of limited technical and financial resources to assess high-risk and high public health impact medicines | Temporary measure to access additional quality products | Already ongoing work for SRA country market | Builds country ownership in stringent QA of essential medicines (ATM and non-ATM)<br>Allows NMRA to focus on strengthening postmarket surveillance and control while building capacity toward stringency | Supports quality assurance in procurement and increased rigor in evaluations |

## Consensus at the WHO and Global Fund Stakeholders Meeting on Quality Assurance of Essential Medicines

Thirty-three participants from about seventeen organizations participated actively in the Joint Stakeholder Meeting on Quality Assurance of Essential Medicines, organized by WHO and the Global Fund, in Geneva on August 30 and 31, 2011.[43] Annex 7 reproduces the executive summary and recommendations of the meeting. Many of these participants had already contributed their perspectives in the interviews that MSH conducted during the month of July (annex 5).

Participants agreed that (1) harmonized, risk-based approaches are needed and are being introduced to achieve maximum impact of QA measures; (2) resources and independent technical expertise for pharmaceutical QA are becoming increasingly scarce worldwide; and (3) the MQAS defines commonly accepted standards that can serve as a basis for an independent qualification system, making quality assurance in procurement a competitive advantage.

Meeting participants recommended the following:

1. Continue to develop a risk-based categorization of essential medicines
2. Harmonize tools to assess procurement agencies
3. Harmonize QA approaches
4. Develop a mechanism to share information

Discussions reflected the views of international stakeholders involved in QA and procurement of donor-funded medicines since representatives of recipient countries had not been invited to the meeting. Engagement of NMRAs will be critical to move forward on the meeting recommendations and the development and implementation of a coordinated approach in which NMRAs actively participate and gradually increase their regulatory capacity for effective QA.

43. "WHO and the Global Fund Joint Stakeholder Meeting Report," Geneva, August 30–31, 2011.

## TOWARD A FIVE-YEAR ROAD MAP

The following initiatives can be developed over the next five years to produce a pragmatic approach (or system) that assures the quality of essential medicines, beginning with those procured with donor funding, but will also impact positively on NMRA capacity to assure the quality of all medicines.

1. Development of risk-based categorization of (non-ATM) essential medicines
    a. WHO as the lead organization will continue to develop criteria and guide implementation of a process for classifying medicines in the WHO Model List of Essential Medicines according to risk categories (high, medium, low) in collaboration with interested and willing stringent regulatory authorities, including the U.S. Food and Drug Administration and the European Medicines Agency, and representatives from NMRAs and the pharmaceutical industry.
    b. The Interagency Pharmaceutical Coordination group (IPC) can build on initial discussions regarding the framework for a pragmatic and risk-based harmonized approach to assure quality of non-ATM essential medicines as described previously, and further define or refine the role of the various mechanisms in addressing medicines classified under medium level of risk.
2. Harmonization of Quality Assurance Policies
    a. WHO, through the Interagency Pharmaceutical Coordination group (IPC), can engage members and other potential collaborators to establish a working group to systematically compile, review, analyze, and propose relevant changes to harmonize the respective member organization's medicines' quality assurance policies and standards.
    b. The respective IPC member organizations will incorporate changes as appropriate, endorse and publish a joint harmonized policy statement on quality assurance of essential medicines procured with donor funds.
    c. The Global Fund, the World Bank, UNICEF, and WHO will work to engage ECHO and other donors to formally adopt and communicate quality assurance policies aligned with the newly harmonized QA policy for donor-funded essential medicines.
    d. WHO is considering an initiative to develop and implement a workable model for Common Technical Documents to standardize requirements for registration dossiers.
3. Harmonization of MQAS-based quality assurance system assessment tools and development of a procurement services agencies' and wholesalers' prequalification body
    a. WHO plans to proceed with updating the MQAS, engaging those organizations that have developed modified MQAS-based tools to assess procurement services, wholesalers, and manufacturers, and to work toward harmonizing existing tools.
    b. Based on development of a harmonized MQAS-based assessment tool, a process can be developed for eventual prequalification of procurement services agencies and a database of approved or prequalified procurement services agencies.
    c. Under the procurement services agencies prequalification initiative, participating agencies can conduct joint manufacturer dossier evaluations and site inspections.

d. A working group can be established to develop IPC-harmonized, MQAS-based standards, criteria, and processes for establishing an independent entity to prequalify, certify, and accredit procurement services that can supply donor-funded essential medicines. The Institute of Tropical Medicine in Belgium (QUAMED project) and the United States Pharmacopeial Convention (Promoting Quality of Medicines Program) can be explored as potential candidates to host the PSA prequalification initiative, as alternatives to WHO. These organizations may be better positioned to provide this service as a cost to be supported by donors or by the procurement services agencies that are assessed and qualified. WHO is already involved in prequalifying priority medicines and their manufacturers and quality control laboratories. WHO could host the database of approved or prequalified procurement services agencies.

4. Phased-strengthening of NMRA-QA capacities

   a. WHO, through the Prequalification of Medicines Programme and other regional registration harmonization initiatives (for example, African Registration Harmonization Initiative), will continue to involve national medicines regulatory authority technical staff in (1) prequalification dossier evaluation, and (2) manufacturing site inspections.

   b. While capacity is being strengthened in such areas as conducting technical dossier evaluations and site inspections, NMRAs can continue to focus on domestic pharmaceutical manufacturing where applicable, as well as postmarketing approval (registration) measures and more effectively controlling what is actually provided to patients and consumers—as very little to nothing is currently done.

5. Information sharing

   WHO plans to host a website that will be open to active participants. WHO will post information on manufacturing site inspections that are planned and completed by WHO and its partners, including information such as the inspection date, site inspected, affiliation of the lead inspector, and contact information for clarification. The website would also provide information on prequalified procurement services agencies, once this initiative begins.

Illustrative key “generic” activities needed for each initiative or project include the following:

- Defining the lead organization (champion), which in most cases will be WHO, as well as key partners from the IPC Group and others
- Engaging potential collaborators, including NMRAs, and establish working groups
- Preparing budget and proposal(s) for funding activities
- Identifying potential funding sources (International Health Partnership+, bilateral donors, internal resources)
- Preparing and implementing respective work plan(s)
- Conducting broader stakeholder consultations

## CONCLUSION

Based on the rate of 253 products over eight years during which the WHO Prequalification of Medicines Programme approved ATM and other medicines, it could be expected that approximately 150 additional medicines from the WHO EML might be approved over the next five years. In addition, 229 products were awarded time-limited approvals through the Expert Review Panel mechanism; it is likewise anticipated that another 190 medicines would be approved for procurement with donor funds during the next five-year period.

Nongovernmental agencies and procurement services agencies will continue to prequalify the medicines they need (not already approved through the WHO Prequalification Programme and SRAs). Assuming increased stringency of product and manufacturer prequalifications, more quality-assured essential medicines will be available for procurement using donor funding; but this is more difficult to project since historical information is not available.

There is consensus that NMRAs should be doing quality assurance assessments and registering products according to stringent standards and methods—however, with a risk-based approach, capacity building can be achieved while donors gradually decrease dependence on prequalifications conducted by the international community.

One factor that could greatly impact the implementation of activities as proposed in the road map is the cost to be borne by donors, or by those who may benefit economically from improved quality of essential medicines. If the cost of implementation is found to be unfundable, these important activities will not take place, and product quality will improve at its own pace, based solely on market dynamics.

# REFERENCES


**European Commission's Directorate-General for Humanitarian Aid (DG ECHO):**

European Commission's Directorate-General for Humanitarian Aid. "Quality Assurance for Medicines and Medical Supplies in Humanitarian Aid." Paper presented at Annual Conference of Humanitarian Aid Partners of the European Commission, Brussels, December 13–14, 2006. http://log.logcluster.org/response/procurement/LOG-02-3-PROCUREMENT-ECHO%20QUALITY%20ASSURANCE%20FOR%20MEDICINE%20AND%20MEDICAL%20SUPPLIES.pdf

Pomatto V., and C. Schuftan. 2006. "Review of Quality Assurance (QA) Mechanisms for Medicines and Medical Supplies in Humanitarian Aid." Concept paper submitted to European Commission's Directorate-General for Humanitarian Aid by GFE Germany. Aachen, Germany: GFE Consulting Worldwide.

European Commission's Directorate-General for Humanitarian Aid. 2006. "Guidelines - Review of Quality Assurance (QA) Mechanisms for Medicines and Medical Supplies in Humanitarian Aid." Submitted to European Commission's Directorate-General for Humanitarian Aid by GFE Germany. Aachen, Germany: GFE Consulting Worldwide.

**Management Sciences for Health**

M. Clark and A. Shrivastav. 2009. "Assessment of Procurement Capacity in 10 States in India," submitted to the UK Department for International Development by the Center for Pharmaceutical Management.

**The Global Fund**

Caudron, J-M. and C. Pouget. 2010. "Report on Quality Assurance of non-ATM Medicines with a Focus on Opportunistic Infections Medicines." Submitted to Secretariat of the Global Fund under the governance of the Portfolio Committee. Geneva: the Global Fund.

Global Fund. 2009. "Analysis of Quality Assurance Policies of Global Fund Partners for the Procurement of Pharmaceutical Products Other than ARVs, Anti-TB and Anti-malarial Medicines (Non-ATM Medicines)." Geneva: the Global Fund.

Global Fund. 2009. "Guide to the Global Fund's Policies on Procurement and Supply Management." http://www.theglobalfund.org/documents/psm/PSM_ProcurementSupplyManagement_Guidelines_en/.

Global Fund. 2010. "Global Fund Quality Assurance Policy for Pharmaceutical Products." http://www.theglobalfund.org/en/procurement/quality/pharmaceutical/.

Global Fund. 2011. "Global Fund Quality Assurance Policy for Pharmaceutical Products: The Expert Review Panel Indicative Terms of Reference." http://www.theglobalfund.org/en/procurement/quality/pharmaceutical/.

Global Fund. 2011. "Global Fund Quality Assurance Policy for Pharmaceutical Products: The Expert Review Panel Mechanism Presentation." http://www.theglobalfund.org/en/procurement/quality/pharmaceutical/.

Global Fund Pharmaceutical Management Unit Quality Assurance and Data Management Team. 2011. "Global Fund Quality Assurance Policy for Pharmaceutical Products. PowerPoint presentation. http://www.theglobalfund.org/en/procurement/quality/pharmaceutical/.

**Stop TB Partnership/Global Drug Facility**

Stop TB Partnership/Global Drug Facility. 2010. "Quality Assurance Policy and Procedures." http://www.stoptb.org/assets/documents/gdf/drugsupply/GDF%20QA%20Policy%20and%20Procedures.pdf.

**United Nations Family Planning Association (UNFPA)**

Hall, Peter, J. Oehler, P. Woo, H. Zardo, L. Chinery, J. S. Singh, S. H. Jooseery, and N. M. Essah. "A Study of the Capability of Manufacturers of Generic Hormonal Contraceptives in Lower- and Middle-Income Countries." *Contraception* 75 (2007): 311–17. http://www.contraceptionjournal.org/article/S0010-7824(06)00446-X/pdf.

UNFPA. 2011. *Quality Assurance Policy for Reproductive Health Medicines*. Retrieved from http://www.unfpa.org/webdav/site/global/shared/procurement/quality%20assurance/UNFPA%20QA%20Policy%20for%20RH%20medicines_31March11.pdf.

**United States Agency for International Development (USAID)**

ADS 312 Additional Help Document. 2011. "GH/OHA/SCMS 'Restricted Commodity' Approval of Pharmaceuticals." http://usaid.gov/our_work/global_health/aids/TechAreas/treatment/info_approval.pdf.

Heltzer, N. 2007. "USAID Office of Foreign Disaster Assistance (OFDA) Pharmaceutical Wholesaler Precertification Project." Submitted to the U.S. Agency for International Development by the Rational Pharmaceutical Management Plus Program. Arlington, VA: Management Sciences for Health.

**United States Pharmacopeia (USP)**

USP. 2007. United States Pharmacopeia Drug Quality and Information Program and Collaborators. "Ensuring the Quality of Medicines in Resource-limited Countries: An

Operational Guide." Rockville, Md: the United States Pharmacopeial Convention; www.usp.org/worldwide/dqi/resources/technicalReports.

J. Primo-Carpenter and M. McGinnis. 2006. "Matrix of Drug Quality Reports in USAID-assisted Countries," prepared by the U,S, Pharmacopeia Drug Quality and Information Program.

**The World Bank**

Heltzer, N., A. Shrivastav, and M. Clark. 2008. "Developing an Assessment System for Procurement Agencies in India." Submitted to the World Bank by the Center for Pharmaceutical Management. Arlington, Virginia: Management Sciences for Health.

**World Health Organization documents**

L. Rago. 2010. "Quality Risk Management in the WHO Prequalification Programme;" http://www.apec-ahc.org/files/tp201105/Lembit_Rago_April_27_Parallel_Track_Track_2.pdf.

WHO. "Discussion Points Relating to Medicines." Presented at UN Prequalification of Diagnostics, Medicines and Vaccines Sixth Consultative Stakeholder Meeting, Geneva, April 4–5, 2011. http://apps.who.int/prequal/trainingresources/Training_Stakeholders2011.htm.

WHO. 2007. "Interagency Guidelines: A Model Quality Assurance System for Procurement Agencies. Recommendations for Quality Assurance Systems Focusing on Prequalification of Products and Manufacturers, Purchasing, Storage and Distribution of Pharmaceutical Products." Previously published as annex 6 of the 40th Report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations (Technical Report Series no. 937). http://www.who.int/medicines/publications/ModelQualityAssurance.pdf.

WHO. 2007. "Survey of the Quality of Antiretroviral Medicines in Selected African Countries", WHO/PSM/QSM/2007.9.

WHO. 2010. "The WHO Prequalification Programme and the Medicines Patent Pool: A Primer," http://apps.who.int/prequal/info_general/documents/FAQ/PQ_PatentPool.pdf.

WHO. 2011. "WHO Prequalification of Medicines: Programme Analysis." (In process). Presented at UN Prequalification of Diagnostics, Medicines and Vaccines Sixth Consultative Stakeholder Meeting, Geneva, April 4, 2011. http://apps.who.int/prequal/trainingresources/Training_Stakeholders2011.htm.

WHO. 2011. "WHO Prequalification of Medicines Programme: The Programme 5 Years from Now." Presented at UN Prequalification of Diagnostics, Medicines and Vaccines Sixth Consultative Stakeholder Meeting, Geneva, April 4, 2011. http://apps.who.int/prequal/trainingresources/Training_Stakeholders2011.htm.

WHO. 2011. "WHO Prequalification of Medicines Programme: Programme Update – Prequalification of Medicines." Presented at UN Prequalification of Diagnostics, Medicines and Vaccines Sixth Consultative Stakeholder Meeting, Geneva, April 4–5, 2011. http://apps.who.int/prequal/trainingresources/Training_Stakeholders2011.htm.

WHO. 2011. "Assessment of Medicines Regulatory Systems in sub-Saharan African Countries: An Overview of Findings from 26 Assessment Reports" (Geneva: WHO, 2010).

WHO. 2011. "Survey of the Quality of Selected Antimalarial Medicines Circulating in Six Countries of sub-Saharan Africa, WHO/EMP/QSM/2011.1.

**Other**

R. Cockburn, et al. 2005. "The Global Threat of Counterfeit Drugs: Why Industry and Governments Must Communicate the Dangers," *PLoS Med* 2 no. 4 (2005), e100,doi:10.1371/journal.pmed.0020100.

R. Bate. 2011. Africa's Epidemic of Disappearing Medicines, http://www.foreignpolicy.com/articles/2011/01/11/africas_epidemic_of_disappearing_medicine?page=0,1, accessed January 11, 2011.

A. A. Amin and G. O. Kokwaro. 2007. "Antimalarial Drug Quality in Africa," *J Clin Pharm Ther* 32, no. 5 (2007): 429–40, doi:10.1111/j.1365-2710.2007.00847.x.

Aedes Foundation. 2010/ "Medicine Themes Day Report," Brussels, September 21–23.

# ANNEXES

## Annex 1: List of Organizations Receiving Requests for Interview

| Name | Type of Organization | Interviewed |
|---|---|---|
| Action Medeor | PSA | √ |
| GIZ (formerly GTZ) | PSA | √ |
| European Union — Directorate-General Department of Humanitarian Assistance | Donor | |
| IDA | PSA | √ |
| Medécins sans Frontières | NGO | √ |
| JSI/Deliver Project | NGO | |
| Missionpharma | PSA | √ |
| PAHO | UN organization | √ |
| PFSCM/SCMS | NGO | √ |
| QUAMED Project (Institute of Tropical Medicine, Belgium) | NGO | √ |
| The Global Fund | Donor | √ |
| The UNION | NGO | √ |
| UNICEF | UN organization | √ |
| UNFPA | UN organization | |
| UNOPS | UN organization | |
| USAID | Donor | √ |
| USP | NGO | √ |
| The World Bank | Donor | √ |
| World Health Organization | UN organization | √ |

*Note:* PSA = procurement service agency; NGO = nongovernmental organization, program implementer

# Annex 2: Survey Questionnaire for Interviews

**Assuring the Quality of Essential Medicines Procured with Donor Funds: Options Analysis**

*Introduction:* Donor health-financed projects involving procurement of commodities have involved large donations for the three high burden diseases: HIV/AIDS, tuberculosis, and malaria (ATM). The WHO global medicines quality-control program (prequalification of suppliers) was developed mainly along those lines with only a limited number of suppliers' products prequalified at this time. Thus, for a wide range of essential medicines there is no centralized, internationally accepted certification process in place that could be the basis for prequalification. This leaves both national programs and donors without proper guidance on procuring good quality medicines for non-ATM, donor-financed projects. This survey is implemented by the World Bank on behalf of the Interagency Pharmaceutical Coordination group, in collaboration with Management Sciences for Health's USAID-funded, Strengthening Pharmaceutical Systems Program. The survey is intended to collect information that builds on the best options for prequalifying WHO-listed essential medicines and identifies any gaps in currently proposed options.

**Questions**

A. The WHO Prequalification Programme is the gold standard in medicine quality assurance; however, it requires 18 months or longer to prequalify a supplier for a particular product, depending on supplier response to deficiencies. Do you think it is realistic to depend solely on this approach for prequalifying the more than 350 medicines on the WHO Model List of Essential Medicines?

B. Which of the following 11 options would be appropriate if WHO and its partners were to establish a risked-based approach to prequalify essential medicines?
*If an option is not appropriate, indicate why not.*
*If an option is appropriate, indicate what would be a possible process to achieve it; kindly include any potential limitations.*
*In replying, consider quality and safety risk for patient, cost-benefit to donors, cost-benefit to national health programs, time to establish the mechanism, time to obtain quality approval results, process for gaining international approval of a specific option, and other aspects.*

   Option 1: Rely on decisions of a stringent regulatory authority (SRA) as defined by the international community.[44]
   - What does "stringent" mean to you?
   - How can certifications submitted by bidders during a tender process be verified if the SRA is in another country?

44. SRA is a national regulatory authority defined as either (1) a member country of the International Conference on Harmonisation (ICH), (2) an ICH observer, (3) or any country whose regulatory authority is associated with an ICH member through a legally binding mutual recognition agreement.

- How would a requirement for marketing authorization from an SRA impact competition in public tenders for essential medicines?

Option 2: Establish an Expert Review Panel (ERP) for essential medicines not included in the current ATM program; the ERP allows interim time-bound medicines approvals as the supplier strives to meet WHO-PQP criteria.

- What are the capacity limitations in comparison to the current ERP mechanism?
- How realistic is it to expand the current ERP to include all essential medicines?
- How could such a mechanism cope with a significant number of procurements for varying baskets of essential medicines in many different countries?
- What are the potential delays and costs with an ERP for essential medicines?

Option 3: Certification of procurement agencies (PAs) using the WHO Model Quality Assurance System criteria (MQAS), whereby the agreed upon "Interagency Product Questionnaire" and specific criteria for a manufacturing site visit are used to prequalify products procured by the PAs.

- How could we define PAs for this purpose?
- How could we deal with conflict of interest if the PA is a one-stop-shop–type supplier?
- How could an international prequalification system for PAs be hosted and funded?

Option 4: Encourage the Global Fund to expand its program on Voluntary Pooled Procurement (VPP) to include essential medicines; the VPP consists of approved PAs for procurement of specific ATM medicines that depend on the WHO-PQP, SRA, and ERP to establish the list of products they can procure.

- Would an expanded VPP speed up the availability of quality-approved essential medicines given that the Global Fund depends primarily on WHO-PQP, SRA, and ERP to establish its list of approved products? *(Note: the Global Fund is already working to include quality medicines for opportunistic infections on its approved product list).*
- Should the Global Fund consider partnering with the WHO on a risk ranking of essential medicines based on: (1) potential threat of a substandard product to the health of the patient; and (2) product characteristics with regard to manufacturing complexity, stability, influence of formulation on bioavailability.

Option 5: Acceptance of medicines and suppliers that have undergone quality assessments for good manufacturing practices (GMPs) and were approved by national regulatory authorities that are not SRAs, as internationally defined.

- Could we accept product quality assessments of some non-SRA national regulatory authorities but not others? What are the criteria for acceptance and nonacceptance?
- Should the international community through PIC/S[45] be encouraged to work closely with (and fund) non-SRA national regulatory authorities to become stringent?

45. PIC/S is the Pharmaceutical Inspectorate Cooperation Scheme, a voluntary organization, which promotes common efforts toward the improvement and harmonization of technical standards and procedures regarding the inspection of the manufacture of medicinal products and the testing of medicinal products by official control

- What if a national regulatory authority does not want to become stringent, as internationally defined, but many of their products are used worldwide?

Option 6: Acceptance of products and suppliers that have undergone quality assessments and been deemed acceptable by implementing organizations such as Medécins sans Frontières.

- What would it take for your organization to procure the prequalified products and suppliers' medicines from a list supplied by other organizations?

Option 7: Acceptance of products and suppliers that have undergone quality assessments and been deemed acceptable by procurement agencies that are certified by USAID (for example, UNICEF, IDA, and Missionpharma)

- What would it take for your organization to procure from a list of products or suppliers that have undergone quality assessments and been deemed acceptable by PAs that are certified by USAID?

Option 8: Acceptance of products that have undergone quality assessments and been deemed acceptable by the 10 humanitarian procurement centres (HPCs) as recognized by ECHO.

- What would it take for your organization to procure from the list of products that were deemed acceptable by the 10 HPCs, as recognized by ECHO?

Option 9: An international agency to be established as a clearing house to collect and publicly share information on all medicines that have been quality approved by any organization or institution.

- Where would it be located and what would be its governing body?
- Should the agency's only responsibility be to rank quality-approved products by an interagency agreed-upon ranking scale, so users could decide if use of specific products is worth the risk?
- Should the agency also do quality assessments of essential medicines for those products not already approved by the other participating agencies?
- How should it handle the issue of confidentiality when products and suppliers being prequalified encounter problems of acceptability?

Option 10: What are other possible iterations of the nine options above considering the safety, cost-benefit, and time to implement criteria?

- For example, advocate for and establish an interagency committee that would agree to use the Interagency Pharmaceutical Product Questionnaire and site visit criteria currently used by the following agencies when prequalifying products and suppliers: WHO, UNICEF, MSF, and International Committee of the Red Cross (ICRC). No results-sharing would take place with this option.
- For example, advocate and establish an interagency committee that would collect the product or supplier quality approvals based on the Interagency Pharmaceutical Product Questionnaire and site visit criteria currently used and share the list with others on the committee—members should include donors, PAs, implementers,

---

laboratories. Currently there are forty members and four partners; http://www.picscheme.org/role.php, accessed on July 5, 2011.

national medicines regulatory authorities, national procurement departments, and nongovernmental implementing organizations.

- How could the above options be organized, funded, and managed?

Option 11: What are other possible options for organizing a list of quality essential medicines and suppliers that donors and national procurement programs could depend on?

C. What unintended consequences might occur when establishing a risk-based option for ranking quality essential medicines?
   1. Increase in medicine prices.
      (Note: A recent study commissioned by the Global Fund[46] showed that issues other than quality were the driving force behind price differences from country to country for medicines used for opportunistic infections).

   2. Short-term supply problem as current suppliers are disqualified.
      (Note: This happened to Stop TB Partnership/Global Drug Facility as it brought second-line tuberculosis medicines under its QA policy).

   3. Other possible unintended consequences?

D. Which existing organization could take up the best option above and carry it forward to advocate with other stakeholders (for example, donors, implementing agencies, national regulatory agencies, national procurement departments) and then carry out the option to fruition?

E. How could QA requirements be differentiated to correspond to risk categories that allow for pragmatic solutions?
   1. Should the medicines on the WHO Model List of Essential Medicines be grouped into high-, medium-, and low-risk categories for the purpose of QA?

   2. Could the groups be assigned high-, medium-, low-risk QA categories for essential medicines based on the following:
      - potential risk of a sub-standard product to the health of the patient;
      - product characteristics with regard to manufacturing complexity, stability, influence, of formulation on bio-availability;
      - other characteristics?

46. J-M. Caudron and C. Pouget, "Report on Quality Assurance of non-ATM Medicines with a Focus on Opportunistic Infection Medicines" (Geneva: the Global Fund, 2010).

# Annex 3: ECHO Criteria for Humanitarian Procurement Centres and Principles for Prequalification[47]

**Humanitarian Procurement Centre criteria**

HPCs must meet the following requirements:

1. Be nonprofit, autonomous, and professional organizations;
2. Be specialized in the technical and commercial management of supplies necessary for the implementation of humanitarian aid operations;
3. Guarantee equal treatment of suppliers and humanitarian organizations;
4. Guarantee high standards of integrity, transparency, pricing practices, performance, and quality;
5. Respect a number of well-defined ethical, procedural, and economic requirements in their operations and in the constitution of stocks; and
6. Accept the controls, including on-the-spot checks.

**Principles for prequalification of suppliers**

1. Reliance on the information supplied by the relevant national drug regulatory authority (DRA);
2. Evaluation of product data and information submitted by manufacturers, including product formulation, manufacturing, and test data and their results;
3. General understanding of the production and quality-control activities of the manufacturers and suppliers and of their commitment to the principles of good manufacturing practices (GMP);
4. Assessment of consistency in the production processes and quality-control activities through compliance with GMP, as described in WHO guidelines;[48]
5. Availability of appropriate quality systems and standard operating procedures (SOPs);
6. Random sampling and testing of pharmaceutical products supplied;
7. Adequate purchasing mechanisms (see WHO MQAS[49]);
8. Good storage practices (GSP);
9. Good distribution practices (GDP);
10. Monitoring of customers' complaints and follow-up to remedy shortcomings;
11. Adequate handling of complaints and recalls; and
12. Ongoing monitoring and requalification.

[47] Source: V. Pommato and C. Schuftan. Review of Quality Assurance (QA) Mechanisms for Medicines and Medical Supplies in Humanitarian Aid: Guidelines. Submitted to the European Commission's Directorate -General for Humanitarian Aid (DG ECHO). Aachen, Germany: GFE Consulting Worldwide. June 2006.

48. World Health Organization, *Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Materials*, vols. 1 and 2 (updated edition), (Geneva: WHO, 1997); and WHO, *Good Manufacturing Practices and Inspection* (Geneva: WHO, 2004).

49. World Health Organization, "Interagency Guidelines" (2007).

**Annex 4: PFSCM Wholesaler Assessment Scorecard**

**Scores for each of the six sections:**

1. Prequalification (2 critical, 5 major criteria)
2. Quality control management (4 major, 1 noncritical or nonmajor criterion)
3. Organization, management, and quality (3 critical, 15 major, 11 noncritical or nonmajor criteria)
4. Procurement (4 major criteria)
5. Facility and warehouse operations (2 critical, 35 major, 5 noncritical or nonmajor criteria)
6. Distribution (5 major criteria)

**Scoring:**

Critical criteria are those that have potential for direct impact on product quality or potential liability to PFSCM; they are scored as pass or fail.

Major criteria are those that may lead to major departure from MQAS recommendations; they are scored from 0 to 2.

Other criteria are not "critical" or "major," but might be considered favorably by PFSCM; they are scored as 0 or 1.

Wholesalers are classified under four categories, based on scoring totals for prequalification (up to 10 points in section 1), QC management (up to 9 points in section 2), and all others (up to 145 points in sections 3, 4, 5, and 6).

| Category | Prequalification (%) | QC management (%) | All other (%) |
|---|---|---|---|
| A | 100 – 90 | 100 – 90 | 100 – 90 |
| B | 100 – 80 | 100 – 80 | 100 – 80 |
| C | 80 – 0 | 80 – 0 | 100 – 80 |
| F | 80 – 0 | 80 – 0 | 80 – 0 |

Category A: Pharmaceutical wholesaler meets 90 percent or more of the criteria required for the prequalification of manufacturers, quality-control management, and all other requirements contained within the checklist. An A Category enables PFSCM to enlist the pharmaceutical wholesaler for all procurement services and extends the number of years required between facility audits to three years. If reports of quality-control issues surface within the three-year audit cycle, PFSCM has the right to conduct audits "with cause."

Category B: Pharmaceutical wholesaler meets 80 percent or more of the criteria required for the prequalification of manufacturers, quality-control management, and all other requirements contained within the checklist. The B Category restricts PFSCM to purchasing pharmaceutical products, which have been approved by a stringent regulatory authority (SRA) and requires the pharmaceutical wholesaler to be evaluated every two years.

Category C: Pharmaceutical wholesaler does not prequalify manufacturers or conduct quality-control management but does meet at least 80 percent of all other requirements listed on the checklist. The C Category restricts PFSCM to purchasing pharmaceuticals products from PFSCM approved vendors. A wholesaler of the C Category will be used primarily for storage and distribution services and will be audited annually to ensure good storage and distribution practices are upheld.

Category F: Pharmaceutical wholesaler, which does not prequalify manufacturers, conduct quality-control management, or meet at least 80 percent of all other requirements on the checklist will not be recommended as PFSCM pharmaceutical wholesaler. Similarly, if the wholesaler does not pass all critical requirements, it will not be recommended.

# Annex 5: Summary of Findings from Interviews and Document Reviews

The consensus was that quality assurance (QA) of all products should be calculated at the same stringency level; but that is not realistic and would not happen for a long time. Therefore other mechanisms must be used for prequalification of essential medicines.

Organizations do not trust medicine quality evaluations conducted by each other. Even though most agreed that harmonization of QA criteria by donors, a risk-based analysis of medicines on the WHO's Model List of Essential Medicines (EML), and transparency of prequalification methods by other organizations would be a big step in the right direction, they would still need to conduct some form of QA assessment for products they procure. However, they concluded that the amount of time spent on their own prequalification activities would likely decrease.

There was consistent agreement among interviewees that the international community must expend greater concerted effort on strengthening national medicines regulatory authorities (NMRAs) and country-based or national procurement centers (NPCs). Interviewees pointed out that it is because of NMRA weaknesses that many donors and others involved in procurement have established their own QA systems.

**General statements**

All respondents agreed that the best approach is to move toward NMRAs conducting the majority of product quality assessments.

Six of nineteen respondents mentioned the need to balance price versus quality. Global market forecasts of medicines to be prequalified (such as IMS health reports) must be provided to manufacturers. That way they can determine the cost-benefit of applying for prequalification of essential medicines. Even though manufacturers may have the volume incentive, extremely low costs may trump their desire to participate in the proposed prequalification schemes. Also, for some essential medicines, there may only be one or two producers due to low volumes, (for example, for pediatric formulations). One respondent indicated that requiring prequalification of essential medicines could increase the procurement price of a product by 20 percent.

Most essential medicines are generics, developed to comply with pharmacopoeial analytical methods and specifications. WHO and other experts need to identify a comparator product for EML products for manufacturers and recipients alike to test against medicines procured.

**WHO Prequalification Programme (WHO-PQP)**

All respondents agreed that the WHO-PQP is very important for ARVs and malaria; the program has done an excellent job establishing and managing an effective prequalification scheme. Ideally, the program would be used for quality of all medicines on the EML, but the time line to prequalify a product is long. Unless the WHO-PQP process is shortened, the program is not practicable given the long list of products needing different degrees of attention, but can still establish therapeutic equivalence of prequalified products. There was also some agreement that

the WHO-PQP should be reserved for new chemical entities (new products being marketed) and for prequalification of active pharmaceutical ingredients (APIs). However, WHO would not work to prequalify sources of APIs until there is a market requiring PQ. For example, ARVs had been targeted for prequalification because there was no previously established market.

**Costs and challenges of the WHO Prequalification Programme (WHO-PQP)**

At a recent stakeholders' meeting in Geneva, WHO-PQP presented the cost to the program to evaluate medicines. From WHO-PQP's point of view, the cost of prequalifying a product varies considerably. It can be as low as US$40,000 if the dossier submitted is of good quality and the manufacturing site passes GMP on first inspection. But the cost is considerably higher if a dossier must be examined several times, when questions sent to the manufacturer and its responses require further review, or if a site must be inspected more than once. In addition WHO-PQP has estimated that the cost of verifying quality is equivalent to approximately 2 percent of the procurement price. To help offset costs for WHO-PQP, there was a proposal from stakeholders for WHO-PQP to levy a fee if a dossier has to undergo multiple assessments.

It was also reported that even if funds could be organized to expand the WHO-PQP, there are several other needs related to human resource capacity and demand for service; for example, there is a need for highly qualified staff that responds to the particular health concerns of that region or country, and for availability of qualified assessors and inspectors at the national level in forthcoming years. There is increasing demand for capacity building and technical assistance; increasing demand for prequalified products for medicines of high public health value, increasing demand of ad hoc services regarding quality risk assessment (Expert Review Panel), constant need to improve communication and collaboration, and reform of information technology services.

**Price versus quality and business needs of manufacturers**

WHO-PQ also reported at the stakeholders' meeting mentioned above that business needs must be considered when manufacturers are asked to participate in the WHO-PQP by WHO, procurement services agencies, and donors. Such business concerns include predictability of sales, capacity utilization (cost-effective volumes), and the need for a guide to the investments necessary to attain WHO-PQP standards. There is a high value to companies that want to achieve global quality standards, both for the local and the export markets; but inconsistencies and complexities in processes and policies among funding and procurement agencies lead to poor forecasting, delays, increased costs, and lack of predictability—just what manufacturers do not want.

Caudron and Pouget [50] [51] reported that price increases should not necessarily be expected because of increased QA demands by donors; for example, the development of the ATM market showed that QA criteria did not lead to an increase in price, but instead stabilized the market; and

50. J-M. Caudron, and C. Pouget, "Analysis of Quality Assurance Policies of Global Fund Partners" (Geneva, 2009).
51. J-M. Caudron, and C. Pouget, "Report on Quality Assurance of Non-ATM Medicines" (Geneva: the Global Fund, 2010).

economies of scale were an important factor in the stabilization. Another reality is the already existing huge variability of procurement prices among countries; for example, in the case of doxycycline 100mg, an essential antibiotic, procurement prices in five countries varied from 94 to 188 percent of the UNICEF price. Other products showed even broader ranges when comparing prices.

**Expert Review Panel (ERP)**

Only 7 of 19 respondents agreed the ERP mechanism functions well to cover gaps in prequalification for target products. If used for expanding the PQ to all medicines on the EML, the mechanism would be handicapped since its requirements are quite similar to those of the WHO-PQP and because it is time-limited. To be more effective, 8 of 19 respondents suggested the need to change the ERP mechanism to a more stepwise, graduated approach to prequalification, allowing at least 24 months for the approval period, as opposed to the current 12 months. During the 24 months the WHO-PQP would monitor for any product changes and to ensure the producer continues to follow GMPs.

**Existing procurement services agencies (PSAs) and nongovernmental organizations (NGOs)**

All respondents commented that a number of PSAs and NGOs are already conducting their own prequalification of essential medicines' manufacturers and products. With a harmonized quality assurance policy and accompanying tools, these organizations could accelerate the goal of prequalification of all essential medicines. To be effective, the following activities are necessary:

- Sharing of GMP audits among PSAs and NGOs would reduce time for dossier reviews and limit QA activities of the PSAs and NGOs, but each organization would continue to use quality-control testing to verify quality of batches to be shipped.
- All PSAs and NGOs would follow the updated WHO-MQAS guidelines, consisting of an Interagency Product Questionnaire and site visits using the same inspection criteria as WHO technical experts.
- PSAs and NGOs would conduct joint GMP audits so they will be able to trust each other's prequalification determinations.
- PSAs and NGOs need to discuss sovereignty issues of countries, confidentiality issues of manufacturers, and their own policies to see how close they could come to harmonization of QA systems.

None of the respondents considered the Voluntary Pooled Procurement mechanism as a focus for expansion of prequalification to cover all essential medicines. It is no different from other PSAs, and all PSAs are familiar with the Global Fund; it may, however, play a role for limited products.

Caudron and Pouget (2010) reported that PSAs' procurement systems are complex because of Global Fund requirements; for example, of those visited, there were as many as four principal recipients and up to thirty subrecipients to satisfy. The capacity of PSAs to perform QA varies, even though most have SOPs and formal QA requirements. For some PSAs there is a potential conflict of interest since the same entity may qualify and also place orders with manufacturers.

There is also a misperception that well-known commercial PSAs with a large market in developing countries can guarantee product quality; however, even if some have specialized staff and facilities, the procurement interest of these companies is to save time and money, which may conflict with QA interests. In essence, QA measures per se by Global Fund PSAs give no reasonable guarantee of product quality.

**Existing nongovernmental entities that provide technical assistance in prequalification and quality control**

The United States Pharmacopeia (USP) is a nonprofit organization located in the United States, India, East Africa, China, and Brazil. The USP is staffed with qualified experts in the field of quality of medicines and foods. USP works in two main activities related to harmonization of quality assurance and prequalification of medicines:

- Prequalifying manufacturers and medicinal supplements (vitamins) for the United States market;
- Managing the USAID-funded program, Promoting the Quality of Medicines (PQM), which provides technical support to manufacturers in poor resource countries to reach higher standards of quality assurance.

QUAMED is a project hosted by the Institute of Tropical Medicine in Belgium. It has developed a database of prequalified suppliers and essential medicines for use by its members. The QUAMED initiative addresses pharmaceutical QA and GMP issues including the following technical activities:

- Facilitation of training sessions on topics related to pharmaceutical quality
- Preparation or support (coaching) of audits at pharmaceutical manufacturers or suppliers
- Support in the assessment of specific pharmaceutical dossiers
- Development of standardized procedures and tools for the evaluation of pharmaceutical sources and suppliers

Representatives of both USP and QUAMED indicated their willingness to serve as possible centralized locations for activities related to expanding the prequalification of essential medicines.

**Accreditation body for PSAs and NGOs**

Eleven of nineteen respondents commented that the international community must establish an accreditation body to verify the findings of PSA and NGO quality inspectors. An accreditation body must be selected that would be recognized by all; plus, it must be transparent concerning the certification process used before PSAs and NGOs would accept certification results. It was suggested by one respondent that the definition of PSAs should be expanded to include national procurement centers (NPCs) since a common goal is to strengthen NPC capacity for procuring essential medicines.

Both QUAMED and USP are possible options for location of the accreditation body since they already have technical experts on board and infrastructures in place; also, they would be considered transparent organizations without conflict of interest by the PSAs and NGOs. WHO

may not be a good place since it is not a regulatory body. Donors must provide funding for the accreditation body regardless of its location so that it can expand to a sufficient number of technical experts for the accreditation work.

### Quality standards and quality testing

Caudron and Pouget (2010) reported that acceptable quality standards are not universally known; some manufacturers are not always genuine and do not follow acceptable QA standards. National testing laboratories often lack resources, reference materials, and the quality management system required to perform effective quality control (QC) monitoring. Also, QC testing gives a false sense of product quality because it is only a snapshot of the sample and would not necessarily identify any variability of the product from the same batch. Therefore NMRAs cannot efficiently detect quality deficiencies of products distributed in the country. It was also reported that no postdistribution (post-market) QC is done in most countries visited. However, there is wide variation between countries: the National Quality Control Laboratory in Kenya is WHO prequalified, and the Pharmacy and Poisons Board has passed the WHO validation of its results and is in the process of building the facility that will enable its quality control lab to be prequalified. In contrast, Niger has virtually no regulatory oversight at all.

### Harmonized criteria for QA of essential medicines

Ten of nineteen respondents agreed that donors must adopt a common approach for QA of medicines and include these criteria in their contracts and agreements so that recipients will better understand the playing field. Two respondents commented that simply having a harmonized approach would stimulate better QA practices by others. Once a few countries are on board with the new QA process, it would then spread to other countries. Countries look more to neighboring countries to see what they are doing; they rarely look at the global picture to establish their own procurement systems.

Caudron and Pouget (2010) reported some confusion had arisen over the fact that QA requirements for essential medicines are less strict when paid with government funds or with unrestricted donor funds than when donors enforce stringent QA requirements.

### Stringent regulatory authority (SRA)

All respondents commented that reaching SRA status by NMRAs would be a good long-term goal. SRA approvals of essential medicines is a good option because the mechanism is sustainable, brings ownership of governments to the forefront, and supports a long-term strategy of improving the overall regulatory environment of countries.

Three of nineteen respondents indicated that the mechanism is not well understood by many at the country level (including some NPCs, NMRAs, and manufacturers). To overcome this, the respondents suggested the following:

- Identify as many SRA-approved essential medicines as possible
- Publish a list of all identified SRA-approved medicines

- Publish a list of all countries considered SRAs today

One respondent stated the need for international organizations (WHO, multilateral, and bilateral donors) to enter into constructive dialogue with governments and convince them to move their regulatory authorities to SRA standards. To do this, the international community must be ready to offer technical assistance to regulatory authorities as needed, as they progress toward becoming an SRA.

One respondent suggested that a system be established for rating the technical capacity of NMRAs and making this information available on their website. WHO already does this for the vaccines program and also has a program of technical support for NMRAs in general. The NMRA ratings by WHO would allow the PSAs and NGOs to do less QA activities (for example, only the dossier review), cutting time and costs for QA. Alternatively, if WHO is unable to do this, the organization selected to do accreditation of PSAs and NGOs, as discussed above, could certify the NMRAs that are following WHO standards and share this with the international community. However, in interviews with WHO respondents, it was clear that rating NMRAs is not a good option. There are 193 NMRAs to consider (193 member countries of the United Nations). The Vaccines Program system for rating NMRAs would not work for essential medicines simply because there are very few vaccines producers in very few countries. On the other hand, there are thousands of manufacturers of essential medicines in many countries. There would never be enough money and experts directed to this purpose, and even if enough resources were to be found, it would be very cost-inefficient since many NMRAs are so weak they would not reach SRA status for many years to come, if at all.

Four of nineteen respondents think the international community should continue accepting some NMRA medicine registrations because of the need to support local suppliers and to simultaneously improve the NMRA regulatory technical capacity; this would require a risk-based analysis of the key essential medicines. However, five of nineteen respondents said they would never accept medicine evaluations by NMRAs that are not SRAs since they have their own internal evidence showing big gaps in the capacity of these NRAs. Four of nineteen respondents agreed that the international community must encourage all NRAs to subscribe to the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) as a means of improving the inspection capacity of member regulatory authorities. However, all must keep in mind that PIC/S activities include GMP audits of manufacturers, not product evaluations.

The best path to becoming an SRA would be a stepwise approach. The steps might include clarification of the following, for example: (1) the bare essentials NMRAs should have; (2) activities at the regional level to promote NMRA becoming SRA (for example, combined inspections with other NRAs); (3) activities that should be done at the national level (for example, establishing a laboratory for product inspection and increasing capacity to inspect for GMPs). Finally, the question must be answered if promoting NRAs to SRA status can be done in a cost-effective manner.

Other recommendations from respondents suggested the best approach to poorly resourced countries is to develop a regional consortium of NMRAs so members would share resources for

registering medicines in their respective countries. WHO respondents suggested that the best way to do this is to first study how NMRAs could cooperate; then, using a risk-based classification of essential medicines, to specify product assessment criteria for each classification of medicines. The system for cooperation among NMRAs must be sustainable and able to provide functional assessments. Resources should not be wasted on activities that have no added value.

A 2004 WHO survey on medicine regulatory authorities in the African region reported that only 4 percent of the member states had developed national regulatory capacity, 33 percent had moderate regulatory capacity (that is, carried out most functions to varying degrees), and 24 percent had basic regulatory capacity (that is, carried out minimum functions). However, 39 percent of the member states had limited regulatory capacity, and the inspection of manufacturing premises, distribution outlets, and ports of entries in these member states was found to be weak or lacking.

The 2010 WHO report on 26 medicine regulatory systems in Sub-Saharan African countries shows the variation in organizational structures and implementation of regulatory functions, selected aspects of marketing authorization, import control, inspections, quality control, market surveillance, and control of clinical trials. Regarding marketing authorization, for example, a South region country provides detailed guidance information on format and content to registration applicants; has 11 expert advisory committees; works exclusively with qualified experts as external assessors (does not have full-time assessors); and recognizes decisions by a defined list of SRAs; however, assessments take 12 to 24 months. A Western region country provides brief but no technical guidance to applicants; follows SOP for assessments; has an advisory committee, external assessors, and sufficient full-time assessors; is supported with a computerized system (SIAMED); and requests certificates of pharmaceutical products. In another West region country, guidance to applicants is insufficiently detailed and outdated; the NMRA works with an advisory committee with no specific expertise, but has full-time assessors and QC laboratory staff as external assessors and insufficient full-time assessors; it does not recognize SRA decisions; and conducts mainly administrative reviews. Another country, in the East region, grants marketing authorization without dossier evaluation; does not provide guidance for applicants; does not have an advisory committee nor use external assessors; and does not recognize SRA decisions.

**WHO's Model Quality Assurance System (MQAS)**

Eleven of nineteen respondents commented on the need for an interagency group to revisit the MQAS model, including input from those currently using it. To some respondents, the MQAS was too complicated for their needs and resources. Most organizations using it today are not following it exactly and have adapted it to their needs. Use of the MQAS as an accreditation tool for PSAs was not accepted from the beginning because of cost implications and political and commercial considerations. The informal group that worked with the Interagency Pharmaceutical Cooperation Group would be a starting point to revisit the MQAS, since those using it subsequently incorporated aspects of the MQAS into their quality assurance programs. The

group would share how they are currently using the MQAS in their organizations and discuss how the MQAS could be modified to serve as an international model for harmonization. It would be important to clarify how substandard products often get through MQAS systems used today and also how substandard products have been identified using this system. The interagency group would then update the MQAS with 2011 criteria. This is because discussions of the current MQAS took place in 2003–04 and were published in 2007; also, these were intended as a guideline, not as a certification document. The updated MQAS should focus more on quality system evaluation, less on how to procure. Finally, to move to harmonization of QA procedures, all PSAs and NGOs interested in procuring essential medicines using donor funding would need to follow the updated MQAS procedures for their QA activities.

**Risk-based assessment of the WHO Model List of Essential Medicines (EML)**

Thirteen of nineteen respondents commented on the need for a risk-based analysis of the EML by WHO, including partners like the Global Fund and other experts from organizations such as MSF, IDA, UNICEF, USP, and QUAMED. Some of the ideas included having high-risk products prequalified only by WHO-PQ, SRA, and ERP mechanisms. Lower-risk products not approved by an SRA would be prequalified by PSAs, NGOs, and strengthened NPCs using a 2011 updated version of the WHO-MQAS. The remaining five respondents had different thoughts about the need for a risk-based analysis: a rating is not important because it would be unnecessary for countries not using those products. They thought it would be better to prioritize prequalifications based on a country's needs. Others said that for some older generics, there shouldn't be a safety risk since they have been marketed and produced for some time. They thought that in the latter case, preshipment quality testing would be sufficient.

WHO has completed a preliminary study of manufacturer-related risks and consequences to patients, to explore the development of a risk-based classification scheme for essential medicines. More work is needed to develop the classification and relate the groupings with a QA approach for each category of risk. Some thoughts on this so far are, as follows: (1) high risk—require more stringent quality assessment such as through WHO-PQ and SRA mechanisms; (2) medium risk—accept assessments by NRAs that meet certain criteria and expertise today, and require developing a system to determine that these assessments are reproducible and transparent; and (3) low risk—procure locally except in countries where NMRAs are considered the weakest. Next step would be for stringent NMRAs, like the U.S. Food and Drug Authority (FDA), to review the preliminary classification and make suggestions for modification, as needed.

**Centralized database for prequalified products and manufacturers**

Ten of nineteen respondents saw the need for a central database to maintain lists of prequalified manufacturers and products. In developing the database, consideration should be given to the following:

- PSAs are often competitors, and their QA system is a business aspect where they have committed money and human resources to establish the quality of products they procure; thus, there is need to clarify steps to change company policy so they could share.

- To the extent possible, organizations should share the different specifications for APIs and finished pharmaceutical products (FPPs).
- Identify what type of organization would manage or host the central database.
- The central database organization would not be a regulatory agency, and there should be no mandate to qualify products for donors or others.
- The database system should be designed to allow access only to the appropriate audience (for example, PSAs, NGOs), but simultaneously also prevent access to sensitive matter such as manufacturers' proprietary information.
- Manufacturer's approval should be obtained for inclusion in the database system; likely it would not be possible to make public the actual GMP audit reports, but it should be possible to publish the results of a positive GMP audit.

PSAs and NGOs may still require some form of QA activities to satisfy their organizations' policies. However, the centralized database would decrease the amount of QA time needed in proportion to the amount of published data in the database.

# Annex 6: Manufacturer–related Risks of Medicines

Manufacture-related risks of medicines and consequences to patients and methods of prevention or detection

| Manufacture-related risk | Adverse consequence | Prevention or detection method | | | EML example |
|---|---|---|---|---|---|
| | | Preregistration evaluation (study data) | Inspection to validate manufacturing procedure? | Quality control test | |
| Active pharmaceutical ingredient (API) is of biological origin | Multiple impurities<br>High content of each impurity<br>Microbial contamination<br>Endotoxins<br>Allergens<br>Multicomponent active ingredients (& consequently, possible variable potency) | Validation of methods of synthesis for API | Validation of manufacturing procedure for API<br>Validation of manufacturing procedure for finished pharmaceutical product (FPP) | Testing of API<br>Testing of FPP | Gentamicin injection<br>Erythromycin tablet |
| Sterility | Infection of patient | | Validated manufacturing procedure | Sterility test | Bupivacaine injection<br>Hydroxycobalamine injection |
| Life-threatening low potency | Low efficacy if potency is low or bioavailability is poor | | Validated manufacturing procedure | Assay test<br>Dissolution test | Streptokinase powder for injection<br>Enalapril tablet |
| Steep dose-response curve or narrow therapeutic index | Toxicity if potency is high<br>Low efficacy if potency is low<br>Low efficacy if bioavailability is low | Pharmacological data prior to first registration | Validated manufacturing procedure | | Digoxin tablet<br>Bisoprolol tablet |
| Low or variable GI permeability (including narrow absorption window) (for oral dosage forms) | Higher risk of poor bioavailability | Clinical data prior to first registration | | | Ciclosporin capsule<br>Methotrexate tablet |
| Low dose solid or semisolid dosage forms | Poor content uniformity may lead to variable efficacy and toxicity | | Validated manufacturing procedure | Assay of individual units | Digoxin tablet<br>Betamethasone cream |

| Manufacture-related risk | Adverse consequence | Prevention or detection method | | | EML example |
|---|---|---|---|---|---|
| | | Preregistration evaluation (study data) | Inspection to validate manufacturing procedure? | Quality control test | |
| Toxic impurities | Toxicity if contents of impurities are high and they lead to a demonstrated adverse effect | Validated method of synthesis<br>Stability testing | Validated manufacturing procedure | Assay in QC of API | Hydralazine powder for injection<br>Hydrocortisone injection |
| Low water solubility (oral dosage forms) | Higher risk of poor bioavailability | Chemical testing prior to first registration | | | Carbamazepine tablet<br>Dapsone tablet |
| Systemic antimicrobial (excludes disinfectants and topical antimicrobials) | Development of resistance if<br>a) potency is low<br>b) bioavailability is low<br>c) usage is profligate | | Validated manufacturing procedure | Assay tests<br>Appropriate use of antimicrobials | Doxycycline tablet<br>Ciprofloxacin tablet |
| Potential risk-mitigation approach | | Documentation-evaluation capability | GMP-inspection capability | Risk-based testing program | |

*Source:* Adapted from Annex 2, WHO & the Global Fund Joint Stakeholder Meeting on Quality Assurance of Essential Medicines, Chateau de Penthes, Geneva, August 30–31, 2011.

# Annex 7: WHO and the Global Fund Joint Stakeholder Meeting on Quality Assurance of Essential Medicines: Executive Summary and Recommendations

While stringent donor-driven quality requirements exist for antiretrovirals, antituberculosis medicines, and antimalarials (ATM medicines), regulatory marketing authorization in the country of use is currently the only formal requirement for most other essential medicines. Donors, procurement agents, and implementers are applying various additional measures to assure medicines quality, such as quality control testing and document reviews with various levels of insight and stringency.

However, most of these measures do not adequately verify whether quality is built into a pharmaceutical product and remains intact at every stage of its life cycle. In the absence of mechanisms to verify compliance of procured medicines with quality standards, the demand for essential medicines is essentially driven by price.

Harmonized, risk-based approaches are being introduced to achieve maximum impact of quality assurance (QA) measures as resources and independent technical expertise for pharmaceutical QA are becoming increasingly scarce worldwide. WHO is leading the work to categorize essential medicines into risk categories as a basis for QA measures in regulation and procurement. The WHO Model Quality Assurance System for Procurement Agencies (MQAS) defines commonly accepted standards, which can serve as a basis for an independent qualification system, making quality assurance in procurement a competitive advantage.

Donors, procurement agents, and implementers represented at the meeting recognized the importance of assuring the quality of life saving essential medicines to stringent standards. They were committed to define and enforce harmonized quality requirements for essential medicines together with the countries that they serve. In working toward this aim, meeting participants agreed on the following recommendations:

**Recommendation 1. Risk-based categorization of essential medicines**

WHO will continue its work, together with regulatory and industry representatives from relevant settings, to characterize risk factors for essential medicines and to develop a structured approach to allocate essential medicines to high-, medium- and low-risk categories. Stakeholders will be consulted on how to use these categories to define and prioritize quality assurance measures.

**Recommendation 2. Tool to assess procurement agencies**

1. Building on past work, an informal, voluntary working group consisting of representatives from QUAMED, PFSCM, UNICEF, MSF, IDA, Crown Agents, MSH, UNOPS, USAID, ICRC, and CHMP[52] facilitated by the Global Fund, will propose a practical tool to assess procurement agencies, based on the WHO-MQAS. Working group members will explore

[52] Centrale Humanitaire Medico-Pharmaceutique (CHMP), France

possibilities to contribute to funding for this work.

2. Once a harmonized assessment tool has been developed, WHO will provide expert input to ensure its consistency with the WHO-MQAS document[53] or subsequent revisions, and will formalize it as an instrument that can be used for qualification of procurement agencies by an independent body.

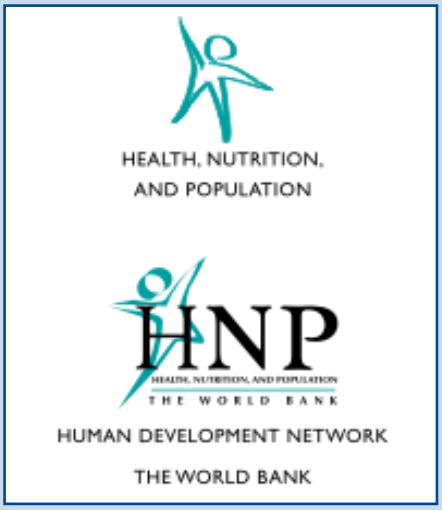
**Recommendation 3. Harmonization of quality assurance (QA) policies**

Stakeholders represented at this meeting will work toward harmonizing their QA policies for essential medicines to maximize the efficiency of their quality assurance measures and to generate a common demand for quality-assured medicines meeting defined standards to impact the market.

**Recommendation 4. Information-sharing**

WHO will host a website, which will be open to participants, to share information on manufacturing site inspections planned and completed by WHO and its partners, including date, site inspected, affiliation of the lead inspector, and the contact details of the person responsible for clarification.

53. "WHO and the Global Fund Joint Stakeholder Meeting Report," Geneva, August 30–31, 2011.




**About this series...**

This series is produced by the Health, Nutrition, and Population Family (HNP) of the World Bank's Human Development Network. The papers in this series aim to provide a vehicle for publishing preliminary and unpolished results on HNP topics to encourage discussion and debate. The findings, interpretations, and conclusions expressed in this paper are entirely those of the author(s) and should not be attributed in any manner to the World Bank, to its affiliated organizations or to members of its Board of Executive Directors or the countries they represent. Citation and the use of material presented in this series should take into account this provisional character. For free copies of papers in this series please contact the individual authors whose name appears on the paper.

Enquiries about the series and submissions should be made directly to the Editor Martin Lutalo (mlutalo@worldbank.org) or HNP Advisory Service (healthpop@worldbank.org, tel 202 473-2256, fax 202 522-3234). For more information, see also www.worldbank.org/hnppublications.

**THE WORLD BANK**

1818 H Street, NW
Washington, DC USA 20433
Telephone: 202 473 1000
Facsimile: 202 477 6391
Internet: www.worldbank.org
E-mail: feedback@worldbank.org