USAID Office of Foreign Disaster Assistance
Pharmaceutical Wholesaler Precertification Project

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RPM Plus works in more than 20 developing and transitional countries to provide technical assistance to strengthen pharmaceutical and health commodity management systems. The program offers technical guidance and assists in strategy development and program implementation both in improving the availability of health commodities—pharmaceuticals, vaccines, medical supplies, and basic medical equipment—of assured quality for maternal and child health, HIV/AIDS, infectious diseases, and family planning and in promoting the appropriate use of health commodities in the public and private sectors.

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LIST OF ABBREVIATIONS

BP	British Pharmacopoeia
cGMP	Current Good Manufacturing Practices
COA	Certificate of Analysis
ECHO	European Commission's Humanitarian Aid Department
EP	European Pharmacopoeia
EOI	expression of interest
GDP	Good Distribution Practices
GH/HIDN	Global Health, Office of Health, Infectious Diseases and Nutrition
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
HPLC	high-pressure liquid chromatography
ISO	International Organization for Standardization
IDA	International Dispensary Association
INN	international nonproprietary name
IP	International Pharmacopoeia
MSF	Médecins sans Frontières
NDRA	National Drug Regulatory Authority
NGO	nongovernmental organization
OAA/T	Office of Acquisition and Assistance, Transportation Branch [USAID]
OFDA	Office of Foreign Disaster Assistance [USAID]
PAHO	Pan American Health Organization
PFSCM	Partnership for Secure Chain Management
PIC/S	Pharmaceutical Inspection Cooperation Scheme
PSA	procurement services agency
PVO	private voluntary organization
RFP	request for proposal
SCMS	Supply Chain Management System
SOP	standard operating procedure
SDRA	Stringent Drug Regulatory Authority
FDA	U.S. Food and Drug Administration
USAID	U.S. Agency for International Development
USG	U. S. Government
USP	United States Pharmacopeia
WHO	World Health Organization

GLOSSARY

Disaster: A serious disruption of the functioning of a community or a society causing widespread human, material, economic or environmental losses which exceed the ability of the affected community or society to cope using its own resources

Certification: The process of confirming that a supplier complies with specified requirements and is acceptable for operational use

Good Distribution Practice: That part of a quality assurance system involving the medicine distribution channel from point of medicine manufacture to the end user

Good Storage Practice: That part of a quality assurance system that includes storage of products up to the point of use

Good Manufacturing Practice: That part of quality assurance that ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing organization

Nongovernmental organizations(as defined by USAID): "Any private or nonprofit entity that is formed or organized independently from any national or local government entity. These can include for-profit firms, academic degree-granting institutions, universities and colleges, labor institutions, foundations, private voluntary organizations, and cooperative development organizations." [1]

Institution within the nonprofit or independent sector that generally are not part of any government but can include organizations that are government and corporate funded.

Precertification (also prequalification): The assessment for acceptability of suppliers within set parameters as applicable

Private voluntary organization (as defined by USAID): "A tax-exempt, nonprofit organization working in, or intending to become engaged in, international development activities. These organizations receive some portion of their annual revenue from the private sector (demonstrating their private nature) and voluntary contributions of money, staff time, or in-kind support from the general public (demonstrating their voluntary nature). USAID refers to non-governmental organizations as private voluntary organizations."

Quality assurance: The overall medicine management plan to ensure that quality requirements for a product or service will be fulfilled

Quality control: A series of analytical measurements carried out according to SOPs to ensure that medicine products meet predetermined, quality acceptability standards

[1] A USAID Resource Guide for Private Voluntary Organizations, October, 2004

Recertification (also requalification): The process of reconfirming acceptability of suppliers within set parameters as applicable

Site master file: A document that provides comprehensive information relative to pharmaceutical manufacturer general information as well as details relative to production and control of manufacturing operations. For the purposes of this report, manufacturer and product information collected by a pharmaceutical wholesaler as part of its manufacturer prequalification process.

INTRODUCTION

In 2006, the U. S. Agency for International Development (USAID), Office of Foreign Disaster Assistance (OFDA), requested assistance from Management Sciences for Health (MSH) Center for Pharmaceutical Management (CPM) to develop a process for precertification of pharmaceutical wholesalers. CPM was asked to prepare a report that would provide criteria (and justification) and draft procedures that OFDA could use to precertify pharmaceutical wholesalers as a source for essential medicines and supplies (FDA and non-FDA approved) for purchase by USAID-funded nongovernmental organizations (NGOs) in developing countries. The criteria were to include transparent standards to afford OFDA the confidence that a pharmaceutical wholesaler satisfying and maintaining the standards will meet USAID minimum standards for pharmaceutical safety, efficacy, quality, and delivered cost.

Where there are acute and immediate requirements for health commodities, precertification of wholesalers as an approved source of pharmaceuticals and supplies would streamline the process of reviewing and approving requests from implementing partners. A precertification process and associated USAID source/origin waiver would also improve efficiency in delivery of health commodities and assure USAID that required supporting documentation was available for reimbursement of essential medicines purchased by an implementing partner for health care interventions.

Report Objectives

The report objectives include—

- Describing a precertification process, including a review of pharmaceutical wholesaler/procurement service agency efforts documented by international organizations
- Preparing criteria and justification, including source documents, that could provide the structure for a wholesaler precertification process that is relatively simple to administer
- Developing draft tools and procedures to precertify wholesalers including beta testing at several domestic and international wholesalers
- Identifying options for implementing a wholesaler precertification program
- Providing options for implementing and managing a pharmaceutical wholesalers' database that can be easily accessed by authorized users and includes performance monitoring

Methodology

This report is based on research on existing literature, documents, reports, and processes regarding precertification or regulation of suppliers, manufacturers, products and procurement of medicines and medical supplies. This research was supplemented by information received from various regulatory, humanitarian, and procurement organizations via e-mail, interviews, and site visits. Pharmaceutical wholesaler precertification prescreening and site inspection tools (see Appendices A and B) stemming from the research were beta tested (see note below) and refined with the assistance of international and regional/local pharmaceutical wholesalers that included:

Two based in the United States—

- MedPharm, Alexandria, VA
- Nubenco, Paramus, NJ

Four based in Europe—

- UNICEF, Copenhagen, Denmark
- MissionPharma, Copenhagen, Denmark
- IDA Foundation, Amsterdam, Netherlands
- Amstelfarma, Amsterdam, Netherlands

Four based in Nairobi, Kenya—

- Mission for Essential Drugs and Supplies (MEDS)
- Omaera Pharmaceuticals
- Phillips Pharmaceuticals
- Lords Healthcare Limited

Additionally, representatives from the World Health Organization (WHO) and the European Commission's Humanitarian Aid Department (ECHO) reviewed draft prequalification tools and provided valuable comments.

Note: A summary of pharmaceutical wholesaler precertification findings and recommendations from brief visits to several international and regional/local wholesalers is attached in Annex A**.**

BACKGROUND

The USAID is the independent federal government agency that provides foreign assistance and humanitarian aid to advance the political and economic interests of the United States. USAID contributes to national interests by supporting people from developing and transitional countries in their efforts to achieve sustained economic and social progress and to participate more fully in resolving the problems of their countries and the world. When an international disaster occurs, USAID coordinates the U.S. Government (USG) response with the affected country, other donor governments, international organization, United Nations (UN) relief agencies, and private voluntary and nongovernmental organizations (PVOs and NGOs)

The Office of Foreign Disaster Assistance (OFDA) whose mission is to "Save lives, alleviate suffering and reduce the economic impact of disasters" coordinates USG responses if—

- It is beyond the affected country's ability to respond
- The affected country requests (or will accept) outside assistance
- It is in the USG's interest

Disaster relief can incorporate assistance to address various needs, including health and nutrition. OFDA works with local PVOs or NGOs who may request USAID funding for procurement of health commodities including essential medicines, vaccines, medical equipment, and medical supplies.

While USAID funds may be used by a PVO or NGO and Missions to purchase U.S. Food and Drug Administration (FDA)-approved essential medicines from U.S. sources, if non-FDA approved medicines are to be purchased, OFDA has the authority to grant a waiver on a case by case basis. For waiver consideration, procurement requests must include documentation that products being considered for purchase are—

- Essential for the planned intervention
- Not available from a U.S. source
- At least 50 percent less than the delivered cost of an equivalent U.S medicine
- Compliant with pharmaceutical procurement procedures outlined in USAID's Automated Directives System (ADS) 312.5.3c[2] regarding source or origin requirements and patent infringement

A copy of the draft OFDA essential medicines approval process consisting of a waiver phase and final authorization or approval phase is attached (Annex B).

[2] ADS 312.5.3c: www.usaid.gov/policy/ads/300/312.pdf

Experiences with International Precertification/Prequalification

Manufacturer prequalification schemes have been implemented by a number of international organizations, based partly on standards and guidelines developed by the World Health Organization (WHO) and the FDA. However, many nonprofit and for-profit health agencies use procurement agencies, pharmaceutical wholesalers, and distributors (sometimes referred to as secondary suppliers) rather than manufacturers to supply their medication requirements. Recognizing this situation, WHO has taken the lead in developing a model quality assurance system for procurement agencies.[3] Other organizations such as Médecins sans Frontières (MSF), Pan American Health Organization (PAHO), European Commission's Humanitarian Aid Department (ECHO), and USAID/Partnership for Secure Chain Management (PFSCM) have undertaken independent efforts to implement a pharmaceutical wholesaler prequalification process. These organizations recognize that prequalification of so-called secondary pharmaceutical suppliers is needed to assure that products offered for sale meet international standards for safety, efficacy, and quality.

Note: Pharmaceuticals are produced by a manufacturer operating under good manufacturing principles. This manufacturer's medicines may be purchased or distributed by a wholesaler who purchases directly from the manufacturer—this is known as the primary pharmaceutical wholesaler. The primary pharmaceutical wholesaler may in turn sell the same product to another pharmaceutical wholesaler that is known as the secondary wholesaler. This process may be repeated numerous times and may provide the opening to allow counterfeit or substandard pharmaceuticals to enter the supply chain. This is the primary reason for precertifying pharmaceutical wholesalers; so that they are able to vouch for or guarantee that there is a direct chain of custody or pedigree for the pharmaceutical product back to the manufacturer, regardless of the number of pharmaceutical wholesalers involved in the distribution chain.

As noted above, WHO has prepared detailed recommendations for assessing procurement service agencies that include—

- General requirements for procurement agencies
- Prequalification
- Purchasing
- Receipt and storage of purchased products
- Distribution
- Reassessment

The recommendations were officially adopted in 2006; however, there is no plan for WHO to assess procurement agencies/wholesalers.[4] On the other hand, groups such as MSF,[5] PAHO,[6]

[3] "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)", WHO Technical Report Series, No.937, 2006, Annex 6.

[4] Personal communication from Rago Lembit, Coordinator, Quality Assurance and Safety: Medicines, Medicines and Standards, World Health Organization, October 2006.

[5] E-mail communication with Cecile Mace, MSF International Pharmacists Coordinator, September 2006.

[6] PAHO Policy in the Procurement of Pharmaceutical Products for Projects Financed by the Global Fund to Fight HIV/AIDS, Tuberculosis and Malaria.

ECHO,[7] and PFSCM have prequalified or are making progress toward prequalification of secondary pharmaceutical suppliers/distributors/wholesalers.

In the case of MSF, local pharmaceutical distributors are primarily used for small purchases. Distributors are requested to provide product information such that MSF can assess the source and then approve or disapprove purchase. They require that a distributor must be licensed by the National Drug Regulatory Authority (NDRA) and must have a pharmacist in charge of quality assurance. In addition, the supplier is inspected to assure compliance with Good Distribution Practices (GDP) and have a quality assurance program in place with specific procedures to select sources of medicine in accordance with WHO recommendations. A communication with the former MSF International Pharmacists Coordinator revealed that the MSF Quality Assurance System was expected to be posted on the MSF website by the end of the 2006, but to date it has not been made available.[8]

Information from PAHO is limited. Their pharmaceutical prequalification policy for procurement of multisource products from secondary suppliers simply states that "suppliers have been pre-qualified by PAHO who provide evidence from the NDRA that they conform to current Good Manufacturing Practices (cGMP) and apply standards in quality assurance and control to the products they are selling."[12]

ECHO recognized that many of their partner NGOs may not have a clear understanding of ECHO procurement procedures for medicines and medical supplies. So they launched a program of pre-qualifying wholesalers based largely on financial criteria including internal control systems, accounting rules, and procurement rules, to assist their partners. Procurement organizations that apply for Humanitarian Procurement Center status and meet strict ECHO selection criteria are designated as Humanitarian Procurement Centers. During the visit to ECHO headquarters, Pablo Ibanez, Deputy Head of Unit for Finance Management, Legal and Procedural Affairs, discussed that the quality of medicines and medical supplies was recognized as an important factor in mitigating risk but ECHO lacks the resources to assure quality; therefore, partners must assume the responsibility to assure quality of procured pharmaceuticals. As part of ECHO's commitment to NGO partner capacity building, a review of quality assurance mechanisms for medicines and medical supplies was commissioned, and the concept paper,[9] including recommendations, was presented at an ECHO sponsored conference in Brussels this past December.

The PFSCM, Arlington, VA, a group that was awarded USG's Supply Chain Management System (SCMS) contract, has received a USAID source/origin waiver that approves SCMS to procure specific multisource pharmaceuticals from International Dispensary Association (IDA), Missionpharma, and the United Nations Children's Fund (UNICEF). The waiver was based on prior USAID experience with these wholesalers and a briefing report prepared by a USAID/SCMS team that visited each of the three pharmaceutical wholesalers. The Action

[7] Personal Communication, Bianca Kamps, International Dispensary Association, August 2006.
[8] E-mail communication, Jean-Michel Caudron, MSF Consultant, October 2006.

[9] Review of Quality Assurance (QA) Mechanisms for Medicines and Medical Supplies in Humanitarian Aid, Veronique Pomatto and Claudio Schuftan, GFE Consulting Worldwide, June 2006.

Memorandum[10] providing waiver approval states that the three suppliers "all have extensive experience in procuring, distributing, and monitoring the quality of pharmaceuticals, medical equipment, and supplies in least developed countries throughout the world." In addition, as part of SCMS efforts to ensure medicine quality, the waiver includes a clause providing SCMS with the right to routinely conduct laboratory testing of procured pharmaceuticals from these sources. The Action Memorandum also states that USAID's Office of HIV/AIDS (OHA)/ SCMS is working with Global Health, Office of Health, Infectious Diseases and Nutrition, USAID's Office of Acquisition and Assistance, Transportation Branch (OAA/T), and OFDA on objective standards to pre-qualify other pharmaceutical wholesalers. Based upon a conversation with a SCMS representative, this is still under development.[11]

Problem Statement

- When a disaster occurs and a government requests for assistance, there is often a request for medicines.
- If medicines are required, local PVOs/NGOs (requesting agencies) supported with USAID funds frequently propose to purchase medicines from local wholesalers/distributors.
- In almost all cases, these medicines are not FDA-approved and requesting agencies may not know if a wholesaler or the non-FDA-approved medicines it supplies meet international standards with regard to proper storage, distribution, safety, quality, efficacy, or USAID price requirements.
- This could potentially lead to inadvertent purchase of counterfeit or substandard/potentially dangerous medicines, or medicines that exceed cost requirements for non-U.S. source medicines.
- Requesting agencies are required to obtain a waiver or pre-approval for the purchase of non-FDA-approved pharmaceuticals prior to procuring medicines from wholesalers or manufacturers.
- As the waiver process requires considerable information, there may be significant delays while documentation is collected. As a result, emergency pharmaceuticals and medical supplies may be delayed.
- Requesting agencies "consistently do not provide all USAID-required documentation for (OFDA) final approval (and waiver approval) of essential medicine purchases."[12] If documentation is incomplete, OFDA will reject reimbursement to the NGOs for purchased pharmaceuticals.

[10] Action Memorandum, Subject: Source/Original Waiver for Certain Pharmaceuticals under Partnership for Supply Chain Management Service (PRSCM) Contract approved September 2006.
[11] Personal communication with David Jamieson, PFSCM, January 2007.
[12] USAID Essential Medicines Procurement Activity, Precertification of Pharmaceutical Wholesalers, Draft Concept Paper, May 2, 2006.

OFDA precertification or pre-approval of pharmaceutical wholesalers and products they supply could enhance procurement efficiency and, at the same time, allay concerns about product safety and quality. However, a USG pharmaceutical wholesaler precertification process with objective standards has not yet been approved although, as mentioned earlier, an USAID waiver has been approved that provides the basis for approving three pharmaceutical wholesalers.[13] It is therefore the principal objective of this report to provide objective criteria for evaluating and precertifying pharmaceutical wholesalers as a source for OFDA partner procurement of essential medicines and supplies for use in developing countries.

[13] "Based upon agency experience and an inspection visit by a USAID team (trip report attached as Annex D, these pharmaceutical wholesalers (IDA, Missionpharma, UNICEF) have systems in place that adequately address quality assurance of non-FDA approved products and that under ADS 312 information is available to attest to the safety, efficacy, and quality of products they offer," extracted from Action Memorandum, Subject: Source/Origin Waiver for Certain Pharmaceuticals under Partnership for Supply Chain Management (PFSCM) Contract, September 2006.

PHARMACEUTICAL WHOLESALER PRECERTIFICATION FRAMEWORK

Definition

For OFDA purposes, precertification of pharmaceutical wholesalers is intended to be a formal transparent process to develop a list of pharmaceutical suppliers meeting USAID requirements for product source eligibility, safety, efficacy, and quality. This would streamline the pharmaceutical procurement process for PVOs and NGOs, and facilitate the OFDA waiver approval process. Precertification of non-U.S. wholesalers could also provide the background information necessary for USAID issuance of a blanket source or origin waiver (for specified pharmaceutical wholesalers and the products they supply).

Process

The backbone of a pharmaceutical wholesaler precertification process is built upon developing justifiable, uniform, transparent criteria that can be efficiently applied to evaluate wholesaler operations. Criteria are needed to assess two major elements—those linked to operational infrastructure and those linked to assuring product quality, safety, and efficacy. Wholesaler operational infrastructure criteria include financial viability, physical premises, warehousing, storage, and distribution. For products, criteria should address procurement practices to ensure that medicines meet USAID price, safety, quality, and efficacy standards. Satisfaction of pre-established criteria is the basis by which a pharmaceutical wholesaler can be certified.

Upon approval of criteria by a process to be delineated by USAID, the primary activities leading to OFDA certification of a wholesaler follow—

Drafting and Publication for Expressions of Interest (EOI)

The EOI should be in accordance with USAID regulations, and available to any pharmaceutical wholesaler desirous of gaining OFDA precertification. Its content should include—

- Purpose, objectives, and indication of the type of information to be submitted
- Procedure for submission of EOI
- Respondent contact details
- Final date for receipt by OFDA unless a “rolling” precertification process is elected (i.e., not a single cut-off date)

A sample draft EOI is included in Annex B.

Evaluation of Precertification Screening Application

The intent of the pharmaceutical wholesaler precertification screening application (see draft attached as Annex E) is to gather detailed information about the wholesaler's viability, operational capability, and systems and product quality. A scoring system needs to be devised to enable a quantifiable basis for—

- Immediate approval of and/or moving toward the site inspection phase
- Request for additional information (if application is incomplete or further explanation is needed)

An alternative option to prescreening and inspection is to grant precertification to a pharmaceutical wholesaler based upon recent inspection and certification by an USAID-approved international inspection team. This is described in the section on OFDA options for implementation.

Site Inspection—Verification of Operational Infrastructure

The purpose of a site inspection is to validate the information contained in the pharmaceutical wholesaler prescreening application. If an on-site inspection is to be performed for an initial inspection, the wholesaler should be provided with an overview of the inspection process and type of documentation that may be requested (e.g., provide a copy of the Pharmaceutical Wholesaler Site Inspection Guide, Annex F). To obtain a realistic view of wholesaler operations, rather than providing a specific inspection date, it probably would be better to state the period of time, such as between the months of "X" and "Y," when an unannounced inspection is to occur. As in the case of the precertification screening application, there should be a quantifiable basis for certification or denial. There may be a case for provisional precertification in the event that the inspector(s) determine that an applicant can correct deficiencies and provide evidence of within a short period of time (i.e., less than 30 to 60 days). If denied, the wholesaler should receive information on deficiencies requiring attention.

While site inspection can confirm that policies, guidelines, and SOPs meeting international standards for prequalification of manufacturers and products, good procurement practice, good storage practice, good distribution practice, and product/systems quality assurance are in place, the ability to store and efficiently retrieve all relevant data and documents cannot be understated. The wholesaler should be able to demonstrate that it has a management information system in place that can document compliance with the standards and procedures specified in its SOPs. Of paramount importance is the wholesaler's capability to provide documents illustrating that the chain of custody for all medicines from the source (manufacturer) to the end user has not been compromised.

On-going Monitoring and Recertification

It is important for OFDA to ensure that a precertified wholesaler maintains quality of services and products. A system should be in place to monitor and record wholesaler performance. Such a

system might include information requested from and supplied by clients (PVOs/NGOs) and unannounced or scheduled site recertification inspections.

Systematic Tracking

A database should be designed to maintain site master files for all approved and pending/unapproved applicants. In addition, the database for precertified pharmaceutical wholesalers should allow for performance tracking. Performance tracking elements could include reliability (product availability and timeliness of delivery), product quality complaints, customer service, and repeat product testing. However, performance data is valuable only if used in the context of an evaluation process that includes transparent criteria.

Summary

The proposed OFDA pharmaceutical wholesaler precertification process is fairly straight forward and is similar to the steps that are recommended by WHO for prequalifying pharmaceutical manufacturers and their products.[14] It includes—

- Solicitation and receipt of an EOI followed by issuance of wholesaler guidelines for submitting information
- Evaluation of wholesaler organization, financial standing, range of products and system operations for supplier and product prequalification, procurement, storage, quality assurance, and quality control
- Site inspections if determined necessary
- Finalization of the precertification assessment
- Continuous tracking of goods and services supplied to ensure the integrity of supplied products.

[14] "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)", WHO Technical Report Series, No.937, 2006, p. 233

PHARMACEUTICAL WHOLESALER PRECERTIFICATION CRITERIA

Introduction

Criteria are standards, rules, or tests on which a judgment or decision may be based. For the purpose of OFDA pharmaceutical wholesaler precertification, meeting uniform, justifiable criteria will provide the confidence required that wholesaler operations are conducted in accordance with Good Distribution Practices (GDP) for Pharmaceutical Products[15] and Good Storage Practices (GSP).[16] In this manner, the risk of products procured not meeting international standards with regards to pharmaceutical safety, efficacy, and quality is minimized.

A formal process of supplier qualification and monitoring is one aspect of good pharmaceutical procurement practices[17] and may involve pre- or post-qualification activities using transparent criteria or standards for evaluating supplier capability to procure pharmaceuticals of defined quality. Supplier considerations include business viability, service reliability, compliance with good storage and distribution practices, ongoing quality assurance/management systems to ensure maintenance of product quality and a management information system that can reliably provide documentation to support all facility operations (e.g., prequalification of suppliers and products, procurement, storage, distribution, quality assurance.). Since it is OFDA's desire to improve the efficiency in managing emergency procurement and waiver processes, only a prequalification or precertification process rather than post-qualification makes sense.

Assuring the quality of medicines is a worldwide concern. There has been considerable quality assurance system work and particularly with prequalification procedures by a number of international organizations (e.g., WHO, MSF, GFATM, World Bank), most typically but not exclusively pertaining to manufacturers rather than wholesalers or a procurement service agency (PSA). In developing draft criteria for wholesaler precertification, available international prequalification background documents were reviewed and important common elements were incorporated into the criteria. It stands to reason that any pharmaceutical wholesaler serving as a source for USAID-funded medicines must meet internationally accepted minimum procurement standards.

In applying criteria to a pharmaceutical wholesaler prescreening or site inspection process, quantitative assessment methodology should be developed, such as a numerical or descriptive system that indicates that standards have been met, exceeded, partially met, or have not been met. For some criterion, if not met, this could be grounds for non-acceptance or at the very least, a request for further explanation or action on the part of the applicant, but for others that are not quite as critical, partial compliance could be acceptable.

[15] Annex 9, Good Distribution Practices (GDP) For Pharmaceutical Products, World Health Organization working document, Rev. 2, 2005
[16] Guide to good storage practices for pharmaceuticals, WHO Technical Report Series, No. 908, 2003
[17] Managing Drug Supply, Management Sciences for Health, p.170-1, 2nd Edition

Criteria

The recommended criteria are divided into two broad categories—

- Assessment of premises/internal operations
- Assessment of activities related to product quality

Included in premises evaluation are financial capacity/viability/organizational structure and operations including, procurement, receipt and storage, distribution, and record keeping/management information system. For products, criteria are applied to manufacturer/supplier prequalification and quality assurance, although the latter is also pertinent to all wholesaler activities.

Premises Criteria

Financial Capacity/Viability/Organizational Structure

The applicant should be able to demonstrate that it has sufficient annual turnover to maintain adequate inventories of essential medicines listed in its catalogue and to fund day to day operations. Financial audits should be conducted on a regular basis,[18] preferably by an independent agency, and should be available for review to determine if funds are available to ensure product availability and quality. Consideration might be given to requesting average inventory and out-of-stock duration for all products listed in the wholesaler's catalogue. This would provide further confirmation of an applicant's ability to meet client requirements. It is worth remembering that "the lack of modern financial management, accounting systems, and management and supervisory responsibility has doomed many pharmaceutical systems to failure."[19]

Applicants shall provide a list of all major clients. If clients include governments and PVO/NGO, agencies, or organizations that are known to procure medicines of known safety, efficacy, and quality (e.g., USG, United Nations Agencies, WHO, Global Fund to Fight AIDS, Tuberculosis and Malaria [GFATM]), this is a definite plus.

The applicant shall provide a list of key personnel and qualifications for the five functional operational units—supplier prequalification, procurement, storage, distribution, and quality assurance. For obvious reasons, responsibility for prequalification and procurement should not be shared by the same person. All personnel should have job descriptions and an organizational chart that reflects lines of responsibility should be available. As per the requirement of most regulatory authorities, at least one person on the staff should be a supervising pharmacist. All key staff should have experience and, ideally, have a background in their respective area(s) of responsibility.

[18] WHO Technical Series Report Series, No. 937, 2006, p.221
[19] Management Sciences for Health. *Managing Drug Supply*, Chapter 13, Managing Procurement, p. 175. 2nd Edition

Licensure

As confirmation that the applicant is approved to supply pharmaceuticals and supplies for human (or animal) use, proof of current pharmaceutical wholesaler license issued by a national and preferably, stringent drug regulatory authority (SDRA)[20] is mandatory.

Procurement

To help ensure that standards of pharmaceutical quality are met, the pharmaceutical wholesaler should have written procurement SOPs that are in line with good procurement practices such as those recommended by WHO.[21,22] SOPs should state that only prequalified pharmaceutical products linked to a prequalified manufacturer are purchased. In addition, the wholesaler must require the manufacturer to provide certain source or "pedigree" documents to authenticate or trace the source and origin of pharmaceuticals it provides for sale. This includes but is not necessarily inclusive of Certificate of Analysis (COA) corresponding to product specifications, such as British Pharmacopoeia (BP), U.S. Pharmacopeia (USP), and European Pharmacopoeia (EP), International Pharmacopeia, and manufacturers' invoice corresponding to batch shown on the COA. If products for sale are relabeled by the wholesaler, the label should include the name of the original manufacturer and batch number on label should be traceable to the original manufacturer's batch number as indicated on its COA.

Receipt and Storage

Written SOPs should address receipt and storage of all products. Storage areas including those designated for receipt, quarantine, general storage, cold storage, controlled medicines, hazardous materials, and damaged or recalled products shall be maintained and operated consistent with FDA, WHO, or SDRA principles of applicable Good Manufacturing Practices (GMP) and good storage practices (GSP) and documentation of same should be available.

Distribution

Written SOPs should be in line with principles of good distribution practice similar to those promoted by SDRA or WHO. The applicant should maintain readily retrievable records that provide acceptable documentation from point of supply to end user including—

- Certificate of pharmaceutical product

[20] USAID practice is that a SDRA is a national drug regulatory authority that closely resembles FDA in its operations. Currently, USAID has designated as SDRAs the NDRAs that participate in the International Conference on Harmonization (ICH) and observers to the ICH (Canada). Source: Action Memorandum, Subject: Source/Original Waiver for Certain Pharmaceuticals under Partnership for Supply Chain Management Service (PRSCM) Contract approved September 2006.

[21] Practical Guidelines on Pharmaceutical Procurement for Countries with Small Procurement Agencies. WHO, Regional Office for the Western Pacific, Manila, Philippines, 2002.

[22] WHO Expert Committee on Specifications for Pharmaceutical Preparations, Technical Report Series 937, Fortieth Report, Annex 6, 2006.

- COA corresponding to batch that included testing against defined standards (BP, USP, IP] EP), GMP certificate consistent with FDA cGMP, or WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce

- Packing list and/or shipping invoice that includes, at a minimum, international non-proprietary name, formulation, strength, unit size, pack size, batch number(s), date of manufacture and expiry, price per unit, and extended price and invoice shall be issued with each consignment.

Prior to shipment, the wholesaler shall ensure that either all products are registered in the consignee country or an import waiver obtained by consignee has been obtained.

Management Information System/Record Keeping

The wholesaler shall be able to demonstrate that its management information system provides documentation that it is operating in compliance with the standards and procedures specified in its SOPs. Of major importance is the wholesaler's capability to provide documents illustrating chain of custody for all medicines from the source (manufacturer) to the end user. If a secondary supplier is a source for product(s), said supplier will provide the wholesaler with records to assure that the chain of custody for any product(s) so sourced has not been compromised.

Product and Manufacturer Assessment Criteria

Prequalification of Suppliers and Pharmaceuticals

For non-approved FDA or WHO approved manufacturing sites and pharmaceuticals, the pharmaceutical wholesaler should have current written SOPs for prequalifying manufacturers and their products to reduce risk of procuring a substandard product. If an applicant wholesaler procures product from another pharmaceutical wholesaler (secondary wholesaler), there should be evidence that the secondary wholesaler follows prequalification procedures in line with international prequalification guidelines such as those published by WHO.[23] The process of wholesaler prequalification includes an assessment of manufacturer and product documentation to determine compliance with wholesaler predetermined product specifications (e.g., BP, USP, EP, IP) and GMP similar to those specified by the FDA or WHO. Product prequalification should be linked to a specific manufacturing site or if multiple sites are used, each location requires a separate assessment.

Site Inspections

Once a wholesaler's manufacturer site master file and product dossier(s) are complete and approved, depending upon various factors such as whether the manufacturer and products are or are not SDRA approved (SDRA as defined by USAID), it may be necessary for the wholesaler's inspection team (internal or contracted) to perform a formal GMP audit of the manufacturing site that is in line with FDA or WHO cGMP guidelines. This inspection must include verifying

[23] A Model for Quality Assurance System for Procurement Agencies, Appendix 6 and 8, WHO Technical Series, No. 937, 2006

information included in previously submitted manufacturing site and product questionnaires. All inspectors should have a background and preferably formal training in GMP inspections. Documented results of the inspection should be available to indicate manufacturer compliance with cGMP and specifically that product(s) to be procured are manufactured in accordance with wholesaler specifications.

As one indication of the comprehensiveness of the pharmaceutical wholesaler's prequalification program, the total number of manufacturer inspections and rejections shall be indicated for the past three years. In addition, there should be a specified frequency of manufacturer/product recertification.

Quality Management

Each pharmaceutical wholesaler wishing to become precertified must document that a quality management system is in place to ensure the safety, efficacy, and quality of all medicines sold to the end user. This quality management system shall encompass all aspects of wholesaler operations including manufacturer and product prequalification, procurement, storage and distribution. A quality manual shall be available that provides detailed Standard Operating Procedures (SOPs) for all previously mentioned wholesaler activities. Quality assurance practices shall be in line with the main principles of FDA or WHO guidelines on GMP for pharmaceutical practices.

Note: Certification from organizations, such as the International Organization for Standardization (ISO), that reflect adherence to international standards and guidelines related to "quality management"(example ISO 9000:2001)[24] provide evidence that an applicant's operations meet high quality standards.

Product Quality Assurance

The pharmaceutical wholesaler shall retain samples of all purchased pharmaceutical batches for a specified time beyond stated product expiry or shall ensure that the manufacturer assumes this responsibility. This is necessary for the wholesaler to respond to possible product complaints by a client or for purposes of random sampling.

Upon receipt of all pharmaceutical consignments, a product verification process should be in place to include at a minimum—

- Physical inspection of samples from each batch
- Comparison of COA against pre-established finished product specifications
- A procedure for random sampling of medicines submitted for laboratory analysis according to international pharmacopeial standard or manufacturer specified standard if no international standard exists

[24] Source: International Organization for Standardization: http://www.iso.org/iso/en/iso9000-14000/understand/basics/general/basics_4.html

Internal or contracted laboratory should be in compliance with principles of good laboratory practice (GLP).

Note: As part of wholesaler precertification or recertification, inspectors may obtain medicine samples for independent quantitative analysis.

Summary

Ultimately, the goal of pharmaceutical wholesaler precertification is to ensure that a sustainable, replicable, systematic evaluation of pharmaceutical products results in affordable quality pharmaceuticals or, at least, minimizes risk of providing a substandard or, in the worst case scenario, counterfeit product. In the instance of the OFDA, precertification should provide an objective basis for gaining USAID blanket source/origin waiver approval for precertified wholesalers and the pharmaceuticals they sell. It is critical that if the pharmaceutical wholesaler precertification system is to achieve an acceptable level of medicine quality, it must be built upon a set of transparent, defensible standards or criteria that address all aspects of wholesaler operations that may impact medicine quality, safety, and efficacy. Criteria are necessary such that an applicant can demonstrate that it is a financially viable organization with qualified personnel in sufficient numbers to seamlessly carry out all pharmaceutical wholesaler activities ranging from prequalification of manufacturers/suppliers and their products to internal operations associated with procurement, receiving, storage, security, sanitation, distribution, product recall, and quality assurance. It also must maintain a management information system that can provide all required documentation that demonstrates adherence to its standard operation procedures.

OFDA OPTIONS FOR IMPLEMENTATION

Introduction

The implementation of a pharmaceutical wholesaler prequalification process includes the steps described in the wholesaler precertification framework section. Depending upon the human resources and budget available to OFDA, there are two primary implementation options—keep the process internal to OFDA or subcontract all or part of the processes to one or more agencies or consultant groups.

In considering implementation options, bear in mind how OFDA/USAID pharmaceutical wholesaler precertification might be viewed by groups outside of the United States. Many international organizations purchasing medicines from pharmaceutical wholesalers/distributors/procurement service agencies or who might recommend pharmaceutical suppliers to their partners face complicated political and resource shortfall issues (human and financial) in regard to precertification. These organizations would welcome a precertification program.[25]

While a U.S.-managed pharmaceutical wholesaler precertification scheme will likely be viewed positively by U.S. agencies and various organizations procuring medicines; international acceptance would be enhanced if responsibility for precertification was shared with or assumed by an independent international organization or consortium of organizations with personnel experienced in establishing and monitoring pharmaceutical manufacturing and product standards.

Strict application of criteria consistent with FDA or WHO guidelines would likely result in precertification disapproval for many local wholesalers/distributors who have previously supplied USG-funded PVOs/NGOs and other international agencies. An abrupt discontinuation of business with long-standing suppliers resulting from lack of precertification could become a thorny issue for the suppliers, host nation government, and local U.S. Missions.

On the other hand, pharmaceutical wholesaler knowledge that precertification will be required could stimulate movement toward meeting internationally accepted guidelines, particularly for those wholesalers with significant USG business. Thus, implementation of a wholesaler precertification program can also be viewed as a part of an educational process leading to improved availability of quality medicines.

Implementation Strategies

Discounting factors external to the precertification process (e.g., political), pharmaceutical wholesaler precertification implementation may include one or a combination of scenarios—

- Immediate precertification of U.S.-based pharmaceutical wholesalers that distribute only FDA-approved or tentatively approved medicines and that are licensed by a State Board of Pharmacy with jurisdiction over the wholesaler's storage and distribution location.

[25] Personal communication with representatives from WHO, MSF, and ECHO.

Should a U.S. wholesaler source non-FDA approved medicines (e.g., non-U.S. source), criteria pertaining to precertification of manufacturers and products as outlined in Section 3 would apply.

Although using U.S. wholesalers to supply FDA-approved or tentatively approved products would obviate the need for USAID waivers and could expedite delivery of required medicines, country import requirements for customs clearance could be an issue as U.S. wholesalers are not required to keep on file documents such as manufacturer cGMP certificate, COA, Certificate of Free Sale, etc. The vast majority of U.S. pharmaceutical wholesalers supply only the domestic market and are neither international drug exporters nor hold an export license although provision for export could probably be arranged. Other points to consider include:

- Delivered pricing for U.S. source and origin medicines are typically far in excess of those available from non-U.S. sources. It is not unusual for U.S. prices to be more than 50 percent higher and often are tripled or even quadrupled the price.

- A number of essential medicines utilized in developing countries are not available from U.S. sources. (e.g., chloramphenicol 250 mg, salbutamol inhaler, metronidazole 200 mg, artesunate 50 mg, procaine penicillin 3 MU powder for injection)

- U.S. source and origin medicines are rarely registered in developing countries.

- Immediate precertification of any pharmaceutical wholesaler and its products who has current prior approved source/origin waiver approval from USAID (see Annex H—copy of USAID Action Memorandum)

  Should OFDA grant approval to use prior approved USAID wholesalers, there still will be a need for a sustainable system to monitor, evaluate, and recertify wholesalers. OFDA has discussed the creation of a pharmaceutical wholesaler database that would be maintained to provide OFDA (and possibly other agencies, partners, and contract organizations) with access (preferably web-enabled) to wholesaler information regarding precertification status, performance history, and possibly pricing from previous procurements.

  The immediate precertification of already approved USG-selected wholesalers and products offers a quick start solution to identifying qualified pharmaceutical wholesalers. However, without application of objective criteria, the pharmaceutical wholesaler precertification process may be challenged by any pharmaceutical wholesaler.

- Precertification of pharmaceutical wholesaler using OFDA-approved precertification criteria. The draft criteria that have been developed form the basis for prescreening and site inspections tools (see Annexes E and F). These tools are the foundation of an objective precertification program and assure that any wholesaler requesting precertification via the EOI procedure described previously will be assessed fairly. Each applicant wholesaler will be required to complete a prescreening questionnaire that will be scored in accordance with a yet to be determined scoring methodology. Those

wholesalers determined acceptable after screening will be notified of acceptance as a precertified wholesaler or, depending on the need to verify submitted data, scheduled for an on-site inspection. The inspection will be carried out by OFDA or contracted inspectors. Should a pharmaceutical wholesaler be deferred for precertification, the applicant will be notified of what further documentation or clarification is needed. The use of transparent criteria together with notification of deficiencies should help address any objection that may be raised by a deferred applicant. At the same time, this process could serve as an educational intervention that may lead to improved pharmaceutical wholesaler operations and, most importantly, the quality of medicines supplied.

- Limited pharmaceutical wholesaler precertification. The wholesaler meets minimum international standards for storage and distribution, procures medicines from secondary USAID-approved wholesalers but does not meet manufacturer prequalification standards.. Under this scenario, the so-called "limited precertified wholesaler" would be required to submit documentation from the approved secondary wholesaler that satisfies OFDA requirements for purchase approval and reimbursement to the PVO/NGO (i.e., minimally, a Certificate of Pharmaceutical Product and manufacturer COA corresponding to the batch sold that includes testing against defined standards [BP, USP, EP, IP])

  Limited precertification may potentially expand the number of approved suppliers. If this scenario was acceptable to OFDA, it would afford PVOs/NGOs and Missions with immediate availability of at least some essential medicines and might persuade local pharmaceutical wholesalers to stock more medicines that meet safety and quality standards. However, the process of determining whether a particular medicine is provided by an approved secondary wholesaler prior to purchase approval by a PVO/NGO could prove extremely onerous.

- Wholesaler precertification rating system based upon degree of risk as regards safety, efficacy, and quality of medicines. Under such a scenario, a system relative to the degree of satisfying OFDA precertification criteria would yield a list of pharmaceutical wholesalers with assigned purchase priority rating (e.g., Level-One wholesaler or Level-Two wholesaler).

  When a disaster or emergency occurs, the PVO/NGO would be instructed to first contact Level-Three wholesalers and, only in the instance where this level wholesaler cannot provide medicines required in the time frame needed, would the PVO/NGO be permitted to contact a Level-Two supplier and so on (assuming a three-level rating). If a PVO/NGO proposed to utilize a precertified wholesaler other than Level Three, OFDA would require that documentation be provided to substantiate that a Level-Three wholesaler could not meet their needs. When only a Level-Two or One precertified wholesaler is available locally, implementation of this scenario could offer immediate availability of small quantities of medicines while awaiting the bulk of requirements to arrive from a Level-Three wholesaler.

Discussion

The primary focus of pharmaceutical wholesaler precertification could be described as an effort to ensure the safety, efficacy, and quality of favorably priced medicines procured from a pharmaceutical wholesaler. Another way of looking at this is to ensure that the risk of procuring substandard or counterfeit medicines is minimized to the extent possible. However, it needs to be recognized that factors such as timeliness of delivery also may weigh heavily on a PVO/NGO decision to request procurement from one wholesaler over another.

The precertification strategies mentioned in OFDA implementation options are meant to provide the OFDA with insights into some possible approaches to precertification and each requires a varying level of effort and resource requirements on OFDA's part. In thinking about the strategies, keep in mind that precertification will most certainly impact current PVO/NGO relationships with pharmaceutical suppliers and the manner in which they carry out procurements. There are advantages and disadvantages associated with each strategy (Table 1).

Table 1. Implementation Strategies

Precertification Scenario	Level of Effort*	Resources Required (Staffing)*	Major Advantages	Major Disadvantages
1. U.S. wholesalers	√	√	• Implementation can be accomplished rapidly • No need for 'waivers' unless non- FDA-approved source/origin medicines are supplied • No need for site inspections • Risk of procuring substandard medicines is minimal	• Drug prices are typically significantly higher than those available outside the United States • Not all essential medicines required by developing countries are available from U.S. sources • Consignee country medicine registration issues are likely
2. USAID-prior approved international pharmaceutical wholesalers	√	√√	• Immediate waiver may be granted to precertified pharmaceutical wholesalers • Risk of procuring substandard or counterfeit medicines is minimized as compared to procurement from non-certified wholesalers	• Requires substantial number of OFDA or contracted personnel for ongoing monitoring and re-evaluation • Strictly applied objective criteria have not been applied to date and need to be developed to provide additional wholesalers an opportunity for approval
3. Application of OFDA criteria	√√√	√√√	• Increases pool of potential precertified pharmaceutical wholesalers • Provides an objective and therefore defensible basis for precertification • Risk of procuring substandard medicines is minimized as compared to procurement from non-certified wholesalers	• Implementation will involve a number of steps and, depending upon availability of resources, could take several months • Requires substantial number of OFDA or contracted personnel with background in and experience with international pharmaceutical standards and/or regulation • Significant resources will be needed to implement wholesaler prescreening applications, site inspections, and ongoing monitoring

4. Limited wholesaler precertification	√√√	√√√	• Could potentially expand the number of precertified wholesalers beyond the number that must meet all OFDA criteria • Increases the possibility of precertifying smaller local (country) wholesale operations • Risk of procuring substandard medicines is minimized as compared to procurement from non-certified wholesalers but not to the degree of those wholesalers meeting all OFDA criteria • Provides an incentive to wholesaler to further develop operations that meet all OFDA criteria and thereby improve a wider range of locally available quality medications	• Implementation will involve a number of steps and depending upon availability of resources, length of time required could take several months. • Requires substantial OFDA or contracted personnel with background in and experience with international pharmaceutical standards and/or regulation • Significant resources will be needed to implement wholesaler prescreening applications, site inspections, and ongoing monitoring • Monitoring to determine that all medicines supplied to PVO/NGO have been sourced from a precertified OFDA wholesaler will be time consuming and difficult to manage
5. Rated precertified wholesalers	√√√	√√√	• Rating of wholesalers based upon the level of adherence to OFDA criteria is likely to result in the largest number of precertified wholesalers among all scenarios • Establishing a rating based upon the likelihood of supplying pharmaceuticals in line with internationally recognized medicine quality standards (similar to those promulgated by FDA, equivalent SDRAs, WHO) will serve to educate wholesalers and PVOS/NGOs about medicine quality and could, in the case of wholesalers, serve to decrease the risk of supplying substandard medicines • For PVOs/NGOs, ratings for precertified wholesalers will provide a rational basis for selecting a suppler • For OFDA, rating of precertified wholesalers will, together with PVO/NGO submission of wholesaler selection documentation, provide a basis for approval (or disapproval) of a procurement request	• Implementation will involve a number of steps and, depending upon availability of resources, could take several months • Requires substantial OFDA or contracted personnel with background in and experience with international pharmaceutical standards and/or regulation • Significant resources will be needed to implement wholesaler prescreening applications, site inspections, and ongoing monitoring • Primarily using medicine quality criteria to rate a wholesaler could result in country level political issues

* Scale for level of effort and resources required is one check (✓) equals least and three checkmarks (✓✓✓) equals maximum.

Implementation Summary

Various strategies or combinations may be employed to accomplish precertification of pharmaceutical wholesalers. It appears to this author that, for reasons including instances when medicines and supplies are required immediately, there is no one strategy that fits all. When a disaster or emergency occurs and pharmaceuticals and/or medical supplies are required, PVO/NGO selection of a wholesaler requires balancing factors such as product availability, risk tolerance to medication quality, and to a more limited extent, price, depending on the situation. To assist OFDA partners with vendor selection and OFDA with approval of requested procurements, precertification strategies are described including major advantages and disadvantages or limitations of each. It is likely that some combination of strategies will need to be considered.

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PHARMACEUTICAL WHOLESALER DATABASE DESIGN

The pharmaceutical wholesaler precertification process from prequalification to monitoring of performance to recertification will result in the creation of significant quantities of data. For stakeholders that might include OFDA, GH/HIDN, OAA/T, NGOs, U.S. Country Missions, and international collaborating partners, a database that includes several modules could be designed with stakeholder access to all or some modules.

Proposed Modules Need Additional Information

- List of USAID/OFDA precertified wholesalers including contact information, catalogues of available items including, international nonproprietary name (INN), strength, manufacturer, pack sizes, and possibly indicative prices

- Pharmaceutical wholesaler master file

    - All data extracted from screening application and site inspection(s)

    - For pharmaceutical wholesalers where precertification is denied or deferred, deficiencies are documented

- Wholesaler performance tracking (for each wholesaler)

    - Delivery time stated in days from date that purchase order is received to date delivered to client

    - Aggregated list of products (complete description including manufacturer) and quantities requested versus what was delivered (confirmed by client)

    - Client complaints (e.g., unresponsiveness to questions, visible product defects, or adverse reactions received from end users)

- OFDA follow-up

    - Action taken resulting from client complaints, e.g., letter to supplier requesting action plan to address complaint; if product quality or adverse reaction related, obtain sample from wholesaler for independent laboratory analysis and take action according to OFDA SOP

Standard Reports

The database should be designed to generate a number of standard reports including—

- OFDA performance
    - Record of all requisitions received and total processing time; problems encountered
- Wholesaler performance
    - Processing time—Time from receipt of purchase order to receipt at port of entry
    - Product quantity ordered versus quantity delivered
- Complaint registry
    - Complaints by category
        - Product—Labeling, physical appearance, adverse drug reaction, etc.
    - Actions taken
- Other
    - As mentioned previously, availability and evaluation of performance data is only valuable if used in an evaluation process that includes transparent criteria

SUMMARY AND DISCUSSION

This report describes a process or framework for wholesaler precertification using objective justifiable criteria that have been incorporated into pharmaceutical wholesaler prescreening and site inspections tools. It also includes options or strategies for implementation of pharmaceutical wholesaler precertification schemes and elements of a pharmaceutical wholesaler database that can be used for ongoing monitoring and assessment by OFDA, its partners, and other interested parties.

The report is based on research into pharmaceutical manufacturer and pharmaceutical wholesaler precertification literature, e-mail communications, and on-site discussions with a number of individuals extensively involved with development or implementation of prequalification schemes for pharmaceutical manufacturer or wholesalers. Tools based upon desk research, discussions, and site visits with pharmaceutical wholesalers and international humanitarian organizations were developed for precertification prescreening and on-site inspection of applicant pharmaceutical wholesalers.

A number of international humanitarian organizations including ECHO, WHO, MSF, and USAID endorse the concept of precertifying pharmaceutical wholesalers. Some organizations have developed guidelines, standards, and specifications that can serve as a basis for PVOs/NGOs to assess wholesaler operations and, in the case of WHO, to provide pharmaceutical wholesalers with tools to assess and improve operations where indicated. OFDA therefore is not alone in its quest to develop a precertification program to assure the safety, efficacy, and quality of purchased pharmaceuticals.

For OFDA, however, the situation faced might not be viewed as the typical case where a planned procurement of pharmaceuticals is to take place. While it is difficult to argue against only precertifying wholesalers that meet all criteria, when a disaster strikes there may not be time to look to such wholesalers for supplying immediate requirements or they may have insufficient inventory. Therefore, in the case of a disaster, implementing a system whereby pharmaceutical wholesalers are rated based upon ability to meet selected as compared to all important transparent criteria and where selection is linked to rating may be logical and appropriate. If, for example, two or three rating levels were established, a system could be implemented whereby Level One or A-rated wholesalers would be contacted first (highest rated for meeting criteria with associated lowest risk of substandard medicine quality), then Level Two (B), and then possibly Level Three (C). Also to be considered is a rating system based upon approval for or availability of a range of prespecified products. Under such system, a “limited certification” might be reasonable

There is an inherent pharmaceutical quality level of risk at every level, even in the case of using U.S. source and origin medicines exclusively. When a disaster or emergency occurs, PVO/NGO selection of a pharmaceutical wholesaler for fulfilling requirements requires balancing factors such as availability, risk level of medication quality, and to a more limited extent, price.

The fact that an international wholesaler precertification scheme has not been implemented should be no surprise given the complexities of attempting to establish such a scheme. As the situation now exists where there is no reliable standard or program for rating pharmaceutical wholesalers to ensure pharmaceutical quality to the extent possible, some combination of strategies seems to be indicated for OFDA-funded partners.

NEXT STEPS

If one assumes USAID/OFDA acceptance of for the pharmaceutical wholesaler precertification criteria framework presented above, an implementation plan is the logical next step. In considering implementation plan development, OFDA may need to consider possible (probable) interest from other USG agencies. Although basic pharmaceutical wholesaler precertification elements would remain the same regardless of participation by more than one agency, requirements and priorities of said agencies would no doubt add complexities to the implementation process. For now, however, the suggested next steps are limited to OFDA.

To assist OFDA with developing a pathway for fully implementing a wholesaler precertification process, the following are offered for consideration—

- Develop a drug quality education module for PVOs/NGOs to familiarize such organizations with precertification rationale
- Implementation and management of the EOI process
- Pharmaceutical wholesaler pre-screening evaluation and response (development of a scoring methodology for immediate approval, recommendation for site inspection, deferral, denial, etc.)
- Site inspection and assessment/recommendation; again, development of scoring methodology and possible adoption of "leveled" precertification (i.e., full as compared to limited)
- Perform site (re)inspections,
- On-going wholesaler monitoring and re-evaluation/re-certification
- Design, development, implementation, and maintenance of a pharmaceutical wholesaler database
- Investigate the availability of contract groups or organizations to perform site inspections and/or maintain wholesaler data base.

Note: OFDA has the option of keeping all processes in-house or developing a Request for Proposal (RFP) for the purpose of outsourcing some or all the precertification procedures and database maintenance and re-certification evaluations. Should functions be outsourced, resultant recommendations and reporting would of require evaluation by OFDA who would retain final decision-making authority.

Additional next steps that could be considered include—

- Formulating a list of pharmaceuticals approved for procurement from precertified wholesalers
- Designing disease specific medication kits (i.e.,cholera kit)
- Consideration of how USAID/OFDA may best collaborate with other stakeholders

ANNEX A. WHOLESALER SITE VISITS—BRIEF SUMMARY OF PRECERTIFICATION FINDINGS AND RECOMMENDATIONS

WHOLESALER: MISSIONPHARMA

Date of Visit: December 11, 2006

In attendance:

Sune Svennignsen, Supply Chain Manager
Jens Rasmussen, Manager, Development Aid
Mikkel Wakefield, Director of Sales
Laurent Lombart, Director, Business Development and Strategic Marketing
Stig Monsted, QA/QC Manager
Bo Birk, Project Manager, Business Development
Ned Heltzer (MSH)
Alexandr Kosyak (OFDA)

BACKGROUND

- Established:1975
- For-profit corporation
- 3 year avg. turnover: USD $70 M
- Warehouse Operation(s): Lynge, Denmark, Gandhidham, India and Ahmedabad, India
- Staff: 85 F/T and 125 P/T
- QA/QC staff: 4 FT
- Wholesale License: issued by the Danish Health Authority; most recent regulatory authority inspection, 2004
- Product Range: Maintains inventory of all drugs on WHO EDL
- Disaster/emergency kits: emergency drug kits (and drug inventory for kits) available and meet WHO requirements ; also prepares custom kits
- Clients: multiple public health agencies in Africa, multiple NGOs, and UN Agencies and USG

MANUFACTURER PREQUALIFICATION

- SOP documentation: Yes. Comprehensive prequalification SOPS in place including manufacturer dossier review as per questionnaire and site inspections
- Inspections: Carries out GMP inspections in accordance with WHO GMP guidelines at manufacturing facilities not licensed by a Stringent Drug Regulatory Authority (SDFA); within India by MP staff; in other countries, assessment is outsourced; inspections conform to USFDA or WHO c/GMP guidelines for pharmaceutical manufacturers.
- Manufacturer requalification: Re-inspection of prequalified manufacturers every 2-3 years
- Site inspections during past 3 years: 65 with 13 rejections
- Prequalification SOP Review: November 2006

PROCUREMENT

- SOPs documented: Yes; specify procurement of prequalified products from prequalified manufacturers
- Pedigree Availability: Documentation available to authenticate source and origin for all drugs (e.g., COA corresponding to batch received, invoice, packing list, COO when requested)

STORAGE and DISTRIBUTION

- Storage arrangement and conditions: in line with GSP/GDP guidelines
- SOP documented: Yes, medicines are stored as per written SOPs and compliance documentation is available.
- Current Good Distribution Practice certificate issued by the Danish Medicines Agency
- Drug registration in consignee country or import waiver: verified prior to shipment
- Packing list/invoice: in line with prescreening application criteria; some information provided on COA

QUALITY MANAGEMENT

- Quality control/quality assurance SOPs documented: Yes
- Drug Quality Inspections: QA/QC department visually inspects samples from each consignment and verifies that COA corresponds to predetermined specifications and drug samples randomly tested by contract laboratories that comply with principles of good laboratory practice (GLP)
- Lab analysis per pharmacopeial standards or in-house manufacturing standards during past two years: 160
- Other QA/QC Certification: ISO 9001 Certification in process

MANAGEMENT INFORMATION SYSTEM

- A system is in place to provide management with tools for organizing, evaluating and efficiently running all departments.

REMARKS

- Responses to a draft precertification questionnaire and information gathered during a limited, scheduled site visit to the Lynge, Denmark, facility, support a preliminary recommendation for precertification as a supplier to all USAID-supported recipients. Prior to issuing a final recommendation for precertification, a more in-depth assessment is advisable.

  Note: Wholesaler operates distribution facilities at two locations that were not visited; these locations need to be assessed.

WHOLESALER: IDA FOUNDATION

Date of Visit: December 15, 2006

In attendance:

Lex de Wijn, Managing Director
Frank van Doren, Sales Manager
Martijn Smid, Area Manager, Asia and Eastern Europe
Mario Stassen, Director Quality Affairs
Julian Suumeijer, Area Manager, Latin America and the Caribbean
Ria Grondman, Responsible Pharmacist
Steven Ijland, Quality Assurance and Regulatory Affairs
Alexandr Kosyak (OFDA)
Ned Heltzer (MSH)

BACKGROUND

- Established: 1972
- Not-for-profit company
- 3 year avg. turnover: USD 68 M
- Warehouse operation(s): Amsterdam and Utrecht, Netherlands
- Staff: 124 FT and 87 PT
- QA/QC staff: 15 FT; 4 PT
- Wholesale license: issued by Dutch Inspectorate of Health Care; inspected by Dutch Drug Regulatory Authority, January 2006.
- Product range: Maintains inventory of all drugs on WHO EDL
- Disaster/emergency kits: emergency drug kits (and drug inventory for kits) available and meet WHO requirements
- Clients: multiple public health agencies in Africa, multiple NGOs and UN Agencies and USG

MANUFACTURER PREQUALIFICATION

- SOP documentation: Yes. Comprehensive prequalification SOPS in place including manufacturer dossier review as per questionnaire and site inspections
- Inspections: Carries out GMP inspections in accordance with WHO GMP guidelines at manufacturing facilities not licensed by a Stringent Drug Regulatory Authority (SDRA) and monitors all companies when drugs are for export only; utilizes staff and contract auditors
- Manufacturer requalification: Re-inspection of prequalified manufacturers every 2-5 years
- Site inspections during past 3 years: 99 with 19 rejections.
- Prequalification SOP Review: July, 2005

PROCUREMENT

- SOPs documented: Yes; specify procurement of prequalified products from prequalified manufacturers
- Pedigree Availability: Documentation available to authenticate source and origin for all drugs (e.g. COA corresponding to batch received, invoice, packing list, COO when requested)

STORAGE AND DISTRIBUTION

- Storage arrangement and conditions: in line with GSP/GDP guidelines
- SOPs documented: Yes; drugs are stored as per written SOPs and compliance documentation is available.
- Good Distribution Practice certificate issued by the Dutch Inspectorate of Healthcare in 2002.
- Drug registration in consignee country or import waiver: verified prior to shipment
- Packing list: Packing list/invoice: in line with prescreening application criteria; some information provided on COA

QUALITY MANAGEMENT

- Quality control / quality assurance SOPs documented: Yes
- Drug Quality Inspections: QA/QC department visually inspects samples from each consignment and verifies that COA corresponds to predetermined specifications and random in-house chemical testing of drug samples (100% for critical products such as ARVs); also outsources some testing to one lab in India and several in Europe; microbial testing is outsourced. Confirmation is required that all labs comply with GLP and performance is monitored.
- Lab analysis per pharmacopeial standards or in-house mfr. standards during past 2 years: 450 (in-house)
- Other QA/QC Certification: ISO 9001:2000 certified: 2000-2007

MANAGEMENT INFORMATION SYSTEM

- A system is in place to provide management with tools for organizing, evaluating and efficiently running all departments.

REMARKS

- Responses to a draft precertification questionnaire and information gathered during a limited, scheduled site visit to the Amsterdam, Holland facility, support a preliminary recommendation for precertification as a supplier to all USAID supported recipients. Prior to issuing a final recommendation for precertification, a more in-depth assessment is advisable.

  Note: Wholesaler operates a distribution facility at another location that was not visited, this location needs to be assessed.

WHOLESALER: UNICEF

Date of Visit: December 12, 2006

In attendance:

Hanne Bak Pedersen, Senior Advisor Pharmaceutical Policy, Supply Division
Soren Hansen, Chief, Warehouse and Logistics, Supply Division
Peter Jakobsen, QA Officer
Murtarda Sesay, Technical Officer, Pharmaceutical Supply Division
Suvi Raution, Chief, Procurement Services Centre.
Fransicso Blanco, Chief, HIV/AIDS and Health Centre, Supply Division
Alexandr Kosyak, (OFDA)
Ned Heltzer (MSH)

BACKGROUND

- Established: 1981
- Not-for-profit organization
- 3 year avg. turnover for essential medications and nutritionals: USD 80 M
- Warehouse operation(s): Copenhagen, Denmark
- Staff: 104 FT (dedicated to essential medicines and nutritionals)
- QA/QC Staff: 1FT
- Wholesale license: Issued by Danish Medicines Agency; GDP License, August 2006
- Product range: Maintains inventory of all drugs on WHO EDL
- Disaster/emergency kits: emergency drug kits (and drug inventory for kits) available and meet WHO requirements
- Clients: UN agencies, governments, international financial institutions (i.e., World Bank), NGOs, philanthropic organizations

MANUFACTURER PREQUALIFICATION

- SOP documentation: Yes. Comprehensive prequalification SOPS in place including manufacturer dossier review as per questionnaire and site inspections
- Inspections: Carries out on-site GMP inspections in accordance with WHO GMP guidelines; manufacturer site inspection based upon "regulatory environment in country of origin" ; utilizes staff auditors and contract auditors
- Manufacturer requalification: Re-inspection every 2-5 years.
- Site inspections during past 3 years: 102 with 38 rejections
- Prequalification SOP Review: April, 2004

PROCUREMENT

- SOPs documented: Yes; specify procurement of prequalified products from prequalified manufacturers
- Pedigree Availability: Documentation available to authenticate source and origin for all drugs (e.g., COA corresponding to batch received, invoice, packing list)

STORAGE AND DISTRIBUTION

- Storage arrangement and conditions: in line with GSP/GDP guidelines
- SOPs documented: Yes; drugs are stored as per written SOPs and compliance documentation is available. Note: stated that pest control has been performed for many years and SOP under development
- Good Distribution Practice certificate issued by the Danish Medicines Agency, August 2006
- Drug registration in consignee country or import waiver: UNICEF is not required to register medicines it supplies but does arrange import waivers via its country field offices prior to shipment
- Packing list: Packing list/invoice: in line with prescreening application criteria; some information provided on COA ; Certificate of Origin is not available but origin is mentioned in Certificate of Analysis

QUALITY MANAGEMENT

- Quality Control / quality assurance SOPs documented: No; Quality assurance manual SOPs for all major operations (manufacturer prequalification, receipt, purchasing, storage, distribution) "will be elaborated in 2007"; stated that QA pharmaceutical practices in line with USFDA or WHO GMP guidelines.
- Drug Quality Inspections: QC department visually inspects samples from each consignment and verifies that COA corresponds to predetermined specifications; Limited random chemical testing based upon prior experience with manufacturer performed by Therapeutic Good Administration, Australia and USP, United States; drug quality focus relies for the most part on manufacturer QA activities (documented at time of inspection by UNICEF auditors)
- Lab analysis per pharmacopeial standards or in-house mfr. standards during past 2 years: 66
- Other QA/QC Certification: Preparing for ISO 9002

MANAGEMENT INFORMATION SYSTEM

- A system is in place to provide management with tools for organizing, evaluating and efficiently running all departments.

REMARKS

- Responses to a draft precertification questionnaire and information gathered during a limited, scheduled site visit to the Copenhagen, Denmark facility support a preliminary recommendation for precertification as a supplier to all USAID supported recipients. Prior to issuing a final recommendation for precertification, a more in-depth assessment is advisable.
- UNICEF assumes no product liability but rather states that this is retained by the drug manufacturer.
- For non-emergency procurements, drug availability information (e.g., is product in stock) is not provided to a purchaser until payment is received (advance payment required).
- UNICEF does not participate in tenders

WHOLESALER: MISSION FOR ESSENTIAL DRUGS AND SUPPLIES

Date of Visit: December 17, 2006

In attendance:

Paschal Manyuru, General Manager
Jane Masiga, Head of Operations
Jonathan Kiliko, Head, Customer Services
Alexandr Kosyak (OFDA)
Ned Heltzer (MSH)

BACKGROUND

- Established: 1986
- Not-for profit, faith based organization
- 3 year avg. turnover: To be supplied
- Warehouse operation(s): Nairobi, Kenya
- Staff:100 FT and 7 PT
- QA/QC Staff: 10 FTE
- Wholesale license: Issued by Kenya Pharmacy and Poisons Board is current; stated that warehouse inspected in 2006 by Kenya Pharmacy and Poisons Board but no report issued to date.
- Product Range: Maintains inventory of most drugs on WHO EDL
- Disaster/emergency kits: does not maintain inventory of emergency kits but has capacity to prepare them
- Clients: Kenya Government, NGOs based in Kenya and USG Kenya (HIV/AIDS ARVs and related drugs); has provided services to NGOs operating in Somalia, S. Sudan, Ethiopia, Rwanda and the Congo

MANUFACTURER PREQUALIFICATION

- SOP documentation: Yes but supplier prequalification activity is limited
- Inspections: In-house staff (Pharmaceutical Technical Committee) perform "mini-inspection" of local manufacturers; MEDS stated that their policy is to support local manufacturers unless not available or significant savings is achievable from importing product; also mentioned that the Ministry of Health is responsible for ensuring quality of drugs locally manufactured or imported; no documentation is available to ensure that manufacturers comply with USFDA or WHO GMP guidelines; drugs are however required to conform to MEDS product specifications
- Drugs procured from India must be WHO prequalified or supplied by IDA
- Site inspections during past 3 years:12 with 4 rejections
- Prequalification SOP Review: SOPs available but no date for last review available at time of visit.

PROCUREMENT

- SOPs documented: Not observed; Local suppliers (manufacturers/wholesalers) account for 70% of procurements
- Pedigree Availability: Documentation is not always available to authenticate source and origin for all drugs, particularly when drugs are procured from a local wholesaler (e.g. COA corresponding to batch not always available, COA is not always complete—pharmacopeial standard not mentioned, address of manufacturer not stated, name of person signing off on COA not stated)

STORAGE AND DISTRIBUTION

- Storage arrangement and conditions: adherence to most GSP/GDP guidelines.
- SOPs documented: Yes; drugs are stored as per written SOPs and documentation is available to ensure compliance; temperature monitoring is performed twice a day but only at the lower storage levels (upper level of drug storage racking not monitored); humidity is not monitored but this planned for the near future; temperature of cold chain products is not monitored during delivery nor has cold chain been validated
- Drug registration in consignee country or import waiver: needs to be determined
- Packing list: Packing list/invoice: in line with prescreening application criteria; some information provided on COA but fully documented COA is not always available

QUALITY MANAGEMENT

- Drug Quality control / quality assurance SOPs documented: Yes
- Drug Quality Inspections: For new suppliers, drug samples are evaluated physically (visually) and complete chemical monograph analysis is performed; for established suppliers, only COA and packaging is inspected upon receipt with random analysis of batches performed by in-house laboratory; stated expectation to achieve compliance with WHO GLP standards in 2007; microbiological analysis is outsourced (U. of Nairobi)
- Lab analysis per pharmacopeial standards or in-house mfr. standards during past 2 years: 555
- Other QA/QC Certification: None

REMARKS

Based upon responses to the draft precertification questionnaire and information gathered during a limited, scheduled site visit, additional documentation of adherence to precertification criteria is needed (particularly associated with manufacturer prequalification and quality management) before a preliminary precertification recommendation is considered.

WHOLESALER: OMAERA PHARMACEUTICALS LIMITED

Date of Visit: December 17, 2006

In attendance:

Benard Otundo, Director
Alexandr Kosyak (OFDA)
Ned Heltzer (SH)

BACKGROUND

- Established:1993
- For profit corporation
- 3 year avg. turnover: USD $13 M
- Warehouse operation(s): Nairobi, Kenya
- Staff: 65 FT
- QA/QC staff: None
- Also owns and operate 28 retail pharmacies and pharmaceutical manufacturer (Sphinx Pharmaceuticals)
- Wholesale license: issued by the Kenya Pharmacy and Poisons Board, current
- Product range: Wide range of drugs including many on WHO EDL list
- Disaster/emergency kits: None
- Clients: public and private sector organizations located in Kenya (e.g. MEDS), DRC, S. Sudan and Burundi; private hospitals and retail pharmacies

MANUFACTURER PREQUALIFICATION

- SOP documentation: None
- Inspections: None; most drugs procured are registered in Kenya (93%) and assumes that Kenya Poison Board establishes and ensures drug quality
- Manufacturer Requalification: Does not prequalify suppliers.
- Site inspections: None
- Prequalification SOP Review: No SOPs

PROCUREMENT

- SOPs documented: No SOPs; product selected based upon price;
- Pedigree availability: readily retrievable documents to authenticate the source and origin for drugs are not available but "might be able to obtain them"; COA can be obtained if requested by client.

STORAGE AND DISTRIBUTION

- Storage arrangement and conditions: require modification to meet GSP/GDP guidelines; there are areas for receiving, general storage and shipping but space was cramped; controlled drug storage inadequate; no designated quarantine area; cold storage temperature is not monitored
- SOPs documented: No SOPs
- Drug registration in consignee country or import waiver: NOT verified.
- Packing list: Packing list/invoice: is not in line with prescreening application criteria; does not include manufacturer, expiry or batch # and COA that might include this data is not available for all drugs

QUALITY MANAGEMENT

- Quality control / quality assurance SOPs documented: No SOPs.
- Drug Quality Inspection: drugs not physically inspected or tested against any standard; for drugs manufactured by the wholesaler's wholly owned subsidiary (Sphinx), chemical analysis of active pharmaceutical ingredients and finished products performed; also, some testing in conjunction with Kenya National QC lab and occasionally the U. of Nairobi.; mentioned 5 percent active pharmaceutical ingredients failure rate but this is undocumented
- Lab analysis: see comment regarding wholly owned manufacturer (Sphinx)
- Other QA/QC Certification: None

MANAGEMENT INFORMATION SYSTEM

- Computer system principally used for accounting functions; we were told that it was in the process of getting upgraded but no details provided.

REMARKS

- The wholesaler had not completed the prescreening application. Based upon first hand observations and information provided by the company director during our brief visit, a number of routine wholesaler operations would NOT meet currently drafted standards for procurement, storage, distribution or quality control/quality assurance.

- Note: Kenya Pharmacy and Poisons Board published its first edition of "Guidelines for Good Wholesaling and Retail Practice for Pharmaceuticals" in June 2006. If inspections of pharmaceutical wholesalers serve to enforce guidelines, improvement in storage and distribution practices can be expected.

WHOLESALER: PHILLIPS PHARMACEUTICALS LIMITED

Date of Visit: December 16, 2006

In Attendance:

Mukesh Mehta, Group managing Director
Janet Handa, HIV/AIDS Coordinator
Alexandr Kosyak (OFDA)
Ned Heltzer (MSH)

BACKGROUND

- Established: 1990
- For profit company
- 3 year avg. turnover: USD 15 M
- Warehouse location(s): Nairobi, Kenya
- Staff: 47 FT
- QA/QC staff: None
- Wholesale license: issued by Kenya Pharmacy and Poisons Board, 2006; inspection report available from March 2006 – no deficiencies
- Product Range: limited in respect to WHO EDL list; only branded products manufactured in countries regulated by stringent drug regulatory authority are sold
- Disaster/emergency Kits: None
- Clients: USAID, International NGOs (e.g. Clinton Foundation, CRS), national wholesalers (e.g. MEDS, JMS), private sector hospitals and pharmacies
- Maintains wholesale distribution centers in 6 African countries

MANUFACTURER PREQUALIFICATION

- SOP documentation: No SOPs; all products are procured from manufacturers that in countries regulated by a Stringent Drug Regulatory Authority and/or prequalified by WHO
- Inspections: None; all suppliers are manufacturers that adhere to USFDA or WHO GMP guidelines and are inspected by a SDRA
- Manufacturer requalification: Not performed; relies on SDRA oversight of manufacturer
- Site inspections during the past 3 years: None; relies on SDRA
- Prequalification SOP Review: No SOPs

PROCUREMENT

- SOPs documented: No written procurement SOPs
- Pedigree Availability: Documentation available to authenticate source and origin for all drugs (e.g. COA corresponding to batch received, invoice, packing list, COO when requested)

STORAGE AND DISTRIBUTION

- Storage arrangement and conditions: in line with most GSP/GDP guidelines; monitoring of storage temperature and humidity is lacking
- SOPs documented: Yes; available for all major activities (e.g. receipt, storage, returned goods, sanitation, pest control) but have not been reviewed for several years
- Drug registration in consignee country or import waiver: can be verified but is responsibility of consignee
- Packing list/invoice: Packing list/invoice: in line with prescreening application criteria; some information provided on COA

QUALITY MANAGEMENT

- Quality control/quality assurance SOPs documented: states availability of quality assurance manual revised in 2003 but not observed during visit
- Drug Quality Inspections: Drug packaging is physically inspected prior to moving goods to storage area; does not perform analytical drug testing of branded products manufactured in countries with a SDRA
- Lab analysis per pharmacopeial standards or in-house mfr. standards: None
- Other QA/QC Certification: None

MANAGEMENT INFORMATION SYSTEM

- System is in place to provide records for day to day operations but an overarching management system for organizing, evaluating and efficiently managing operations was not observed

REMARKS

- Responses to a draft precertification questionnaire and information gathered during a brief, scheduled site visit to this wholesaler support a preliminary recommendation for "limited" precertification as a supplier to all USAID supported recipients. Prior to issuing a final recommendation for precertification, a more in-depth assessment is advisable.

- Note: this consultant has recommended a limited precertification since the wholesaler operates under a business model where only branded drugs manufactured in countries with a stringent drug regulatory authority (SDRA) are procured. Should this model change and drugs are procured from manufacturers in countries without a SDRA, additional SOPs would need to be implemented before unrestricted precertification could be recommended.

- Of interest is that Phillips has a sister company, Pharma Specialties (not inspected) that supplies generic drugs manufactured in India as well a limited number of drugs manufactured in Kenya. According to the Group Managing Director, all batches are analyzed by an independent lab in India (Vimta) and if requested, products will also be analyzed by a WHO approved lab in South Africa (Cenqam).

WHOLESALER: LORDS HEALTHCARE LIMITED

Date of Visit: December 19, 2006

In Attendance:

Mohamed Khar, Director, Sales and Marketing
Alexandr Kosyak (OFDA)
Ned Heltzer (MSH)

BACKGROUND

- Established: 1989
- For profit company
- 3 year avg. turnover: USD 4 M
- Warehouse operation(s): Nairobi, Kenya
- Staff: 50 FT and 7 PT
- QA/QC staff: 1 FT
- Wholesaler license: issued by Kenya Pharmacy and Poisons Board, 2006
- Product Range: Wide range of drugs including many on WHO EDL list
- Disaster/emergency Kits: does not supply disaster type kits
- Clients:: Global fund (ARVs and antimalarials), Kenyan NGOs including MEDS, local Government, private sector hospitals and retail pharmacies

MANUFACTURER PREQUALIFICATION

- SOP documentation: No written SOPs; for ARVs, TB and antimalarials, procure from WHO preapproved suppliers; all drugs procured are registered in Kenya
- Inspections: No formal inspection program; on occasion, "visited" manufacturers in India and stated that some companies have been rejected
- Manufacturer requalification: None
- Site inspections during past 3 years: No formal inspections
- Prequalification SOP Review: None

PROCUREMENT

- SOPs documented: No written procurement SOPs
- Pedigree Availability: Documentation available to authenticate source and origin of all drugs (e.g. COA corresponding to batch received, invoice, packing list, COO when requested)

STORAGE AND DISTRIBUTION

- Storage arrangement and conditions are NOT in line with GSP/GDP guidelines; storage area for solid orals congested; controlled drugs were stored in an insecure fashion (in desk); temperatures are recorded weekly and at the time of our visit, temperature in warehouse exceeded manufacturer specifications for some products
- SOPs documented: No written storage or distribution SOPs.
- Packing list/invoice: Packing list/invoice: in line with prescreening application criteria; some information provided on COA

QUALITY MANAGEMENT

- Quality control / quality assurance SOPs documented: There is no quality assurance manual or documentary evidence that QC procedures are in place
- Drug Quality Inspections: Drugs are not physically inspected or tested against any standard; wholesaler relies on manufacturer QA; packaging is inspected when order is prepared for shipment to client
- Lab analysis: None
- Other QA/QC Certification: None

MANAGEMENT INFORMATION SYSTEM

- Some aspects of wholesale operations are computerized (ex. invoicing) and documents such as COAs were available but a system for organizing, evaluating and efficiently managing operations was not observed. A computer software upgrade that is planned might address deficiencies.

REMARKS

- Based upon responses provided to a draft precertification questionnaire, first hand observations and information provided by the company sales and marketing director during our brief visit, a number of routine wholesaler operations would NOT meet currently drafted criteria for procurement, storage, distribution or quality control/quality assurance. However, given that this company procures a number of drugs of known quality from WHO preapproved manufacturers and appeared open to improving the quality of internal operations, a limited wholesaler precertification (specified products) could be considered if major deficiencies pertaining to storage, distribution and QA/QC are addressed.

- Note: Kenya Pharmacy and Poisons Board published its first edition of "Guidelines for Good Wholesaling and Retail Practice for Pharmaceuticals" in June 2006. If inspections of pharmaceutical wholesalers serve to enforce guidelines, improvement in storage and distribution practices can be expected.

WHOLESALER: AMSTELFARMA

Date of Visit: December 20, 2006

In attendance:

Nico Roozendaal, Director
J. van Haperen, Responsible Pharmacist
Alexandr Kosyak (OFDA)

BACKGROUND

- Established: 1986
- For profit company
- 3 year avg. turnover: To be provided
- Warehouse location(s): Lelystad, Holland with administrative office in Heemstede.
- Staff: 25 FT
- QA/QC staff: 4 FT
- Wholesale License: issued by Ministry of Health, Welfare and Sport, 2006; regularly inspected by the Dutch Pharmaceutical Inspectorate; last inspection 2006 (report in Dutch)
- Product range: Maintains wide range of essential drugs and small range of medical supplies
- Disaster/emergency kits: None
- Clients: Not specified

MANUFACTURER PREQUALIFICATION

- SOP documentation: Yes. Comprehensive prequalification SOPS in place including manufacturer dossier review as per questionnaire and site inspections
- Inspections: Carries out GMP inspections at manufacturing facilities not licensed by a Stringent Drug Regulatory Authority (SDRA) (e.g. Indian and China); inspections conform to USFDA or WHO c/GMP guidelines for pharmaceutical manufacturers.
- Manufacturer Requalification: dossiers every year; site inspections every 3-4 years if deemed necessary
- Site Inspections during past 3 years: 19
- Prequalification SOP review: November 2004 with next review planned in first quarter of, 2007

PROCUREMENT

- SOPs documented: Yes; specify procurement of prequalified products from prequalified manufacturers
- Pedigree Availability: documentation is available to authenticate source and origin for all drugs (e.g. Mfr. COA corresponding to batch, invoice, packing list, COO when requested)

STORAGE AND DISTRIBUTION

- Storage arrangement and conditions in line the GMP/GDP guidelines
- SOPs documented: Yes; drugs are stored as per written SOPs and compliance documentation is available; new employees receive GDP training
- Drug registration in consignee country or import waiver: for all products, registrations status, Certificate of Pharmaceutical Product and product dossier is available
- Packing list: in line with criteria in prescreening application.

QUALITY MANAGEMENT

- Quality control / quality assurance SOPs documented: Yes
- Drug Quality Inspections: QA/QC department visually inspects goods received and utilizes independent laboratories (Farmalyse, Zaandam, and Lelypharma, Lelystad) for chemical analysis of all batches originating in China or India
- Lab analysis per pharmacopeial standards or in-house during past 2 years: 25 products and 120 batches
- Other QA/QC Certification: None

MANAGEMENT INFORMATION SYSTEM

- A system is in place to provide management with tools for organizing, evaluating and efficiently running all departments

REMARKS

- Responses to a draft precertification questionnaire and information gathered during a limited, scheduled site visit to the Lelystadt, Holland facility, support a preliminary recommendation for precertification as a supplier to all USAID supported recipients. Prior to issuing a final recommendation for precertification, a more in-depth assessment is advised.

- Note: Wholesaler is the owner of Waterland Laboratories that is licensed by Dutch Health Authorities to have drugs contract manufactured.

APPENDIX B. DRAFT OFDA APPROVAL PROCESS

The OFDA essential medications approval process may be separated into two distinct phases—

1. The waiver (sometimes referred to as pre-approval)
2. The final authorization (sometimes referred to as final approval)

Waiver

The waiver allows USAID/OFDA to waive the requirement to purchase only FDA-approved medications provided that all necessary documentation is provided, reviewed, and found acceptable. The waiver review consists of screening the intended medications list for appropriateness, suitable quantities, adherence to accepted formularies, acceptable manufacturers, and review of the proposed wholesaler or supplier.

If an NGO anticipates procuring pharmaceuticals by the waiver mechanism, it is the NGO's responsibility to identify a medicine supplier (manufacturer, distributor, or wholesaler) willing to work with the NGO to—

- Determine the quantity required
- Calculate the cost
- Request appropriate documents supporting that the products being procured are safe, effective, and quality products

The NGO must provide a separate cover letter to OFDA—

- Stating their intent to purchase non-FDA approved medications.
- Justify and demonstrate why FDA-licensed medications will not be used. Justifications may be based on the non-availability of the product from the United States, or the U.S. delivered price would be at least 50 percent more than from another source.
- Provide a list of all pharmaceutical products they propose to procure.
- Provide quantities and prices of intended purchase.
- Provide the disease condition(s) within the scope of the project proposal that is to be treated with each medicine.
- Provide assurance that the medicines are on the recipient country's formulary—if there is no national formulary in the recipient country, the medicines should be listed on the WHO Essential Drugs List. http://www.who.int/medicines/publications/essentialmedicines/en/

- Provide certification that the pharmaceutical wholesaler supplying the essential medications is certified to market medicine products.

- Obtain certification from the pharmaceutical wholesaler that manufacturers supplying medicines hold current GMP certificates demonstrating that they meet acceptable standards for the manufacturing of pharmaceuticals; certificates based on the "WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce"; certificates for free sale of the product, etc. http://www.who.int/medicines/areas/quality_safety/regulation_legislation/certification/en/index.html

- Assure that the product is approved for marketing in the country.

Upon receiving the letter justifying the need to procure non-FDA licensed pharmaceuticals and supporting documentation, OFDA will review the documentation and provide a decision to the NGO.

- If the review is favorable, the proposed product list and proposed supplier have been determined to be acceptable; the OFDA pharmacy advisor will prepare a waiver outlining the conditions.

- This process will be done on a case-by-case basis with each proposal. No "global" waiver may be granted for any grantee to routinely procure pharmaceuticals outside of USAID guidance.

- At this time, no non-FDA licensed manufacturers or suppliers are approved for the procurement of non-FDA licensed products (i.e., OFDA has not approved "blanket" purchases for any supplier).

Note**:** The NGO faces financial risk as most manufacturers, distributors, or suppliers will not provide this type of information prior to procuring the product. Therefore, the NGO must obtain assurances from the proposed medicine wholesaler that it is willing and able to provide this information following purchase and delivery of essential medications to the NGO. The NGO must be willing to purchase the needed products and obtain documents that demonstrate safety, efficacy, and quality, and submit those documents to OFDA with the understanding that use of grant funds is not guaranteed and is subject to final OFDA authorization for the purchase.

Final Authorization

Final authorization allows USAID/OFDA funds to be used for reimbursement of medication purchases by the NGO. In particular, OFDA must verify that all medicines purchased are safe and effective, have not less than 12-months shelf life remaining from the delivery date, and have been delivered to the area of intervention.

It is incumbent on the NGO that the USAID cognizant technical officer receives all required documentation within 90 days of the end of the grant period. This includes legible and organized copies of—

- OFDA waiver
- Invoice(s)
- Packing lists with batch number listed for each item
- Delivery notices
- Documentation attesting to the safety, efficacy, and quality manufacturing of each medication—an example of this type of information/documentation would include a certificate of analysis for each product procured stating that the product meets USP or BP standards
- Project budget showing essential medicine purchases are within budget limits

  It is important that the NGO organize the documents listed above prior to submission to OFDA. Generally, it is recommended that a cover letter including invoice number(s) with cross-reference to the packing list should accompany the documents. Each line on the packing list should be numbered and the associated certificate of analysis for that line should be numbered accordingly. This will allow OFDA to quickly ascertain that all required documents are present for review.

  When OFDA has completed the authorization review, the NGO will be notified whether the entire invoice amount has been approved for reimbursement. If the review is found deficient or unacceptable, a memo is prepared for the file and a letter is sent informing the NGO which pharmaceuticals are unacceptable and that OFDA funding of those products is disallowed.

Factors that may cause the essential medication purchase to be disallowed include—

- Drug wholesaler is not certified for this activity
- Incomplete supporting documentation submitted
- Drug purchased (or delivered) has less than 12 month's shelf life from delivery date
- Certificate of analysis does not match batch number of medicine delivered
- Certificate of analysis does not have information regarding the analytical laboratory
- Certificate of analysis indicates that the pharmaceutical product does not meet internationally recognized standards
- Quantity invoiced does not match delivery notice.

APPENDIX C. USAID PHARMACEUTICALS POLICY ADS 312.5.3c

312.5.3c PHARMACEUTICALS

The following policies apply to pharmaceuticals.
1) Approval Requirement - To be eligible for USAID financing, all pharmaceutical and biological products, including oral rehydration salts, must comply with the U.S. Food and Drug Administration (or other controlling U.S. authority) regulations governing United States interstate shipment of such products unless the M/OP/COM approves the procurement of the product prior to financing. The following types of pharmaceuticals and biological products, which do not meet this requirement, must be approved by M/OP/COM prior to financing:

a. Prescription pharmaceuticals which are not FDA-approved products;
b. Nonprescription pharmaceuticals which are not FDA-approved products or covered by a final over-the-counter drug monograph; and
c. Biological products which are not FDA-approved products from an FDA-approved establishment.

2) Source/Origin Requirement - The source and origin of USAID-financed pharmaceuticals is limited to the United States. (See E312.5.3c, para. 2) for exceptions)

3) Patent Infringement - The procurement of pharmaceuticals outside the United States that infringe on U.S. patents is prohibited.

4) Generic Description - All pharmaceuticals must be generically described in the solicitation document unless they are being purchased for resale under a CIP. Under CIPs, when the procurement is undertaken by public or private sector entities purchasing for resale, where brand name acceptance is an important factor, brand name procurement is allowable.

5) Price Rules - CIPS - In addition to the applicable price rules in Subpart G of 22 CFR 201 (AID Regulation 1) (See Mandatory Reference, 22 CFR 201, Subpart G), bulk pharmaceuticals are subject, at the pre-financing stage, to the special price rules found in Part II-D of the "USAID Commodity Eligibility Listing" (See Mandatory Reference, USAID Commodity Eligibility Listing).

The following essential procedures must be followed when dealing with pharmaceuticals.

1) Approval Requirement - Submissions of proposed pharmaceutical procurements for approval by M/OP/COM must include the generic name, dosage form, strength or concentration, unit package size, the intended therapeutic use, name of the manufacturer, and any other relevant factors bearing upon a specific application.

2) Source/Origin Requirement
Exceptions to the general rule that USAID-financed pharmaceuticals must be of U.S. source and origin shall be made in accordance with the requirements in Subpart F of 22 CFR 228 (AID Regulation 28), after clearance by the Office of Procurement (M/OP/COM)(See Mandatory Reference, 22 CFR Part 228, Subpart F). However, if the USAID Geographic Code 941 is the authorized source for procurement under the assistance agreement, an exception from the U.S. source requirement to permit a specific pharmaceutical procurement from a code 941 country requires only the approval of the Office of Procurement (M/OP/COM).

a. Under assistance other than CIPs, a waiver of the U.S. source policy will be considered if:
    1. The pharmaceutical product is essential to the activity;
    2. The product, in the same or substantially equivalent form, is not available from the United States, or the delivered price from the United States would be at least 50 percent more than from another source; and Information is available to attest to the safety, efficacy and quality of the product, or the product meets the standards of the U.S. Food and Drug Administration or other controlling U.S. authority.

b. Under CIPs, waiver of the U.S. source policy will be considered if:
    1. The pharmaceutical product is essential;
    2. The product, in the same or substantially equivalent form, is not available from the United States; and
    3. The product meets the standards of the U.S. Food and Drug Administration or other controlling U.S. authority.

3) Patent Infringement - USAID must obtain express authorization of the owner of the patent before it finances a pharmaceutical product manufactured outside the United States which would involve use of, or be covered by, an unexpired patent of the United States which has not previously been held invalid by an unappealed or unappealable judgment or decree of a court of competent jurisdiction. This requirement cannot be waived

APPENDIX D. USAID WHOLESALER TRIP REPORTS

1. Visit to IDA Facilities in Amsterdam, Netherlands, February 6-7, 2006

In Attendance: USAID, Management Sciences for Health, IDA

Background

This visit was intended to become more familiar with the quality assurance and quality control practices of this organization which was founded in 1972. There are approximately 180 employees—35 are employed in sales and marketing with the balance employed at various sites located primarily in the IDA's Netherlands headquarters and warehouses. Its in-warehouse inventory includes over 700 items, approximately half of which are pharmaceutical products on the WHO Essential Medicines List (EML). The warehouse in the Netherlands is a bonded facility so there are no import requirements on bringing products in or out of it. Historically, IDA had approximately 100 suppliers but they are winnowing that inventory down to a target of 15. At this time, there are approximately 50-60 suppliers. IDA's product registration dossier activities are in the process of being transferred to its offices in India where most of its sources are located. Attachment A is a brief presentation background on this organization. In addition to single products, the organization has prepared aggregate kits for emergencies in accordance with WHO guidelines. The kits for the tsunami consist of three pallets each with eight cartons. The kit is intended to supply basic health supplies for 10,000 persons for three months. The product expiry of the packaged materials are monitored and if expiry occurs the items will be replaced (none has reached expiry yet). The kits can be prepared to any specifications, e.g., palliative care, and can include controlled substances.

IDA has an annual turnover of approximately 80 million Euros per year of which nearly 50 percent is for ARVs. The ARVs are sold to 40 countries. It stocks approximately 700 products and has an additional 2,300 products within reach. The warehouse has about four turnovers per year and receives/ships approximately 15–20 containers per week.

The laboratory has 5–6 employees performing about 4,000 physical examinations per year and 400-600 analyses per year in a one-shift operation. The lab is equipped with two dissolution apparatuses, two high-performance liquid chromatographies (HPLCs), and a number of titration rigs. The activity level in the laboratory was high and appeared to be under control. The India facility will have 20 laboratory staff members.

Products—Its pharmaceutical product line is manufactured primarily in India but there are also some products from China. The products bear an IDA label and carry an IDA patient insert. The product labels also carry the name of the manufacturer and the site of manufacture, manufacturer lot number, and expiry date. The products which are on the EML also carry an EML symbol. The products are sourced from approved manufacturer sites and all sources are routinely monitored at three year intervals. The WHO prequalified suppliers are similarly monitored. The IDA also purchases European export-only products from some firms but plans to phase this activity out in preference to Indian source products. The majority of its suppliers do their stability studies for

climatic zones I and II, and IDA is pushing them to perform stability testing for zones III and IV which would be more appropriate for the tropical regions where IDA's products are distributed.

Approximately two to three batches of product per month expire and are disposed of in approved waste facilities, either low or high temperature incinerators. Small amounts of expired materials are disposed of without comment but larger volumes of expired products are investigated to determine the source of the forecast errors (root cause analysis?).

Inspections—There are approximately 85 inspections planned for this calendar year. Inspections are conducted by the IDA staff and two competent contractors in accordance with WHO GMP criteria. Inspection reports are annotated with observed deficiencies linked to WHO GMP citations.

All inspection data is carried in pdf format on IDA's intranet and all aspects of the processes and plans can be accessed rapidly.

Other—There are 15 buyers of which three purchase ARVs only. There are six buyers in India and one in China, two more buyers are expected soon.

Facility Overview

1. Tour of receiving dock and quarantine area

    a. There are two facilities in the Amsterdam area one of which is owned by IDA and the other a leased space. There is a new warehouse planned for India and the leased facility will be closed when the new one is completed. The IDA uses both physical and electronic quarantine for incoming goods.

2. Released goods storage areas

    a. The released goods areas were well maintained and orderly

3. Shipping areas

    a. The shipping areas were well maintained and orderly

4. Testing laboratory facilities

    a. The testing laboratory facilities had five full-time staff members with two dissolution apparatuses and HPLCs. There were numerous titration apparatuses. Although an extensive audit was not conducted, the facility appeared to be under control.

For pharmaceutical and other medical products which are not FDA-approved or WHO prequalified—

1. Vendor prequalification procedures including documentation assessments

a. There are extensive assessment processes including inspections, documentation assessments, and product testing. IDA is winnowing down the number of suppliers in its inventory to help assure quality products and have better control.

2. GMP compliance assessments, product testing, ongoing quality assurance programs including follow-up visits and routine product surveillance programs

    a. GMP assessments are conducted by IDA staff and contractors, and are well documented. Follow-up inspections are conducted at intervals.

For all products—

1. Customer complaint files and resolution documentation

    a. Customer complaint files are maintained and appropriate follow-up actions are initiated and documented

2. Product recalls and adverse medicine event reports receipt and follow-up procedures quality testing

    a. There are infrequent recalls and those that have occurred are documented. There have been no adverse event reports which have been substantiated on follow-up.

With regards to products available—

1. Product lists with prices

    a. These were made privately available to Robert Staley, Procurement Director for SCMS

2. Country registrations of products, how are these registrations are assured, and by whom

    a. IDA registers its own products—all products are own label contract manufacture and IDA registers the manufacturer site as required

3. Ability to provide import required quality and shipping documentation, import requirements of receiving country

    a. IDA supplies the required documentation to deliver their products through customs

4. Time frames from receipt of order to delivery, and handling of routine and emergency orders

    a. The time frames vary depending on amounts and whether the products are held in their limited buffer stocks

5. Business capacity issues—current transaction and shipping volumes and scale-up options

a. The current transactions and shipping volumes are under control and the current model could likely be doubled. Direct deliveries of larger quantities would allow significant scale-up since the materials would not have to transit their warehouses. This would also require an alternative sampling and verification model.

6. Document retention and access—certificates of analyses, clean report of findings, pro forma invoices

    a. These are all adequately maintained and accessible

2. Visit to UNICEF, February 08, 2006

Background

UNICEF has a turnover of approximately $1 billion per year which consists of about $500 million in vaccines which are directly delivered; and $80 million pharmaceutical products of which approximately $20 million are routed through its warehouses in Copenhagen and Dubai, and $60 million are sent directly to the country; it will be closing its warehouse in Johannesburg. The remaining product turnover includes medical supplies, educational materials, etc. All products are examined against procurement documents and selected pharmaceutical samples are sent for analyses. Approximately 35 samples are sent for analyses per year; this number includes both new products and routine surveillance samples. The analytical work is performed by the Therapeutic Goods Administration (TGA) of Australia. In the past, UNICEF also sent work to the Danish Government laboratories but they were much more expensive than the TGA. The UNICEF warehouse operations are expected to cover their expenses through direct charges to non-UN users such as the International Red Cross-Crescent and charge-backs to other UN organizations.

Facility Overview

1. Tour of receiving dock and quarantine area

    a. The receiving and quarantine areas appeared adequate and under control. Sampling is conducted at the receiving area and physical examination is performed in an adjacent area.

2. Released goods storage areas

    a. The released goods areas were orderly and appeared adequate and under control

3. Shipping areas,

    a. The shipping areas were orderly and appeared adequate and under control.

4. Testing laboratory facilities if nearby

a. The UNICEF makes use of the Therapeutic Goods Administration (TGA) laboratories in Australia. There are 35 samples for new product qualification and routine surveillance submitted annually for examination. The routine samples are selected from the $80 million pharmaceutical products purchased per year and a number of new product registrations.

For pharmaceutical and other medical products which are not FDA approved or WHO prequalified—

1. Vendor prequalification procedures including documentation assessments

    a. Prequalification procedures and documentation assessments appear to be adequate and under control.

2. GMP compliance assessments, product testing, ongoing quality assurance programs including follow-up visits, and routine product surveillance programs,

    a. The procedures for GMP review appear adequate and under control. The UNICEF purchases 30 to 50 percent of its pharmaceutical products from countries without strict regulatory authorities (European Union export only, non-PIC/S, not United States or Japan)

For all products—

1. Customer complaint files and resolution documentation

    a. Customer complaint files and resolution documentation were reviewed and appeared to be adequate and under control

2. Product recalls and adverse drug event reports receipt and follow-up procedures quality testing

    a. Product recalls and adverse drug event reports are few and appear to be adequately addressed and under control

With regards to products available—

1. Product lists with prices

    a. Robert Staley was comfortable with the responses he received

2. Country registrations of products, how are these registrations assured, and by whom

    a. UNICEF handles registration requirements and has staff members available in each of the countries to help get products through registration

3. Ability to provide import required quality and shipping documentation, import requirements of receiving country

a. UNICEF is able to meet the country requirements for getting materials through customs

4. Time frames from receipt of order to delivery, handling of routine and emergency orders

    a. Dealing with emergencies is a UNICEF strength and these events are smoothly and effectively addressed; routine operations appeared to be adequate and under control

5. Business capacity issues—current transaction and shipping volumes and scale-up options

    - The SCMS transaction load and shipping volumes would not likely pose an unusual challenge to UNICEF

6. Document retention and access—certificates of analyses, clean report of findings, pro forma invoices

    - The documentation retention and access procedures appear to be adequate and under control

3. Visit to Missionpharma, February 9, 2006

Background

Missionpharma is a for-profit PLC which was established approximately 30 years ago. Its business is approximately 90 to 95 percent with the public sector and generated through responses to tenders. The organization's turnover is approximately $70–80 million per year which consists of approximately 75 percent generic medicines and 25 percent non-medicine products. The product volume is about 2,000 containers per year. Approximately 70 percent of its shipping is surface. Missionpharma maintains an inventory of approximately 800 medicine presentations primarily obtained from firms which have products on the WHO prequalified list. Over 60 percent of its products are obtained from India and the balance from European sources (both EU marketed and export only) and China. As with the other wholesalers, the organization's suppliers generally supply products stability tested and labeled for Climatic Zone II. It performs about 6,000 physical examinations per year and 150 product analyses. Approximately 10 percent of the products are blister packs. The outdated products are about 4 to 5 percent a year which are disposed of at a licensed facility. The warehouses are bonded and do not require customs clearance although it is investigating marketing in Denmark. Missionpharma employs wireless thermometers in its controlled temperature space. It received 33 complaints last year and had no recalls. Last year it prepared hospital kits tailored for different types of hospitals in Ethiopia. One adverse event report was received last year which was confused and couldn't be followed through but was documented at the offices. It has a large World Bank prime procurement contract in the Congo and have eight senior staff members assigned there for the implementation. They perform initial and routine follow-up inspections on their suppliers.

Facility Overview

1. Tour of receiving dock and quarantine area

    a. The receiving dock and quarantine area were orderly and appeared to be under control; both physical and electronic quarantine procedures are in use

2. Released goods storage areas

    a. The released goods storage areas were orderly and appeared to be under control

3. Shipping areas

    a. The shipping areas were orderly and appeared to be under control

4. Testing laboratory facilities, if nearby

    a. The testing lab facilities used by Missionpharma are located in India and could not be visited. It reported that the facility is ISO 17025 accredited. The records indicated analytical summaries for approximately 150-200 products and about 10 failed; the QA staff adequately discussed these findings and their resolution—rejected products.

For pharmaceutical and other medical products which are not FDA approved or WHO prequalified—

1. Vendor prequalification procedures including documentation assessments

    a. The qualification protocols appeared to be adequate and under control

2. GMP compliance assessments, product testing, ongoing quality assurance programs including follow-up visits and routine product surveillance programs

    a. Although we did not have sufficient time to review these matters in depth their protocols and discussions appeared to be adequate and under control.

For all products:—

1. Customer complaint files and resolution documentation

    a. Complaint files were presented and their resolution discussed; the system appears to be adequate and under control

2. Product recalls and adverse drug event reports receipt and follow-up procedures quality testing

    a. There are few recalls or adverse events reported and the protocols appear adequate and under control

With regards to available products—

1. Product lists with prices

    a. Robert Staley discussed these matters with the staff and was satisfied with the responses

2. Country registrations of products, how are these registrations assured, and by whom

    a. Missionpharma handles its own product registrations which include the manufacturer-site information

3. Ability to provide required import quality and shipping documentation and import requirements of receiving country

    a. Missionpharma provides all of the required documentation to meet the receiving country requirements.

4. Time frames from receipt of order to delivery, handling of routine and emergency orders

    a. Their handling of routine and emergency orders appeared to be adequate and under control

5. Business capacity issues— current transaction and shipping volumes and scale-up options,

    a. Their current warehousing could handle a significant increase in volume and their transaction capacity appeared to be adequate for an increase; it is likely that the larger SCMS orders would be direct deliveries which would not transit the warehousing

6. Document retention and access— certificates of analyses, clean report of findings, pro forma invoices

    a. Its document retention and access appeared to be adequate and under control.

APPENDIX E. DRAFT WHOLESALER PRESCREENING APPLICATION

USAID Office of Foreign Disaster Assistance Pharmaceutical Wholesaler Precertification Project

Pharmaceutical Wholesaler Precertification Screening Application

Section 1. Wholesaler General Information
1.1 Date:
1.2 Legal business name:
1.2.1 Doing business as (if different than legal business name)
1.2.2 Physical address of all locations providing warehouse and distribution services:
1.3 Phone number:
1.4 Fax number:
1.5 E-mail address:
1.6 Website URL:
1.7 Name of person completing application, including position/title:
1.8 Attach list of commodities normally stocked and include manufacturer and country of origin
1.9 If you keep an inventory of disaster-type kits, please attach a listing of kits, kit contents and price/kit.
1.10 Please attach a list of any human or veterinary pharmaceuticals (e.g., essential medicines, vaccines) maintained in stock that may be used for emergencies (other than those contained in a prepackaged emergency kits.

Section 2. Business Viability and Organizational Structure			
2.1 Year when business established as a pharmaceutical wholesaler:	Year:		
2.2 Annual turnover for pharmaceuticals in U.S. dollars (USD) x past three years 2003, 2004, 2005; if an audited financial statement is available, kindly attach.	$	$	$
2.2.1 Provide turnover for human pharmaceutical stocks for past three years	$	$	$
2.2.2 Provide turnover for veterinary pharmaceutical products; if none are sold or stocked, mark "N/A" in box.	$	$	$
2.3. Annual turnover for pharmaceuticals in USD x past three years 2003, 2004, 2005; if an audited financial statement is available, kindly attach.	$	$	$
2.3.1 Can you provide documentation to confirm actual sales and purchases?	Yes ☐	No ☐	
2.4 Please attach a copy of your organizational chart and indicate name of individual for key positions and length of time employed.			

2.5 Indicate the number of personnel employed within the following key functional departments (indicate if full-time <FT> or part-time <PT> **and** attach resume for each department lead). Note: The same employee may work for more than one department. If applicant operates in more than one physical location, provide PT or FT personnel for each location.	Location #1	Location #2	Location #3	
2.5.1. Management	PT FT	PT FT	PT FT	Comment:
2.5.2. Prequalification of pharmaceutical manufacturers/suppliers	PT FT	PT FT	PT FT	Comment:
2.5.3. Quality Assurance/Quality Control (the overall management plan to ensure that quality requirements for a product or service will be fulfilled and analytical measurements carried out according to standard operating procedures (SOPs) to ensure product quality and safety).	PT FT	PT FT	PT FT	Comment:
2.5.4. Purchasing:	PT FT	PT FT	PT FT	Comment:
2.5.5 Storage:	PT FT	PT FT	PT FT	Comment:
2.5.6 Distribution and shipping:	PT FT	PT FT	PT FT	Comment:
2.5.7 Pharmacist(s)	PT FT	PT FT	PT FT	Comment:
2.5.8 Total number of PT and FT personnel including support staff	PT FT	PT FT	PT FT	Comment:
2.6 Please **attach** a list of all the following types of clients:				
2.6.1 Government clients for the past 2 years				
2.6.2 International health organizations/nongovernment clients for past 2 years.				
2.7 Please indicate (below) the availability of the following licenses/certificates/inspection reports (including date of issue and expiry date) issued by a national/regional regulatory authority and other certifying organizations **and attach copies**.				
2.7.1 Pharmaceutical Wholesaler License (if applicant operates more than one facility, provide information for each facility including facility address, contact information and licenses)	Year:		N/A ☐	
2.7.2 Other certifications or licenses issued by a regulatory authority (e.g., ISO):	Other:			
2.7.3 Regulatory authority inspection report (attach copy of reports for past three years):	Year:		N/A ☐	
Section 3. Manufacturer/Supplier Prequalification				
3.1 Do you have written SOPs for prequalifying pharmaceutical manufacturers/suppliers?	Yes ☐		No ☐	
3.1.1 Indicate date (month/year) of most recent SOP review or revision:	Date Reviewed:		Date Revised:	
3.2 Are product and manufacturer prequalification SOPs for non-U.S. manufacturers and products consistent with the World Health Organization's (WHO) "A Model for Quality Assurance System for Procurement Agencies," Appendix 6 and 8, WHO Technical Series, No. 937, 2006? Reference: http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf	Yes ☐		No ☐	Comment:

3.2.1 Do medicines that you supply conform to U.S. Pharmacopeia (USP), British Pharmacopoeia (BP), European Pharmacopoeia (EP), or International Pharmacopeia (IP) specifications (unless not available for a product)? Reference: http://www.pharmacopoeia.org.uk/	Yes ☐	No ☐	Comment:
3.2.2 For medicines not listed in official compendia, do you provide product specifications?	Yes ☐	No ☐	Comment:
3.3 Does your staff or a contracted external inspection group perform on-site inspections that conform to U.S. Food and Drug Administration (FDA) or WHO cGMP guidelines for all manufacturers that do not have a current manufacturing license issued by a Stringent Drug Regulatory Authority (SDRA) as defined by USAID or WHO? Please indicate individual and qualifications of personnel performing site inspections in the comment section. (SDRAs include: FDA, Japan, all 25 European Union countries, Canada, Australia, and Switzerland). Reference: http://www.ich.org/cache/compo/276-254-1.html	Yes ☐	No ☐	Comment:
3.3.1 If pharmaceutical manufacturer site inspections are performed, do you inspect all manufacturing facilities where a medicine to be purchased is **not** registered and currently marketed in the country of manufacture?	Yes ☐	No ☐	Comment:
3.3.2 If manufacturing site inspections are carried out, specify qualifications and background of inspection staff	Qualifications and background:		
3.4 For the past three years, state the number of current Good Manufacturing Practices (cGMP) site evaluations performed by your inspection team and number of that failed to meet cGMP standards. If you do not perform GMP inspections, tick N/A.	# inspections/ rejections: /	N/A ☐	Comment:
3.5 If you prequalify manufacturers, do you maintain a site master file for each manufacturer?	Yes ☐	No ☐	Comment:
3.6 For prequalified manufacturers, what is the frequency (in years) of re-inspection?	Years:		Comment:
3.7 Do you maintain pharmaceutical product dossiers for each product purchased from a supplier?	Yes ☐	No ☐	Comment:
Section 4. Procurement			
4.1 Do you have written procurement SOPs?	Yes ☐	No ☐	
4.1.1 Indicate date (month/year) of most recent review or revision	Date Reviewed:	Date Revised:	Comment:
4.1.2 Do your SOPs specify that only prequalified pharmaceutical products linked to a prequalified manufacturer will be procured (if you do not prequalify suppliers, tick N/A)?	Yes ☐	No ☐	N/A ☐

4.2 Can you provide readily retrievable documents to authenticate the source and origin for all pharmaceuticals (see 3.7 above)? At a minimum, this includes Manufacturer Certificate of Analysis (COA) corresponding to your product specifications (i.e., BP, USP, EP) and manufacturer invoice/packing list corresponding to batch shown on COA. **Note:** In some countries this is referred to as a drug pedigree or documentation ensuring that wholesaler has, in its possession, documents to demonstrate that the supply chain from original manufacturer to wholesaler is secure.	Yes ☐	No ☐	Comment:
4.3 If you repackage medicines, in addition to holding a wholesaler license, are you licensed as a manufacturer?	Yes ☐	No ☐	Comment:
4.3.1 Is your manufacturing license issued by a SDRA? (see 3.3. above)	Yes ☐	No ☐	Comment:
4.3.2 Does labeling of repackaged medicines include the name of the original manufacturer?	Yes ☐	No ☐	Comment:
Section 5. Storage			
5.1 Are storage areas for all pharmaceuticals in line with applicable Good Storage Practices similar to those published by the EU or WHO? Reference: 1.http://www.who.int/medicines/services/expertcommittees/pharmprep/QAS_068Rev2_GDPdraft.pdf 2.http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/docs/doc2001/may/gdpguidelines1.pdf	Yes ☐	No ☐	Comment:
5.2 Are drugs stored under normal storage conditions: 15–25ºC or depending on climatic conditions up to 30ºC?	Yes ☐	No ☐	Comment:
5.2.1 Are records maintained that indicate compliance with temperature storage requirements?	Yes ☐	No ☐	Comment:
5.2.1.1 Paper records?	Yes ☐	No ☐	
5.2.1.2 Electronic records?	Yes ☐	No ☐	
5.2.1.3 Indicate frequency in times per day that temperature is recorded:			
5.2.2 For drugs that must be stored under defined storage conditions (e.g., do not store over or under "X"ºC or protect from moisture, light), is documentation available that indicates compliance with indicated storage condition? For example, your policy states storage location for such products and storage location is monitored (for temperature and/or moisture) and measurements recorded.	Yes ☐	No ☐	Comment:
5.3 Do you have written SOPs and associated records of documentation applicable to all storage activities including but not limited to the following (if available, indicate month/year reviewed or revised)?	Yes ☐	No ☐	

5.3.1 Receipt (receiving)	Date Reviewed:	Date Revised:	Comment:
5.3.2 Product quarantine (i.e., products are not released to general storage for distribution until physical inspection is completed)	Date Reviewed:	Date Revised:	Comment:
5.3.3 Narcotics	Date Reviewed:	Date Revised:	Comment:
5.3.4 Cold storage	Date Reviewed:	Date Revised:	Comment:
5.3.5 Rejected products (damaged/returned/expired, etc.)	Date Reviewed:	Date Revised:	Comment:
5.3.6 Product samples from all batches received	Date Reviewed:	Date Revised:	Comment:
5.3.7 Sanitation (cleaning)	Date Reviewed:	Date Revised:	Comment:
5.3.8 Pest control	Date Reviewed:	Date Revised:	Comment:
5.3.9 Security (i.e., restricted entry to drug storage areas, alarm system)	Date Reviewed:	Date Revised:	Comment:

Section 6. Distribution			
6.1 Are distribution SOPs in line with principles of Good Distribution Practice? Reference: www.who.int/medicines/publications/pharmprep/TRS_937.pdf p.179-204	Yes ☐	No ☐	Comment:
6.2 Indicate availability of the following documents that provide documentation from manufacturer to consignee (attach copy of each document):			
6.2.1 Certificate of Pharmaceutical Product. Reference: http://www.who.int/medicines/areas/quality_safety/regulation_legislation/certification/modelcertificate/en/	Yes ☐	No ☐	Comment:

6.2.2 Certificate of Analysis corresponding to batch that includes testing against defined standards (BP, USP, International Pharmacopoeia), EP; if no compendia standard exists, COA indicates manufacturer standard utilized:	Yes ☐	No ☐	Comment:
6.2.3 GMP certificate consistent with FDA cGMP or WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce	Yes ☐	No ☐	Comment:
6.2.4 Shipping invoice and/or packing list that includes at a minimum, international non-proprietary name, formulation (i.e., capsule, injection, topical) strength, unit size, pack size, batch number(s), date of manufacture and expiry, price per unit and extended price. State exceptions, if any.	Yes ☐	No ☐	Exceptions:
6.3 Prior to shipment, do you verify that all drugs are registered in the consignee's country or if not registered, an import waiver has been obtained by consignee?	Yes ☐	No ☐	Comment:
Section 7. Quality Management			
7.1 Do you have a quality manual that includes policy statements, SOPs, and documentation for all activities including—			
7.1.1 Internal audit	Yes ☐	No ☐	Comment:
7.1.2 Prequalification of manufacturer	Yes ☐	No ☐	Comment:
7.1.3 Prequalification of product	Yes ☐	No ☐	Comment:
7.1.4 Purchasing	Yes ☐	No ☐	Comment:
7.1.5 Receipt of products	Yes ☐	No ☐	Comment:
7.1.6 Storage	Yes ☐	No ☐	Comment:
7.1.7 Distribution	Yes ☐	No ☐	Comment:
7.1.7 Indicate date (month/year) of most recent review or revision	Date Reviewed:	Date Revised”	
7.2 Are your quality assurance practices in line with the main principles of FDA on GMP for pharmaceutical practices (reference: http://www.fda.gov/cder/dmpq/cgmpregs.htm) or WHO guidelines? (http://whqlibdoc.who.int/publications/2004/9241546190_part1.pdf)	Yes ☐	No ☐	Comment:

7.3 Do you retain samples of all pharmaceutical batches extending to or beyond the product expiration date?	Yes ☐	No ☐	Comment:
7.4 Do you visually inspect (labeling, appearance of tablets, etc.) a sample of all batches received prior to release for sale?	Yes ☐	No ☐	Comment:
7.5 Do you perform random laboratory testing against defined standards for pharmaceutical products?	Yes ☐	No ☐	Comment:
7.5.1 If you perform random laboratory testing, what is the average number of tests performed for the past two years and indicate # of failing products, if any?	200_: / (# tests / # failed)	200_: / (# tests / # failed)	Comment:
7.5.2 If you perform laboratory testing in-house, does your laboratory comply with principles of Good Laboratory Practices? Reference: http://www.olis.oecd.org/olis/1998doc.nsf/LinkTo/env-mc-chem(98)17	Yes ☐	No ☐	Comment:
7.5.3 Do you outsource any product testing? Please attach name and address of lab(s) and contact information.	Yes ☐	No ☐	Comment:
7.5.3.1 If you outsource product testing, does your contract laboratory comply with principles of Good Laboratory Practices? If yes, please provide copy of current GLP certificate.	Yes ☐	No ☐	Comment:
Section 8. Management Information System/Record Keeping System			
8.1 Do you maintain an electronic and/or manual MIS that can provide prompt retrieval of all records that document activities including but not limited to:			
8.1.1 Prequalification of manufacturers/suppliers	Yes☐	No ☐	Comment:
8.1.2 Procurement	Yes ☐	No ☐	Comment:
8.1.3 Receipt	Yes ☐	No ☐	Comment:
8.1.4 Storage	Yes ☐	No ☐	Comment:
8.1.5 Drug quality tests	Yes ☐	No ☐	Comment:
8.1.6 Disposal of outdated/damaged/recalled/substandard drugs	Yes ☐	No ☐	Comment:
8.1.7 Distribution	Yes ☐	No ☐	Comment:

8.1.8 Client complaints (e.g., service, product)	Yes ☐	No ☐	Comment:
8.1.9 Pharmaceutical recalls	Yes ☐	No ☐	Comment:

Section 9. Applicant Comments

Please include any additional explanatory comments and refer to Section and number :

ATTESTMENT: I _____ (insert name) am authorized by _____ (name of company) to provide the information requested in this application and certify that all information is correct and true and documentation is available upon request that will validate all responses. We also agree to unannounced inspection visits by OFDA representatives and understand that if information provided in this application cannot be substantiated, eligibility for USAID/OFDA precertification may be withheld until proof of corrective action is taken and another inspection can be scheduled.

Date: Signature:

Print Name:

Title and Position: Phone:

E-mail:

FOR OFDA USE

Application is complete and site inspection is/is not (circle one) recommended.

Comments:

Reviewer Name and Signature:

Date:

APPENDIX F. WHOLESALER SITE INSPECTION GUIDE

USAID Office of Foreign Disaster Assistance Pharmaceutical Wholesaler Precertification Project

Pharmaceutical Wholesaler Site Inspection Guide

Section 1. General Information			
Note to inspectors: Verify information below uploaded from wholesaler prescreening application			
1.1 Date:			
1.2 Legal business name:			
1.2.1 Doing business as (if different than legal business name)			
1.2.2 Physical address of all locations providing warehouse and distribution services:			
1.3 Phone number:			
1.4 Fax number			
1.5 E-mail address:			
1.6 Website URL:			
1.7 Name of person completing application, including position/title:			
1.8 Attach list of commodities normally stocked and include manufacturer and country of origin			
1.9 If you keep an inventory of disaster-type kits, please attach a listing of kits, kit contents and price/kit.			
1.10 Please attach a list of any human or veterinary pharmaceuticals (e.g., essential medicines, vaccines) maintained in stock that may be used for emergencies (other than those contained in a prepackaged emergency kits.			
Section 2. Business Viability and Organizational Structure			
2.1 Verify date when business established as a pharmaceutical wholesaler	Verified: Yes ☐ No ☐		
2.2. Annual pharmaceutical turnover in U.S. dollars (USD) for past three years confirms turnover stated in screening questionnaire (documentation available to confirm sales).	Yes ☐	No ☐	Comment:
2.2.1 Is annual turnover for pharmaceutical products x past three years as stated in prescreening application?	Yes ☐	No ☐	Comment:
2.2.3 If an audited financial statement has been submitted, is original available for review?	Yes ☐	No ☐	Comment:
2.3. If an audited statement has not been submitted with prescreening application, is documentation available to verify sales and purchases?	Yes ☐	No ☐	Comment:

2.4 Company organizational chart clearly defines authority, responsibility, and interrelationships of personnel to assure that processes for product selection and quality will not be compromised (e.g., purchasing and prequalification are not carried out by the same person).	Yes ☐	No ☐	
2.5 There are current written job descriptions for all key personnel (prequalification, quality assurance/quality control, purchasing, storage, distributions and shipping, pharmacist in charge).	Yes ☐	No ☐	Comment:
2.5.1 Documentation available to confirm previously submitted list of full-time and part-time personnel.	Yes ☐	No ☐	Comment:
2.6 Verify license to operate a wholesale pharmaceutical distribution facility issued by Stringent Drug Regulatory Authority (SDRA) is current. If applicant operates more than one facility, verify licensure information for each facility.	Yes ☐	No ☐	Year:
2.6.1 If applicant has indicated certifications or licenses from organizations (e.g., ISO), verify availability of such licenses.	Yes ☐	No ☐	Year:
2.6.2 Inspection report from DRA is available for review and if deficiencies noted, evidence available that deficiencies have been addressed.	Yes ☐	No ☐	
2.7 Documentation available to verify that previously submitted client list (for past two years) includes U.S.- and non-U.S.-based international humanitarian and government entities.	Yes ☐	No ☐	
Section 3. Manufacturer/Supplier and Product Prequalification			
3.1 If applicant has indicated availability of prequalification SOPs for pharmaceuticals and manufacturers/suppliers, verify availability and date of last review/revision.	Yes ☐	No ☐	Comment:
3.2 Are product and manufacturer standard operating procedures (SOPs) for non-U.S. manufacturers and products consistent with the World Health Organization's (WHO) "A Model Quality Assurance System for Procurement Agencies," Annex 6, contained in WHO Technical Series, 937, 2006?	Yes ☐	No ☐	Comment:
3.2.1 Verify that pharmaceuticals supplied by applicant conforms to U.S. Pharmacopeia (USP), British Pharmacopoeia (BP), European Pharmacopoeia (EP), or International Pharmacopeia (IP) specifications (unless not available for a product).	Yes ☐	No ☐	Comment:
3.2.2 For medicines not listed in official compendia, applicant provides product specifications to manufacturer or accepts manufacturer specifications.	Yes ☐	No ☐	Comment:
3.3 If applicant states that staff or a contracted external inspection group perform pharmaceutical manufacturer on-site inspections that conform to FDA or WHO cGMP guidelines at manufacturing facilities that do not have a current manufacturing license issued by a Stringent Drug Regulatory Authority (SDRA) as defined by USAID or WHO (U.S. Food and Drug Administration (FDA), Japan, European Union countries, Canada, Australia and Switzerland) or hold pre-approval by WHO, random review of inspection reports provides validation. Also confirm that inspection staff named in prequalification application carry out inspections.	Comment:		

3.3.1 If pharmaceutical manufacturer site inspections are performed, documentation is available that inspections are carried out at all manufacturing facilities where a medicine to be purchased is **not** registered and currently marketed in the country of manufacture.	Yes ☐	No ☐	Comment:
3.4 If manufacturer inspections are carried out, documentation is available to confirm inspections and re-inspection as per stated frequency of re-inspection in precertification screening application.	Yes ☐	No ☐	Comment:
3.5 Site master files are available for all prequalified manufacturers.	Yes ☐	No ☐	Comment:
3.6 Pharmaceutical product dossiers are available for all procured pharmaceuticals.	Yes ☐	No ☐	Comment:
Section 4. Procurement			
4.1 Procurement SOPs are available and current.	Yes ☐	No ☐	Comment:
4.1.1 Verify date of most recent review or revision	Date Reviewed:	Date Revised:	
4.1.2 Prequalified products are purchased from prequalified manufacturers linked to those products	Yes ☐	No ☐	Comment:
4.2 For all manufacturers and products procured, the following documentation is available: Certificate of Analysis (COA) corresponding to wholesaler specifications and manufacturer invoice corresponding to batch shown on COA.	Yes ☐	No ☐	Comment: Yes ☐
4.3 If wholesaler repackages medicines, in addition to holding a wholesaler license, a current manufacturer license has been issued.	Yes ☐	No ☐	Comment:
4.3.1 Is documentation available to confirm that manufacturing license has been issued by a SDRA? (See 3.3 above)	Yes ☐	No ☐	Comment:
4.3.2 Labeling of repackaged medicines include the name of the original manufacturer.	Yes ☐	No ☐	Comment:
Section 5. Storage			
5.1 Storage areas for all pharmaceutical conform with applicable Good Distribution Practices similar to those published by the U.S. FDA or WHO?	Yes ☐	No ☐	Comment:
5.2 Drugs are stored under normal storage conditions: 15-25ºC or depending on climatic conditions up to 30ºC?	Yes ☐	No ☐	Comment:
5.2.1 Records are maintained that indicate compliance with temperature storage requirements?	Yes ☐	No ☐	Comment:
5.2.1.1 Paper records?	Yes ☐	No ☐	Comment:
5.2.1.2 Electronic records?	Yes ☐	No ☐	Comment:
5.2.1.3 Records documenting frequency of recording temperatures are available.	Yes ☐	No ☐	Comment:
5.2.2 For drugs that must be stored under defined storage conditions (e.g. do not store over or under "X"º C or protect from moisture, light) documentation is available that indicates compliance with indicated storage condition? For example, your policy states storage location for such products and storage location is monitored (for temperature and/or moisture) and measurements recorded.	Yes ☐	No ☐	Comment:

5.3 Written SOPs and associated records of documentation applicable to all storage activities including but not limited to those listed below are available; indicate month/year reviewed or revised. If not available, so indicate.			
5.3.1 Receipt (Receiving)	Date Reviewed:	Date Revised:	N/A ( )
5.3.2 Product quarantine (i.e. products not released to general storage are for distribution until physical inspection is completed)	Date Reviewed:	Date Revised:	N/A ( )
5.3.3 Narcotics	Date Reviewed:	Date Revised:	N/A ( )
5.3.4 Cold Storage	Date Reviewed:	Date Revised:	N/A ( )
5.3.5 Rejected products (damaged/returned/expired, etc.)	Date Reviewed:	Date Revised:	N/A ( )
5.3.6 Product samples from all batches received	Date Reviewed:	Date Revised:	N/A ( )
5.3.7 Sanitation (cleaning and maintenance)	Date Reviewed:	Date Revised:	N/A ( )
5.3.8 Pest Control	Date Reviewed:	Date Revised:	N/A ( )
5.3.9 Security (ex. Restricted entry to drug storage areas, alarm system)	Date Reviewed:	Date Revised:	N/A ( )
Section 6. Distribution			
6.1 Distribution SOPs are in line with Good Distribution Practices	Yes ☐	No ☐	Comment:
6.2 Comprehensive records are available for review that can trace products purchased from manufacturer to receipt by consignee. See list that follows:			
6.2.1 Certificate of Pharmaceutical Product	Yes ☐	No ☐	Comment:
6.2.2 Certificate of Analysis corresponding to batch that includes testing against defined standards (BP, USP, International Pharmacopoeia, EP); if no compendia standard exists, COA indicates manufacturer standard utilized	Yes ☐	No ☐	Comment:
6.2.3 GMP certificate consistent with US FDA c/GMP or WHO Certification Scheme.	Yes ☐	No ☐	Comment:
6.2.4 Verify that shipping invoice includes: international non-proprietary name, formulation, strength, unit size, pack size, batch number(s), date of manufacture, expiry, price per unit and extended price.	Yes ☐	No ☐	Comment:
6.3. Prior to shipment, wholesaler verifies that all drugs are registered in the consignee's country or if not registered an import waiver has been obtained by consignee.	Yes ☐	No ☐	Comment:
Section 7. Quality Management			
7.1 A quality assurance (QA) manual is available that includes policy statements and SOPs for all activities and documentation to support these activities including: including internal audit, prequalification, purchasing, receipt of products, storage and distribution and documentation is available to confirm adherence with SOPs.	Yes ☐	No ☐	Comment:
7.1.1 Internal audit?	Yes ☐	No ☐	Comment:
7.1.2 Prequalification of manufacturer?	Yes ☐	No ☐	Comment:
7.1.3 Prequalification of product?	Yes ☐	No ☐	Comment:

7.1.4 Purchasing	Yes ☐	No ☐	Comment:
7.1.5 Receipt of products?	Yes ☐	No ☐	Comment:
7.1.6 Storage?	Yes ☐	No ☐	Comment:
7.1.7 Distribution?	Yes ☐	No ☐	Comment:
7.2 Verify date that QA manual has been reviewed or revised.	Date Reviewed:	Date Revised:	
7.2.1 Verify that QA practices are in line with the main principles of U.S. FDA on GMP for pharmaceutical practices (reference: http://www.fda.gov/cder/dmpq/cgmpregs.htm) OR WHO guidelines (http://whqlibdoc.who.int/publications/2004/9241546190_part1.pdf)	Yes ☐	No ☐	Comment:
7.3 If applicant has stated that samples of procured products are retained, are samples stored in accordance with manufacturer labeling?	Yes ☐	No ☐	Comment:
7.4 If applicant has stated that they visually inspect a sampling of all batches received prior to a drug's release for sale, is there evidence of this activity?	Yes ☐	No ☐	Comment:
7.5. If applicant has stated that they perform random laboratory testing against defined standards, is there documentation available to support this?	Yes ☐	No ☐	Comment:
7.5.1. If laboratory testing is performed, records are available to verify the number of products tested over the past two years and number of tests where product has failed to meet standards.	Yes ☐	No ☐	Comment:
7.5.2 If laboratory testing is performed in-house, is documentation available to confirm that the laboratory complies with principles of WHO Good Laboratory Practice (GLP)?	Yes ☐	No ☐	Comment:
7.5.3 If wholesaler utilizes a contracted laboratory for pharmaceutical testing against defined standards, is there documentation available to document that the lab operates in line with WHO GLP. Is GLP certificate available? State authority issuing certificate.	Yes ☐	No ☐	Comment:
Section 8. Management Information System/Record keeping			
8.1 Evidence is available that all records are securely maintained and the MIS, whether electronic or manual or both can provide reliable availability of documents/records for all activities including but not limited to:			
8.1.1 Prequalification of manufacturers/suppliers	Yes ☐	No ☐	Comment:
8.1.2 Procurement	Yes ☐	No ☐	Comment:
8.1.3 Receipt of products	Yes ☐	No ☐	Comment:
8.1.4 Storage	Yes ☐	No ☐	Comment:
8.1.5 Drug quality testing	Yes ☐	No ☐	Comment:
8.1.6 Disposal of outdated/damaged/recalled/substandard drugs	Yes ☐	No ☐	Comment:
8.1.7 Distribution	Yes ☐	No ☐	Comment:

8.1.8 Client complaints (e.g. service, product)	Yes ☐	No ☐	Comment:
8.1.9 Pharmaceutical recalls.	Yes ☐	No ☐	Comment:
8.2 Backup systems are in place to prevent loss of data.	Yes ☐	No ☐	Comment:
8.3 Communication access is available via phone, fax and computer.	Yes ☐	No ☐	Comment:

Comments:

Inspection of facility and pharmaceutical documentation reveals that information is/is not (circle one) available to attest to the safety, efficacy and quality of pharmaceuticals that are not FDA approved as required by ADS 312.

Inspector name(s):

Signature(s):

Date:

APPENDIX G: DRAFT EXPRESSION OF INTEREST

Introduction

This EOI is being issued to identify pharmaceutical wholesalers that wish to become precertified by the United States Agency for International Development (USAID), Office of Foreign Disaster Assistance (OFDA), to provide pharmaceutical commodities to OFDA-supported Private Voluntary/Nongovernment organizations (NGOs/NGOs). It is the intent of OFDA to only permit pharmaceutical wholesalers that are precertified to provide products to OFDA supported NGOs/NGOs.

1. Background

The USAID Office of Foreign Disaster Assistance is the organization with United States Congressional mandate to coordinate U.S. Government responses to international disasters. OFDA works in coordination with the affected country, other donor governments, international organization, UN relief agencies and private voluntary and non-governmental organizations (NGOs and NGOs). OFDA's support to Private Voluntary Organizations (NGOs) and Non-Government Organizations (NGOs) can include funding for medicines and supplies required to support relief efforts.

To be eligible for using USAID/OFDA financing, all pharmaceutical and biological products must comply with the U.S. Food and Drug Administration (or other controlling U.S. authority) regulations governing U.S. interstate shipment of such products unless the OFDA approves procurement of non-FDA licensed pharmaceuticals. This is known as a waiver process. In general, the waiver review process consists of a screening of the medications intended for purchase for appropriateness, suitability of quantities, adherence to accepted formularies, acceptability of manufacturers and review of the proposed wholesaler or supplier.

If a NGO or NGO decides that it is in the best interest of their program and the U.S. Government to procure non-FDA approved medications from a pharmaceutical supplier (manufacturer, distributor or pharmaceutical wholesaler), they must provide OFDA with certain information including, among others:

- Non-availability of the product from a U.S. source or the delivered price from the U.S. would be at least 50 percent more than from another source
- Certification that the pharmaceutical wholesaler providing the essential medications is certified to market drug products
- Evidence from the drug wholesaler that the product manufacturer holds a current Certificate of Good manufacturing Practices demonstrating that it meets acceptable standards for the manufacturing of pharmaceuticals
- Documentation attesting to the safety, efficacy and quality of each medication; this would include at a minimum, a certificate of analysis (COA) with batch number and evidence

that the product has been tested against internationally recognized compendia standards (USP, EP, BP, IP, and meets/exceeds such standards

- Product delivered has at least 12 month's shelf life remaining (unless exception has been approved by OFDA)

- Packing lists/invoices with batch number corresponding to COA

2. Purpose

In the context of improving efficiency of access to and affordability of non-FDA approved essential drugs that meet U.S. requirements for safety, efficacy and quality when a disaster or emergency situation occurs, it the intent of the OFDA to precertify pharmaceutical wholesalers via a transparent and uniformly applied process. The precertification of wholesalers will streamline the process of preparing and approving procurement requests from U.S. Missions, PVOs/NGOs and NGOs.

3. Process

The precertification process will include completion of a prescreening application requesting detailed information relative to the applicant wholesaler's:

- business viability and organizational structure
- prequalification of pharmaceutical products and manufacturers
- purchasing, storage and distribution of pharmaceutical products and
- quality assurance system.

Based upon predetermined criteria, an applicant may be precertified with or without an on-site inspection or additional information may be requested. A list of precertified wholesalers will then be shared USAID/OFDA partners and it is expected these wholesalers will be the first points of contact when an emergency procurement is required.

Note: Although not the basis for precertification, it may be useful for applicants to become familiar with the contents of the World Health Organization, Annex 6, "A Model Quality Assurance System for Procurement Agencies", WHO Technical Report Series, No. 937, 2006.

4. Procedure for submission of EOI

A. Submit a cover letter expressing interest in obtaining OFDA wholesaler precertification, including contact person, name and address of principal location, e-mail address and phone number to:

USAID/OFDA
Reference: OFDA Pharmaceutical Wholesaler Precertification
Address:
E-mail:
Telephone:

B. Upon receipt of your EOI addressed to the e-mail address above or in writing, a link to the prescreening pharmaceutical wholesaler application will be e-mailed to you. The application should be completed electronically and returned via e-mail and courier. Your application will be processed in the order received. Applications that are not complete will be returned and will require resubmission for consideration. Resubmitted applications will then fall to the back of the queue.

APPENDIX H. ACTION MEMORANDUM, SUBJECT: SOURCE/ORIGIN WAIVER FOR CERTAIN PHARMACEUTICALS UNDER PARTNER FOR SUPPLY CHAIN MANAGEMENT SERVICE (PFSCM) CONTRACT, AUGUST 30, 2006

U.S. AGENCY FOR INTERNATIONAL DEVELOPMENT

ACTION MEMORANDUM

TO: GH/OHA, S. Ken Yamashita

FROM: OHA/SCMS, Carl Hawkins

SUBJECT: Source/Origin Waiver for Certain Pharmaceuticals under Partnership for Supply Chain Management Service (PFSCM) Contract

Background

We are recommending that you approve a source/origin waiver to code 935 for pharmaceuticals:

a) Manufactured at a site approved by a Stringent Regulatory Authority (SRA), or
b) Offered by the International Dispensary Association Foundation (IDA), Missionpharma, or UNICEF

This waiver does not apply to ARVs, which are covered under other waivers. The Director of OHA has been delegated the authority to sign such waivers through ADS 103.3.16, effective 2/6/1996 (See Appendix A).

1. Source, Origin and Nationality. Under USAID source, origin and nationality rules in 22 CFR 228, a waiver of source/origin/nationality can be made on the basis that offshore procurement is necessary to promote efficiency in the use of foreign assistance resources, including to avoid impairment of foreign assistance objectives.

This waiver is necessary to promote efficiency in the use of U.S. foreign assistance resources in that it will allow for the purchase of pharmaceuticals that are critical to the PEPFAR program. It is the stated policy of the PEPFAR program that the Emergency Plan will purchase the lowest-cost drugs, regardless of origin, when demonstrated to be safe, effective and of high quality. A critical component of the

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WASHINGTON, D.C. 20523

PFSCM contract is to provide pharmaceuticals in support of the entire PEPFAR program in a timely and efficient manner, including instances of stock-outs where time is of the essence. This waiver will permit the OHA/SCMS to create and maintain a list of safe and effective multi-source generic pharmaceuticals from which USAID Missions, other USG posts, and other PEPFAR implementing entities can order through the PFSCM contract, rather than processing waivers on a transaction-by-transaction basis. This waiver does not apply to PEPFAR-related purchases made outside the PFSCM contract.

This expanded list of eligible pharmaceuticals will be on the PFSCM ordering website. GH/OHA/SCMS will oversee additions and corrections and monitor the maintenance of the list, which the contractor will administratively manage. The fact that a product is on the list does not necessarily mean that it will be bought. Each procurement of pharmaceuticals is monitored and approved by OHA/SCMS for technical and programmatic appropriateness. The in-country team, the PFSCM contract team, and OHA/SCMS will consider whether it is the appropriate product, whether the dosage is correct, possible alternatives, potential sources, cost, and a variety of other factors.

A critical objective of the PEPFAR program is the sustainability of HIV/AIDS host-country programs. This requires us to use existing sources of pharmaceuticals (with due regard for safety, efficacy and quality) to provide the availability and readiness of adequate stocks of generics that will ensure the sustainability necessary for effective and efficient supply chain management support to PEPFAR activities under this contract. Most often the pharmaceuticals being used in country programs are not from the U.S. and an equivalent U.S.-manufactured pharmaceutical is not registered by the host government drug regulatory authority. Without access to high quality, low cost pharmaceuticals that are approved for use and are being used in the countries in which USAID works, PEPFAR country programs will be unable to get pharmaceuticals to those who need them and unable to reach the targets in support of prevention and treatment programs.

Due to international price competition and local registration requirements, there are virtually no U.S. source/origin generic drugs available in the developing countries in which USAID is implementing health programs. Second, in order to build up the supply capacity of in-country programs we are supporting, we must focus on using sources and manufacturers that the host government has approved or will be using.

2. Cost. With regard to the cost differential consideration, i.e., that the US cost be at least 50% more than the non-US cost, experience has shown that non-US sourced generic drugs nearly always meet the requirement (in fact, they are usually an order of magnitude less expensive). An analysis of over 200 commonly used multi-source generics showed a median price ratio between international prices and those available from the Federal Supply schedule of 1:3.8 (in other words, the same product on the FSS was nearly four times more expensive).

3. Safety, Efficacy and Quality. ADS 312 requires that information is available to attest to the safety, efficacy and quality of pharmaceuticals that are not FDA-approved. For this waiver, the following assurances are available:

a. Stringent Regulatory Authorities (SRAs). Because the SRAs designated by USAID have standards similar to the USFDA, SRA approval clearly meets the safety, efficacy and quality requirements of ADS 312. SRA approval was considered adequate for ARVs under the Administrator's 2005 waiver.

USAID practice is that an SRA is a national drug regulatory authority (NDRA) that closely resembles FDA in its operations. Currently, USAID has designated as SRAs the NDRAs that participate in the International Conference on Harmonization (ICH) - they are:

U.S. FDA;
Japanese Ministry of Health, Labor, and Welfare;
European Agency for the Evaluation of Medicinal Products (EMEA) centralized procedure; and
European Free Trade Area (represented by the Swiss Medic).

USAID also has designated as an SRA the Canadian NDRA, the Therapeutic Products Directorate, Health Canada, an observer to the ICH.

b. IDA, Missionpharma, and UNICEF. Based on agency experience and an inspection visit by a USAID team, these pharmaceutical wholesalers have systems in place that adequately address quality assurance of non-FDA approved products and that under ADS 312 information is available to attest to the safety, efficacy and quality of the products they offer. The Trip Report is at Appendix B.

IDA, UNICEF, and Missionpharma are organizations that have well-established reputations for providing high quality generic pharmaceuticals, medical equipment

and supplies to governments, United Nations' agencies and NGOs in developing countries.

UNICEF is a major supplier to both private and public sector health and population program recipients.

Another value added component of IDA, UNICEF, and Missionpharma is that these wholesalers actively strive to register appropriate drug products in least developed countries. Active efforts to achieve drug registration greatly enhance USAID's ability to provide needed drug products in a timely manner.

IDA is the world's largest not-for-profit provider of pharmaceuticals and medical supplies, offering a wide range of quality assured products from stock. IDA is USAID's principal wholesaler for non-US pharmaceuticals, used by USAID in the past on a case-by-case waiver basis for both large and small procurements of non-US pharmaceuticals. For example, Appendix C is a list of over 200 products that have procured from IDA under the RPM Plus project. IDA provides high quality generic pharmaceuticals, medical equipment and supplies to governments, United Nations agencies and NGOs in developing countries. IDA is a preferred supplier to WHO, International Committee of the Red Cross, Doctors without Borders, UNHCR and has previously supplied pharmaceuticals to USAID-funded projects.

Founded in 1975, **Missionpharma** is a for-profit organization with an original objective of supplying low-cost generic pharmaceuticals to missionary clinics associated with the Scandinavian churches. It has since expanded and is one of the world's leading suppliers of generic pharmaceuticals and medical devices to governments, United Nation agencies and NGOs in developing countries. In addition to supplying products from WHO pre-qualified manufacturers, Missionpharma runs its own comprehensive prequalification system, based on the following criteria:

- Valid manufacturer's license and GMP certificate according to WHO guidelines.
- Assessment of Site Master File.
- Evaluation of product dossiers including conducted bioequivalence studies.
- Performing a formalized GMP audit at the manufacturing site.
- Verification of quality control procedures and source of Active Pharmaceutical Ingredient (API).

In addition, Missionpharma has a quality control system for verifying product quality that includes inspection of the actual product and comparison of

Certificates of Analysis against finished product and API specifications. It uses a network of qualified independent laboratories undertaking further analysis of the product quality when required. In case of product complaint or recall, there are Standard Operating Procedures (SOPs) to ensure that corrective and preventive actions are taken in each case.

UNICEF, established in 1946, has a mandate to provide supplies wherever needed in the developing world. A central warehouse is located in Copenhagen, Denmark and HIV/AID drugs and supplies are warehoused and distributed from this site.

UNICEF requires all manufacturers responding to its solicitations to be pre-approved by the WHO and annually demonstrate that they comply with the standards set by the WHO. WHO Geneva Headquarters acts as an adviser to UNICEF on matters related to the quality of pharmaceutical and biological products and has formulated criteria for evaluating the acceptability of vaccines for purchase by UN agencies. All quality assurance functions are provided to UNICEF by WHO. These include random lot testing, inspection of the supplier's facility and the National Control Authority Laboratory by qualified experts, periodic re-inspection and follow-up investigation of adverse events reported. Governments that lack a functioning National Regulatory Authority to ensure pharmaceutical quality are encouraged by WHO to procure through UNICEF in order to ensure the provision of pharmaceuticals of known quality. Procuring through UNICEF is the most effective means to ensure that medications of known quality are procured.

The inspection report concluded that IDA, UNICEF and Missionpharma all have extensive experience in procuring, distributing, and monitoring the quality of pharmaceuticals, medical equipment and supplies in least developed countries throughout the world. The general findings of the report were:

(1) Prequalification. In reviewing the quality testing and monitoring systems, it is our opinion that these three organizations make significant efforts to assure drug quality. Each of the three organizations requires that suppliers undergo a rigorous prequalification process. This process includes an initial application by the supplier that documents business solvency and capacity, ability to supply needed products, and quality of products provided. If the preliminary application is approved, a manufacturing site inspection is scheduled to assess compliance with Good Manufacturing Practice (GMP). Criteria used by inspectors are GMP criteria recommended by the World Health Organization. After a supplier has

successfully completed the prequalification process, routine follow-up GMP inspections are conducted at three year intervals to assure continuing compliance.

(2) Testing. In addition to the prequalification process, samples from the new supplier's drug product are routinely subject to visual inspection and selected testing in reference laboratories to confirm the content and quality of the drugs provided.

(3) Warehousing. The team also reviewed warehousing practices at each of the three companies. It is apparent that state-of-the-art warehouse equipment and facilities are fully available. Standard Operating Procedures are in place to maintain proper control of inventory and related documents and records.

This waiver is based primarily on agency experience with these organizations. We are working with GH/HIDN, OAA/T and OFDA on objective standards under which other organizations might also "pre-qualify" as pharmaceutical wholesalers.

5. Additional quality assurance (QA) testing. As a part of its efforts to ensure ongoing quality of supplies and gather independent data on the QA procedures of its suppliers, PFSCM has a Standard Operating Procedure for QA testing and has reserved the right to routinely conduct its own QA testing of the pharmaceuticals it buys.

6. US patent laws and Express Authorization. Multi-source generics are off patent and, therefore, do not infringe U.S. patent laws or require express authorization by the US patent-holder.

This Action Memorandum has been cleared by Renata Cameron, OAA/T, thereby satisfying the ADS 312.5.3c requirement for M/OAA approval for purchase of non-US produced and non-FDA approved pharmaceuticals.

7

Recommendation

That you approve a source/origin waiver for pharmaceuticals, other than ARVs, for the Supply Chain Management Service (PFSCM) contract; an authority delegated to you by ADS 103.3.16.

Approve _____

~~Disapprove~~ _____

Date 8/30/04

APPENDIX I. REFERENCES, RECOMMENDED READING, AND LINKS

1. European Commission Humanitarian Aid (ECHO). <http://ec.europa.eu/echo/index_en.htm> (accessed May 2, 2007)

2. World Health Organization (WHO). 2004. *A Compendium of Guidelines and Related Materials. Volume 2: Good Manufacturing Practices and Inspection.* <http://whqlibdoc.who.int/publications/2004/9241546190.pdf> (accessed May 2, 2007)

3. WHO. 2005. Go*od Distribution Practices for Pharmaceutical Products* (draft). Geneva: WHO. <http://www.who.int/medicines/services/expertcommittees/pharmprep/QAS_068Rev2_GDP draft.pdf>

4. National Association of Boards of Pharmacy (NABP). 2006. *Model Rules for the Licensure of Wholesale Distributors*. Mt. Prospect, IL: NABP. < http://www.nabp.net/> (accessed May 4, 2007)

5. WHO. 1999. *Operational principles for good pharmaceutical procurement.* Geneva: WHO <http://www.who.int/3by5/en/who-edm-par-99-5.pdf> (accessed May 4, 2007)
.

6. British Association of Pharmaceutical Wholesalers (BAPW). *THE BAPW Gold Standard Good Distribution Practice by Pharmaceutical Wholesalers.* <http://www.bapw.net/policy_and_media/BAPW_gold_standard_of_good_distribution_practice.pdf> (accessed May 4, 2007)

7. Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM). *Policies on Procurement and Supply Management*. <http://www.theglobalfund.org/en/about/procurement/> (accessed May 2, 2007)

8. WHO. 2005. *WHO Expert Committee on Specifications for Pharmaceutical Preparations.* Technical Series 929, Thirty-ninth Report. Geneva: WHO <http://www.who.int/medicines/publications/pharmprep/en/> (accessed May 2, 2007)

9. WHO. 2006. *WHO Expert Committee on Specifications for Pharmaceutical Preparations.* Technical Series 937, Fortieth Report. <http://www.who.int/medicines/publications/pharmprep/en/> (accessed May 2, 2007)

10. U.S. Code of Federal Regulations, Title 21—Food and Drugs, Part 205 Guidelines for State Licensing of Wholesale Prescription Drug Distributors. <http://www.access.gpo.gov/nara/cfr/waisidx_99/21cfr205_99.html> (accessed May 2, 2007)

11. GFATM. Compliance Lists—A List of Products and Suppliers Compliant with the Global Fund Quality Assurance Policy. <http://www.theglobalfund.org/en/about/procurement/compliance/default.asp> (accessed May 2, 2007)

12. European Economic Community. 1992. COUNCIL DIRECTIVE 92/25/EEC of 31 March 1992 on the wholesale distribution of medicinal products for human use. <http://www.ikev.org/docs/eu/392L0025.pdf> (accessed May 5, 2007)

13. U.S. Department of Health and Human Services. Food and Drug Administration. 2006. *Guidance for Industry Quality Systems Approach to Pharmaceutical CGMP Regulations, September 2006.* <http://www.fda.gov/Cder/guidance/7260fnl.htm> (accessed May 2, 2007)

14. Healthcare Distribution Management Association. <http://www.healthcaredistribution.org/index.asp> (accessed May 2, 2007)

15. World Bank. 2000. Technical Note: Procurement of Health Sector Goods. Washington, DC: World Bank. http://web.worldbank.org/WBSITE/EXTERNAL/PROJECTS/PROCUREMENT/0,,contentMDK:20062738~menuPK:84284~pagePK:84269~piPK:60001558~theSitePK:84266,00.html (accessed May 2, 2007)

16. ASEAN Cosmetic Association. 2005. ASEAN GMP Training Module Storage. (workshop). http://www.aseancosmetics.org/presentation/Storage_Module%20.ppt (accessed May 2, 2007)

17. U.S. Agency for International Development. Automated Directive System Chapter 312, Eligibility of Commodities, Section 312.5.3C. <http://www.usaid.gov/policy/ads/300/312.pdf> (accessed May 2, 2007)

18. The International Conference on Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH). <http://www.ich.org/cache/compo/276-254-1.html> (accessed May 2, 2007)

19. European Medicines Agency. <http://www.emea.europa.eu/> (accessed May 2, 2007)

20. Mission for Essential Drugs and Supplies.<http://www.meds.or.ke/contacts.php> (accessed May 2, 2007)

21. GTATM. 2006. Guide to the Global Fund's Policies on Procurement and Supply Management. <http://www.theglobalfund.org/pdf/guidelines/pp_guidelines_procurement_supplymanagement_en.pdf>

22. Pharmaceutical Inspection Convention and the Pharmaceutical Co-operation Scheme. <http://www.picscheme.org/index.php> (accessed May 2, 2007)

23. GFATM. Quality Assurance Information. <http://www.theglobalfund.org/en/about/procurement/quality/> (accessed May 4, 2007)

24. United Nations Children's Fund (UNICEF). UNICEF Supply Catalogue—Pharmaceuticals and Nutrition. <http://www.supply.unicef.dk/catalogue/> (accessed May 2, 2007)

25. NABP. Verified-Accredited Wholesale Distributors Program. <http://www.nabp.net/vawd/vawdapplication.pdf> (accessed May 3, 2007)

26. WHO. Guidelines on the implementation of the WHO certification scheme on the quality of pharmaceutical products moving in international commerce. (accessed May 4, 2007) <http://www.who.int/medicines/areas/quality_safety/regulation_legislation/certification/guidelines/en/index.html>(accessed May 4, 2007)

27. Organization for Economic Co-operation and Development (OECD). OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring. <http://www.oecd.org/document/63/0,2340,en_2649_34381_2346175_1_1_1_1,00.html> (accessed May 4, 2007)

28. Pan American Health Organization. 2003. *Guideline for Good Manufacturing Practices Inspections*. <http://www.paho.org/english/ad/ths/ev/gpm-guideline-inspect-eng.pdf> (accessed May 4, 2007)

29. Broun, D. 2005. *Global Fund Policy on Quality Assurance for Pharmaceutical Products, Procurement of Single and Limited Source Pharmaceuticals*. Tenth Board Meeting. Geneva, GFATM. <http://www.theglobalfund.org/en/files/boardmeeting10/gfb1009_annex4.pdf>

30. Republic of Kenya. Pharmacy and Poisons Board. 2006. Guidelines For Good Wholesaling and Retail Practice For Pharmaceuticals. Nairobi: Kenya.

31. U.S. Department of Health and Human Services. Food and Drug Administration. 2004. *Pharmaceutical cGMPs for the 21st Century - A Risk-Based Approach. Final Report - Fall 2004.* Washington, DC: U.S. Government Printing Office. <http://www.fda.gov/cder/gmp/gmp2004/GMP_finalreport2004.htm>

32. World Bank. 2003. *Assessment of Agency's Capacity to Procure Health Sector Goods.* Washington, DC: World Bank, April 2003. < http://go.worldbank.org/2GBDECUNI0> (accessed May 5, 2007)