INTRODUCTION

Today, global access to quality medicines increasingly is threatened by many factors, including the presence of both substandard and counterfeit medicines. Substandard medicines\(^1\) can occur even when they are manufactured according to quality standards and Good Manufacturing Practices (GMPs). Counterfeit medicines\(^2\), on the other hand, which account for a larger percentage of poor quality medicines in resource-limited countries, occur because there is a deliberate intention to mislead. In both instances, however, the result is poor quality medicines that deny practitioners and patients of achieving expected health outcomes. Poor quality medicines can be especially burdensome in developing countries where they not only fail to produce needed results, but also absorb limited resources, undermine faith in already tenuous health systems, and may promote antimicrobial resistance to devastating infectious diseases such as HIV, malaria, and tuberculosis. Poor quality medicines represent a failure of standards and conformity assessments to standards, and such failures can and do arise at multiple points in the medicines continuum; from discovery, to development, to registration, through manufacturing and distribution, to utilization. The globalization of pharmaceutical markets has exacerbated this growing problem of poor quality drugs, particularly in countries that lack strong drug regulatory systems and oversight. Whatever standards and conformity assessments there are for medicine supply chains—from suppliers to manufacturers, and thereafter from practitioners to patients—these supply chains are becoming increasingly fragmented and fragile.

The United States Pharmacopeial Convention (USP) offers standards that help ensure the quality of processes and products. The process standards include good manufacturing practices and supply-chain management standards. Product standards are offered in monographs with tests, procedures, and acceptance criteria to allow ingredient and product testing. End product or in-process testing at key points along manufacture and supply continua are key components in the series of safety nets that result in quality medicines. For medicines, including natural source and rDNA biologicals, USP’s compendia are the United States Pharmacopeia (USP) and National Formulary (NF) for excipients. While not regulated in the U.S. as medicines but rather as foods, dietary supplements are included in USP’s compendial approaches, and USP is alluded to as a source of standards in the Dietary Supplement Health and Education Act (DSHEA)

\(^1\) Legally registered product that does not meet official USP standards for identity, quality, purity, strength, packaging and labeling.
\(^2\) Product that is deliberately mislabeled for identity and/or source. Usually there is no active ingredient or a different active ingredient than stated on the label.
amendments to the Food, Drug and Cosmetic Act (FDCA). Recently, USP published a Dietary Supplements Compendium for dietary supplements and their ingredients (known as traditional medicines outside the United States). Although USP is not a conformity assessment (enforcing) body, it offers conformity assessments through third party verification programs for dietary supplements and their ingredients as well as medicinal ingredients. USP also provides programs to support training and education in compendial and allied standards. These programs, in turn, can support certification activities for compendial and health professionals.

In this white paper, the USP Council of the Convention Section on Global Public Health presents background information and proposals to stimulate Convention discussion on the roles and responsibilities of a volunteer-driven, practitioner-based standards setting body in promoting global public health through its standards-setting and allied public health activities.

**BACKGROUND AND STATUS OF USP’S GLOBALIZATION EFFORTS**

1. **BURDEN OF COUNTERFEIT, SUBSTANDARD, OR ADULTERATED MEDICINES**

   Approximately 15% of all drugs in circulation are believed to be substandard or counterfeit, with the clinical and financial burdens falling most heavily on developing countries. In some parts of Africa and Asia, as much as 50% of the medicines in commerce may be counterfeit. More than one-third of chloroquine-containing and antibacterial medicines collected in Nigeria and Thailand were found to be below compendial standards as a result of degradation and poor manufacturing. Countries with limited resources face many challenges that can result in poor quality medicines, including weak regulatory systems, poorly staffed and equipped national drug control laboratories (official medicines control laboratories), and poor enforcement due to corruption or lack of political will. Heat and humidity common to many developing countries can reduce quality during manufacture, storage, and distribution. In recent years, many countries—irrespective of their development—have been challenged by episodes of economically-motivated adulteration. Melamine, diethylene glycol, and over-sulfated chondroitin sulfate have created morbidity and mortality within countries and across regions of the globe.

2. **USP AND ADULTERATION**

   As the United States entered the 20th Century, the state of its supply of medicines was poor and deteriorating. This was the era of Dr. Harvey Wiley (a President of the USP Convention) and his poison squad. And it also was an era in which Congress, in 1906, first established a statutory role for USP in helping to assure drug quality. By 1938, Congress had established the modern role we know today for USP-NF as official compendia under the FDCA. Under the FDCA, a drug with a name recognized in USP-NF must comply with compendial identity standards or be deemed adulterated, misbranded, or both. Such drugs must also comply with compendial standards for strength, quality, and purity, unless labeled to show all respects in which the drug differs. Although USP-NF standards have an important

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5 http://www.fda.gov/AboutFDA/WhatWeDo/History/CentennialofFDA/HarveyW.Wiley/default.htm

6 Federal Food, Drug, and Cosmetic Act §201(j), §§501(b), 502(e)
role in federal law, the enforcement of compendial standards is the responsibility of the U.S. Food and Drug Administration (FDA) and other governmental authorities.

3. **USP AND GLOBALIZATION**

Historically, USP’s Convention membership has been sympathetic to international public health opportunities and has always strongly supported the work of the World Health Organization (WHO) and its regional offices (particularly the Pan American Health Organization) and other international organizations that work to promote global public health. In the 1990s and the first decade of the 21st Century, USP accelerated its international efforts. A key decision occurred in the first year of the 2005-2010 cycle when the USP Board of Trustees endorsed development of overseas sites, first in Europe, then in India, China, and finally, in Brazil. Subsequently, the Board advanced a new strategic plan that emphasized the importance of working internationally, which resulted in USP defining key regions and countries of the world for special focus (Attachment 1). USP’s overseas sites were located where USP could have the greatest public health impact—in countries where the largest amount of active pharmaceutical ingredient and dosage form manufacturing is occurring.

This effort has accelerated with more focused initiatives, including language translations; increased global availability of USP’s products and services; and technical assistance provided to ministries of health, regulatory agencies, and national drug control laboratories. USP’s international effort has been forging closer ties with governmental agencies, resulting in the potential for increased cooperation in standards development. At the same time, USP’s standards-setting role and allied financing model (sale of books and reference materials to support its work) at times limits understanding of its broader public health service role and creates the perception that USP is too commercial in nature.

USP’s dependence on revenue from the sale of its books and reference materials stems from the fact that, unlike other pharmacopeias in the world, USP is non-ministerial and receives no government funding for its standards activities. While other pharmacopeias receive financial support from their governments and may also sell their products and services to manufacturers as an additional means of support, USP must rely solely on self-generated income to fund its activities.

USP’s regional focus usually allies well with this traditional financing model, which brings products and services directly to first parties (manufacturers of medicines and pharmaceutical ingredients) who wish to demonstrate adherence to quality standards by use of the USP and NF marks—a traditional value of USP irrespective of whether USP and NF are recognized in national law. However, only a small fraction of the world’s ~200 countries have a significant number of manufacturers whose purchases of USP’s products and services can help finance USP’s other public health activities. For regions without a significant manufacturer presence, USP must find additional resources to support its work in promoting access to quality medicines.

USP’s international initiatives have met with other challenges as well. For example, an attempt to create monographs for articles legally marketed outside of the U.S. (non-U.S. authorized monographs) failed because of constraints on the opportunity (monographs only for neglected infectious diseases) and also in execution (staff were challenged to understand the differentiation in monograph stipulations needed to control the same article in different countries).

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Many organizations in the United States have advanced successfully into global activities. In some ways, USP came somewhat late to these opportunities and, despite impressive success in a few short years, it remains to be seen whether the organization can advance from its national base to act successfully on the world stage in a way that has real impact on global health.

4. USP’S INTERNATIONAL PROGRAMS

The following summarizes USP’s specific international activities and initiatives that, along with the development of its overseas sites, have been part of its globalization.

a) The USP Council of Experts: International Health Expert Committee

In the 2005-2010 cycle, the USP Council of Experts formed an International Health Expert Committee (IHEC) that met at least yearly to consider key issues and opportunities to promote access to quality medicines. In addition, the Expert Committee formed advisory panels to cover key topics. A brief summary of the work of the Expert Committee and its advisory panels appears below:

- **CIPIH Advisory Panel** – This advisory panel, led by committee member Stan N. Finklestein, M.D., developed a paper entitled *How Does the Regulatory Framework Affect Incentives for Research and Development?* in response to a request by the WHO’s Commission on Intellectual Property Rights, Innovation, and Public Health (CIPIH).

- **African Health Advisory Panel** – This advisory panel, led by committee member Andrew Walubo, M.D., conducted a study on the issues of the healthcare system in Sub-Saharan Africa, including the drug distribution system, drug regulatory authority, and drug quality-control laboratories. Dr. Walubo developed a paper entitled *The Drug Situation in the Sub-Saharan Africa* that identified major problems such as widespread killer diseases (malaria, HIV and TB), counterfeits, lack of skilled personnel, and weak regulatory mechanisms. Following a suggestion from the IHEC, Dr. Walubo also wrote two business proposals for strengthening the quality control laboratories and drug regulation’s personnel skills in South Africa, and drug quality testing in rural Uganda using Mini Laboratory tools.

- **Spanish Translation Advisory Panel** – This advisory panel, led by committee member Dr. Enrique Fefer, Ph.D., and supported by staff member Mr. Damian Cairatti, has provided oversight to the translation of the *USP–NF* into Spanish, now in its third consecutive official edition, including Supplements and corresponding online versions. The panel has also undertaken translation of the 4,400 redesigned monographs that will be part of the 2010 revision of *USP–NF*.

- **Russian Translation Advisory Panel** – This advisory panel, led by committee member Roman Koslov, M.D., Ph.D., completed the publication of the *USP-NF* Russian Edition (unofficial) with plans to publish updates in 2009 and 2010 to bring the book to official status. An electronic version is under consideration.

- **Chinese Translation Advisory Panel** – This advisory panel was led by committee member Professor Zhong-Yuan Yang. A Memorandum of Understanding (MOU) between USP and the Chinese State Food and Drug Administration specifies four areas
of collaboration including USP-NF Chinese translation and third party verification of pharmaceutical ingredients.

- **Collaboration with WHO** – The IHEC provided comments on WHO Guidances (normative documents), which are developed by WHO staff with input from experts from around the world. The guidances most relevant to USP are advanced through two WHO Expert Committees: the Expert Committee on Specifications for PharmaceuticalSpecifications and the Expert Committee on Biological Standardization.

b) **USP Drug Quality and Information Program**

The USP Drug Quality and Information Program (USP DQI) is a cooperative agreement with the United States Agency for International Development (USAID) in which USP is funded to provide technical assistance to developing countries. The program was begun in 2000 as a follow-on to the Rational Pharmaceutical Management Plus program. The agreement was extended in 2005 and, more recently, is on track for extension and expansion in 2009. While the program initially focused on drug information, drug quality initiatives were added in 2003 and have become the primary objective. Through staff located in USP’s Rockville headquarters, USP DQI works with governments in more than 30 countries, USAID missions, WHO, and other partners to evaluate a country’s readiness and capacity to provide quality medicines. Working through in-country mechanisms, USP DQI obtains targeted funds to develop or strengthen drug registration processes, drug quality assurance systems, national drug quality control laboratories, and postmarketing surveillance systems. USP DQI also assists manufacturers in developing countries to improve their good manufacturing practices (GMP) to reach WHO prequalification status. The USP DQI program has established a presence in USAID-priority countries on four continents, advancing strategies to improve drug quality and the appropriate use of drugs. Examples of current work appear in Attachment 2.

c) **John Snow, Inc. and Population Services International**

In 2007, USP received funding outside its USAID cooperative agreement to support additional activities in developing countries. This included sub-contracting awards with John Snow, Inc. (JSI) and Population Services International (PSI). JSI implements DELIVER, a separate USAID Project. USP’s role in the project is to provide technical services (i.e., development of standard operating procedures, GMP audits, and laboratory testing) to ensure the quality of antimalarial medicines being procured for and/or by developing countries. USP has also partnered with PSI in the ACT Watch project, a study funded through a private grant from the Bill and Melinda Gates Foundation. USP’s objective in this initiative is to assess the quality of Artemisinin-based Combination Therapy (ACT) antimalarial medicines in developing countries in sub-Saharan Africa and Southeast Asia.

d) **USP’s Verification Programs**

In the early years of the 21st Century, USP began third party verification programs designed to fill regulatory gaps for dietary supplements and their ingredients and medicinal ingredients. As conceived, the program was designed to mimic a regulatory process for articles, with careful document review, testing, GMP audits, and post-market surveillance. The status of articles that have been verified appears below. The program has had slower than expected uptake for several reasons, including cost of execution and the absence of regulatory and/or consumer recognition. Yet, it remains an opportunity that might be useful in developing countries, perhaps with suitable
USP’s role in assuring global access to quality medicines. USP’s program was adapted successfully as part of the USAID cooperative agreement to independently qualify an artesunate-amodiaquine combination medicine from China for use in Liberia. Its use in developing countries might be especially valuable where good manufacturing and supply chain process standards and conformity assessments to these and other standards are weak or non-existent. It might also be used to prepare manufacturers for more stringent regulatory assessments, including WHO’s prequalification program.

<table>
<thead>
<tr>
<th>Verification Program</th>
<th>Number of Companies</th>
<th>Verified Products/Ingredients</th>
<th>Number of Products/Ingredients Undergoing Verification</th>
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<tr>
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<td>175*</td>
<td>15</td>
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<tr>
<td>DS Ingredients</td>
<td>13</td>
<td>38</td>
<td>10</td>
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<td>Pharmaceutical Ingredients:</td>
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<tr>
<td>• Drug Substances</td>
<td>7</td>
<td>16</td>
<td>3</td>
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<td>• Excipients</td>
<td>3</td>
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<td>0</td>
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<tr>
<td>Total</td>
<td>33</td>
<td>281</td>
<td>28</td>
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* This number represents over 296 million labels on over 800 unique SKUs of products represented by various label brands, such as Nature Made, Kirkland Signature, Sunmark, B&J, Yourlife, Equaline, Longs, etc.

e) **USP’s Pharmacopeial Education Programs**

At USP’s 2000 Membership Meeting, a resolution was adopted encouraging USP to consider creating an educational program to further the understanding and optimal use of the robust standards, monographs, and information contained in the USP-NF. An education program was launched in 2002 and has grown into a unique department capable of offering over thirty different continuing education courses that are taught in various countries across the world. During the past year, USP’s Pharmacopeial Education Department has conducted over 100 programs reaching nearly 3,000 science professionals in 20 countries. These educational programs provide highly useful information to manufacturers, purchasers, retailers, healthcare professionals, and government testing laboratories. As USP creates new standards or revises existing standards, corresponding educational courses are created to help inform and train the world’s science community on these changes. USP strives for increased access to its educational offerings by developing Internet-based courses and by working with international organizations and governments to offer educational programs at national, regional, and local levels. Despite some success, USP’s education and training programs remain in some ways “pilot” approaches that need careful consideration in the coming years to make them as value-added and robust as they can be. In many developing countries, these programs could be amplified with courses on GMPs, supply chain management, and registration topics. Partnering with ministries, agencies, academia, manufacturers, practitioners, and their associations—aided by revolutions in information technology that support distance learning—add further opportunities for success.
SUMMARY AND PROPOSALS FOR CONSIDERATION

USP advanced its international presence and activities vigorously in the 2005-2010 cycle based on decisions of the USP Board of Trustees and supported by Convention members through resolutions adopted at the 2005 Convention (as well as prior Conventions). This progress complemented the ongoing work of the USP DQI cooperative agreement with USAID. Together, the joint efforts bring USP into all parts of the world.

While USP’s offerings are small relative to need, USP has experienced resistance at times from other public health bodies whose missions appear to mimic those of USP. As discussed above, this resistance comes from confusion between USP’s standards-setting activities and its public health mission to promote access to quality medicines throughout the world. Also, USP’s role as a non-governmental, non-profit, standards-setting body and its associated freedom of action is confusing to many. For the most part, USP believes the issues arising in this context are readily resolved through better understanding and communication, evolving with recognition that there is far more than enough work and “space” for all parties to make a valuable contribution.

USP’s own resources must always be husbanded carefully, and the organization’s financial situation no longer allows funds to support non-core compendial activities, including activities in developing countries. Nevertheless, USP’s scarce financial resources should not overshadow the rich resources reflected in the knowledge, skills, and commitment of its volunteers—Convention delegates, the Board of Trustees, and the Council of Experts—or the expertise of its staff and stakeholder groups. Bolstered by its existing products and services, USP could have a significant impact working with others in developing countries. Funding alternatives such as cooperative agreements, grants, and contracts would allow USP to expand its work to improve global access to quality medicines.

With these challenges and limitations in mind, this white paper from the Council of the Convention Section on Global Public Health calls on all USP volunteer experts and their cumulative wisdom to consider ways to marshal USP’s forces internationally for the next cycle in accordance with USP’s mission. Ideas for consideration include:

1) Global approaches to registration and control of medicines through both ministerial and non-ministerial approaches. An example of an approach to global registration and control appears in Attachment 3.

2) Special programs to advance regional networks of activity and interest to promote access to quality medicines. A summary of a white paper from the African Health Advisory Panel of the IHEC appears in Attachment 4.

3) Approaches that lead to the availability of “global comparator pharmaceutical products” (in the U.S., the reference listed drug) and global primary reference materials coupled with any acceptable procedure to achieve sound measurements of medicines and their ingredients to assure their identity, strength, quality, and purity.⁸

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4) Approaches that support continuing equivalence of all medicines relative to a comparator pharmaceutical product using life cycle management, quality by design, and harmonized compendial approaches.

5) Approaches that support drug control laboratories to promote market access, market surveillance, and compendial updating. An example of a regional network approach appears in Attachment 5.

6) Compendial approaches that rapidly advance harmonization to avoid duplicative testing, reduce cost of medicines, and promote quality medicines irrespective of country or region.

7) Spectral libraries using multiple portions of the electromagnetic spectrum coupled with advanced informatics and instrumentation for all materials (food and drug products, ingredients, and impurities, together with their packaging), along with global surveillance networks to signal outbreaks of substandard, fake, and/or adulterated medicines. Libraries of acceptable materials and products would also include known or likely adulterants for drugs and contaminants for foods.

8) Approaches using modern informatics including Web based systems to bring useful information to practitioners and patients throughout the world—in their languages and at a level where comprehension is possible—to allow understanding of the importance of quality medicines used rationally to maintain health and treat disease.

9) Expanded activities, alternately funded, that advance the types of products and services that USP DQI can offer. Examples of areas of focus and opportunity appear in Attachment 6.

Taken together, the opportunities are immense for USP’s cadre of volunteers and staff, working through appropriate partners and with suitable funding, to promote global access to quality medicines rationally used. The Council of Convention Section on Global Public Health is pleased to offer this white paper to Convention members for their consideration.
## ATTACHMENT 1

**USP’s International Activities**

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<thead>
<tr>
<th>Partners</th>
<th>USP World Region</th>
<th>North America</th>
<th>Latin America</th>
<th>West Europe</th>
<th>East Europe</th>
<th>Middle East, North Africa (MENA)</th>
<th>Sub-Saharan Africa</th>
<th>South Asia</th>
<th>Asia Pacific</th>
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<tr>
<td>Ministries of Health</td>
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**“Where”**

- HEADQUARTERS AND SITES
- RELATIONSHIPS WITH NETWORKS
- MEMORANDUMS OF UNDERSTANDING (MOUs)
- ANNUAL SCIENCE MEETINGS (ASMs)/STAKEHOLDER FORUMS
- MARKETING & SALES
- USAID/CONTRACTS

**“Who”**

**“How”**
GENERAL OVERVIEW OF HOW USP DQI WORKS IN ALL COUNTRIES

When USP DQI is invited into a country by USAID, staff first establishes a cooperative working relationship with the country leadership including the Ministry of Health, national steering committee, drug regulatory agency (DRA), drug quality control laboratory, infectious disease programs, pharmacists associations, related pharmacy schools, and provincial health authorities. The first step is to assess the current QA/QC situation, determine gaps in their programs, and propose how USP DQI can assist them. The goal is to strengthen their QA/QC capacity by addressing drug registration, good manufacturing and good laboratory practices (GMPs and GLPs), laboratory testing capability, post-marketing surveillance, as well as good storage and distribution practices. USP DQI partners with international organizations (IOs) and Nongovernmental Organizations (NGOs) working in the region by coordinating efforts and shaping activities to meet individual needs of the country. USP DQI published “Ensuring the Quality of Medicines in Resource-Limited Countries: An Operational Guide,” which discusses all aspects of drug quality; four co-authors were from DRAs of developing countries; others were partners from World Health Organization (WHO), Management Sciences for Health (MSH), PATH and other organizations.

ASIA AND NEAR EAST REGION

USP DQI has worked in the Mekong sub-Region since 2003, primarily in Cambodia, Laos, Thailand, and Vietnam, specifically targeting antimalarial medicines. USP DQI staff has provided technical assistance by:

- Supplying essential lab supplies and equipment;
- Conducting laboratory and surveillance training—lab set-up, GLP, basic and advanced testing, equipment maintenance, Minilab®1 use, sampling procedures, documentation, and data analysis and reporting;
- Establishing surveillance programs in 39 sentinel sites.

Surveillance in Cambodia, Thailand, and Vietnam covers antimalarial and other anti-infective medicines, including selected antibiotics, anti-tuberculosis and antiretroviral drugs. The results allow local, national and regional governments to take law enforcement action and to alert health professionals and the public to problems.

1 Minilab® is a small portable (suitcase) laboratory equipped to do basic drug quality testing in the field.
USP DQI also collaborates with INTERPOL and WHO to thwart counterfeit medicines production in Southeast Asia. Data from the medicines monitoring programs in Cambodia, Laos, Thailand, Vietnam, and the Philippines has been used in covert operations that have led to arrests and seizures of fake medicines. Within this collaboration, USP DQI staff also trained customs, drug regulatory, and police officials on how to identify fake medicines using Minilabs®, as well as on proper sampling techniques.

**Vietnam** and **Laos** each hosted a “Training on the Quality, Safety and Rational Use of HIV/AIDS Medicines,” a seminar to inform pharmacists about managing the treatment of HIV/AIDS, in September 2008. USP DQI organized and facilitated the seminars.

**Laos** and **Cambodia** recently received training on good practices for medicines procurement, distribution, storage, and dispensing, focusing on antiretrovirals. **Cambodia** and **Vietnam** were recently trained on expanding quality monitoring to anti-infective medicines.

**Cambodia** has filmed public service announcements on the importance of drug quality and the danger of counterfeit medicines as part of its public awareness campaign, which will air in local languages in Cambodia, Laos, Thailand, and Vietnam. The campaign also featured articles in Health Messenger and the WHO DVD Dealers in Death. USP DQI organized a workshop and offered technical assistance to help the Cambodian Department of Drugs and Foods establish a pharmacovigilance center, which has since been awarded associate membership in the WHO International Drug Safety Monitoring Program. Analysts in the national drug quality lab were also trained on bioavailability and bioequivalence.

**Cambodia/Thailand** are cooperating to conduct a study of antimalarial drug quality in Cambodian/Thai border provinces using randomized sampling methodology to document possible links to antimicrobial resistance and drug quality.

**Thailand** has received training in Good Manufacturing Practices to improve skills for the Center of Excellence and Minilab® training for sentinel site staff.

The **Asian Network of Excellence in Quality Assurance of Medicines** (ANE/QAM) comprising three institutions was established with USP DQI/USAID assistance to share their expertise in drug quality to serve the needs of the region. The institutions include Mahidol University Faculty of Pharmacy and Chulalongkorn University/Pharmaceutical System Research and Intelligence (PSyRIC), which are located in **Thailand**, and the University of Santo Thomas Center for Drug Research, Evaluation & Studies, which is located in the **Philippines**. USP DQI helps strengthen the unique capabilities of each Center through training and technical consultation. PSyRIC is building a public drug quality database to centralize results of surveillance testing.

**Philippines** began monitoring the quality of antimalarial drugs at two sentinel sites in 2005. Recently, a five-day Minilab® training was conducted at the Bureau of Food and Drugs in Manila for six selected sentinel sites targeting antituberculosis medicines in the Filipino market.

**Bangladesh** is now able to manufacture zinc tablets locally; USP DQI has assessed three company facilities and is providing technical guidance to two to help them meet WHO prequalification status to provide medicines for UNICEF.

**Nepal** recently had three manufacturers assessed by USP DQI for GMPs on zinc tablets in order to become UNICEF-prequalified. In 2009, a chlorhexidine manufacturer was also assessed. Nepal was one of the first countries in which USP worked in the early days of the USAID agreement. In that work, a network of eight drug information centers was established.

USP DQI assessed three companies in **India** for GMPs for the manufacture of antituberculosis drugs and also has begun reviewing dossiers that manufacturers will submit to WHO for pre-qualification status.
For Avian Influenza, USP DQI developed monographs for oseltamivir and testing guidelines compatible with the Minilabs® capability. A quality monitoring system for oseltamivir has been established in the Asia and Near East Region, with mapping all suppliers and distributors in an attempt to improve the quality of stockpiled and circulated oseltamivir.

**SUB-SAHARAN AFRICA**

Many of the activities in the Sub-Saharan African (SSA) region focus on antimalarial drugs and countries making the transition to Artemisinin Combination Therapies (ACTs) as first-line treatment. USP DQI and WHO are collaborating on a Study of the Quality of Antimalarials in Sub-Saharan Africa (QAMSA) which will establish baseline data on the quality of ACTs in select African countries.

Phase 1 countries include Benin, Cameroon, Ethiopia, Ghana, Kenya, Madagascar, Nigeria, Senegal, Tanzania, and Uganda. In Ethiopia in February 2008, USP DQI staff conducted initial training for two representatives from each country on Sampling Procedures and Basic Tests using the Minilab®; staff then traveled to Madagascar in June 2008 to validate the first round of sampling. USP DQI financially sponsors Madagascar, Senegal and Uganda by supplying Minilabs®, lab ware, reagents, and reference standards; WHO sponsors the remaining seven. USP DQI will continue to provide technical oversight, train additional country reps and lab analysts, oversee sample analyses, and disseminate the data obtained to all countries involved in the QAMSA study. Data will be available in early 2009.

While in Ethiopia for the QAMSA training, USP DQI staff also conducted an assessment of the country’s QA/QC capabilities in preparation for establishing a Drug Information Center (DIC) and a postmarketing surveillance system. The final disposition of these activities will depend upon obtaining sufficient funding from USAID/Ethiopia. In August 2008, staff conducted a training course on Basic Tests and Sampling Procedures for Establishing Antimalarial Drug Quality Monitoring in the Oromia region. If done correctly, these tests can evaluate the quality of antimalarials as a component of establishing a sustainable system of medicines quality control in the country. In January 2009, staff conducted a training workshop on Good Laboratory Practices and compendial analytic methods for the Drug Administration and Control Authority (DACA) and its Drug Quality Control and Toxicology Laboratory (DQCTL). Beginning in 2009 and going through 2012, USP DQI has proposed a plan to assist DACA DQCTL become WHO pre-qualified and achieve ISO/IEC 17025:2005 accreditation.

USAID obligated funds in the Fall of 2008 for USP DQI to conduct QA/QC assessments of Mali, Benin, and Liberia. In summer 2008, USP DQI staff began evaluating the drug regulatory authorities’ (DRA) capacity for drug registration and quality control in order to establish a postmarketing surveillance program for antimalarials in these countries. Staff assessed Benin in July, Mali in September, and Liberia in November. USAID and USP DQI staff also traveled to Liberia in February 2009 to provide technical assistance in finalizing draft legislation relating to quality assurance issues in the country.

USP DQI has been working in Ghana, Senegal, and Madagascar since 2003 assessing QA/QC capabilities, as a way of helping to strengthen the institutions in charge of medicines in their countries, and establishing drug monitoring programs for antimalarial medicines. Each country has received priority equipment, reagents, and pharmacopeial references, and has been provided with Minilabs® for testing at sentinel sites. Each has been trained in lab set-up, GLP, basic testing, equipment maintenance, and Minilab® use; Senegal and Madagascar have been trained in advanced testing methods. The three countries are in different stages of their programs contingent, primarily, on the diligence of the DRA and cooperation of all key players.

- Ghana has been instructed in good registration procedures and trained on the use of SIAMED drug registration software. WHO experts also assessed their registration division and issued recommendations to improve the DRA’s registration of medicines. In February 2009, USP DQI conducted a training in sampling and testing of antimalarials using Minilabs®.
- In Senegal, USP DQI facilitated cooperation among agency partners to advance their work; the current work plan includes establishing a pharmacovigilance program focused on adverse drug reaction (ADR) reporting of ACTs.

- Madagascar has made particular progress with training and monitoring activities, as well as with acting on problems that have been discovered. USP DQI helped install SIAMED drug registration software and trained staff in good registration practices, and trained national drug quality control laboratory (NDQCL) analysts in testing for Bacterial Endotoxins. With the Malaria Action Coalition, USP DQI assisted in establishing a national pharmacovigilance program focusing on ADRs for ACTs; USP DQI returned to Madagascar in June 2008 to collect and assess the pharmacovigilance data that had been obtained. During that visit, USP DQI helped establish a DIC in Antananarivo, Madagascar—the first in the country. The DIC will provide drug information to health professionals as well as to consumers.

USP DQI conducted a GMP assessment of Shelys Pharmaceuticals in Tanzania for the manufacture of Zinc sulfate tablets (for treatment and prevention of acute diarrheal disease in children), and returned in 2007 to assess their progress toward WHO pre-qualification status. In Fall 2008, USP DQI traveled to Tanzania to conduct a GMP assessment of a second pharmaceutical manufacturer, Zenufa.

Uganda was one of three countries initially selected to receive funds in 2005 from the President’s Malaria Initiative. USP DQI staff conducted a QA/QC assessment in 2006 and has provided lab equipment and trained NDQCL staff on GLP and major testing methods. In May 2008, USP DQI established a drug quality monitoring program in five provinces in Kampala, and in December 2008, trained staff on new drug applications on SIAMED drug registration software. In 2009, USP DQI will help Uganda establish a pharmacovigilance program in the country.

In 2006, USP DQI conducted an assessment of the existing drug information unit of Kenyatta National Hospital of Kenya; however, USAID funding was not made available and no additional action has been proposed.

During 2001-2004, USP DQI worked with USAID-Mozambique to provide technical assistance and support to the Center for Drug Information (CiMed).

USP has presented, co-organized, sponsored and/or led and facilitated meetings on drug quality and pharmacovigilance in Egypt (2006), Morocco (2007), and Tanzania (2006).

**LATIN AMERICA AND THE CARIBBEAN (LAC)**

Currently, USP DQI participates in two initiatives to help combat AMR in the LAC region: Amazon Malaria Initiative (AMI) and South American Infectious Disease Initiative (SAIDI).

Since 2002, USP DQI has partnered with USAID, Pan American Health Organization (PAHO), Centers for Disease Control and Prevention (CDC), Management Sciences for Health/Strengthening Pharmaceutical Systems (MSH/SPS), and eight country members – Bolivia, Brazil, Colombia, Ecuador, Guyana, Peru, Suriname, and Venezuela – to participate in the Amazon Malaria Initiative. USP DQI collaborates with local drug regulatory authorities and existing national drug quality control laboratories to assure the quality of antimalarials by strengthening the laboratories and advancing drug registration procedures. Following USP DQI training, each country develops antimalarial drug quality monitoring systems of sampling, testing, and data reporting.

In 2008, USP DQI sponsored two interns from the OMCLs of Colombia and Peru to participate in an “Internship on the Application of USP’s Quality Management System to its Laboratory Operations.” USP DQI plans to host another intern in 2009.
The AMI program began to reach out to Central American countries in 2008. At a July 2008 workshop on “Gas Chromatography, Headspace, and Residual Solvents” held in Colombia, representatives from the national labs of Guatemala and Panama participated. Representatives from Honduras first participated in an AMI workshop in Ecuador in August 2008, where GLP, HPLC, UV, and dissolution techniques were taught; Guatemala and Panama also participated. The first USP DQI activity to be hosted in Central America was the November 2008 “Workshop to Improve Management of Supply and QA Systems for Malaria Medicines in Central America,” held in Guatemala and attended by representatives from Costa Rica, El Salvador, Honduras, Nicaragua, and Panama. During that trip, USP DQI staff also performed a Rapid Assessment of Guatemala’s national laboratory.

Beginning in 2004, USP DQI has partnered with USAID, CDC, MSH/SPS, PAHO, Alliance for Prudent Use of Antibiotics (APUA), Links Media, and three country members – Paraguay, Peru, and Bolivia – to participate in SAIDI. SAIDI assesses the current drug quality capacity at the national level and helps each country develop effective, sustainable interventions to contain AMR. USP DQI trains analysts from local, regional, and national quality control laboratories to create a sampling plan for collecting and testing samples of antibiotic and anti-tuberculosis medications. That data is used to help DRAs take action to improve the quality of medications in the market.

Following an audit by ACLASS, Peru was recommended in January 2009 for ISO/IEC 17025:2005 accreditation for 5 laboratory tests.

EUROPE AND EURASIA


- DICs located in medical schools, hospitals, and other institutions were set up in Russia, Moldova, and Romania. With initial assistance from USP DQI, the DICs provide current, reliable drug and therapy information to healthcare professionals and patients. A major goal was reached in 2006 when all the DICs became self-sustaining.

- In Russia, Belarus, Ukraine, and Kyrgyzstan, USP DQI established Continuing Education Distance Learning Centers in cooperation with the Institute of Antimicrobial Therapy, the Department of Clinical Pharmacology of Smolensk State Medical Academy, and the regional DICs. Courses are intended to improve the qualifications of doctors and focus on antimicrobial therapy, socially important diseases, and DIC management.

- Developed by a group of Russian scientists in 2001, the Infectious Diseases Textbook provides Russian and Newly Independent States healthcare professionals with information on antibacterial, antiviral (including HIV/AIDS), antifungal, antiprotozoal, and antihelmintic drugs. The third edition of the Textbook, published in 2007, also provides information on HN51 avian influenza and the quality of antimicrobials and other new drugs on the market. In 2008-2009, USP DQI plans to design and implement a study to assess the impact of the Textbook and the distance learning programs in Russia.

- In 2003, USP DQI and the Institute of Antimicrobial Therapy published a Russian translation and adaptation of the 2002 Guide to Infection Control. This manual explains guidelines for reducing the rate of nosocomial infections and describes practical measures intended to improve quality of care, minimize risk, save lives, and reduce costs.
In an effort to improve the implementation of the DOTS strategy and reduce the spread of MDR-TB, in 2003 USP DQI helped collect samples of anti-TB drugs from Kazakhstan and followed up with a training workshop on drug quality. In 2005, USP DQI and RPM Plus conducted a training workshop on how to use Minilabs® for representatives from the drug regulatory agencies and national quality control laboratories of Kazakhstan, Kyrgyzstan, Tajikistan, and Uzbekistan.

In 2009, USP DQI plans to conduct training courses to expand drug quality monitoring in Russia, focusing on anti-TB drugs. After translating the Minilab® Manual into Russian, USP DQI will provide the necessary Minilabs®, reference standards, and lab supplies for its Russian counterparts.
THE WAY FORWARD: A GLOBAL HEALTH CARE SECRETARIAT

EXCERPT FROM RESPONSE PREPARED BY USP’S ADVISORY PANEL OF THE INTERNATIONAL HEALTH EXPERT COMMITTEE IN RESPONSE TO WORLD HEALTH ORGANIZATION’S COMMISSION ON INTELLECTUAL PROPERTY RIGHTS, INNOVATION, AND PUBLIC HEALTH (CIPIH)

Despite what now can only be described as a deeply challenged set of systems to treat neglected diseases in developing countries, much has occurred that offers hope. Opportunities relate to transnational collaborative activities, such as WHO’s Pre-Qualification program and the EDQM Certificate of Suitability, that advance beyond information exchange and harmonization to collaboration for action. These initial efforts to move beyond national decision-making, which can be flawed and resource-constrained, set the stage perhaps for a truly global regulatory and practitioner/patient enterprise. By means of enhanced collaboration, public and private officials and regulators of developing countries may be in a remarkable position to advance basic research, discovery, drug development, registration, utilization, and related approaches for medicines (with allied activities) to prevent and treat diseases that have plagued humankind for centuries—and to develop medicines to treat other conditions as well. In the past several years, national, sub-regional, regional, trans-regional, and global activities for collective action have appeared and offer hope. These not only have yielded needed registration and other standards but also have engaged regulators in the conduct of bilateral and multilateral conformity assessment activities. They have thus moved beyond information sharing and harmonization to yield useful results; i.e., they are action oriented.

The concluding theme of this paper is that regional and global collaboration efforts should be strengthened and, when possible, expanded and consolidated. Further consolidation is based on a vision of a collaborative global health care secretariat with multiple components, involving representatives from all countries, and yielding decisions suitable for national adoption. The components would focus on a) discovery; b) research and development; c) sound regulatory decision-making and, when appropriate, rapid registration decisions; d) optimal pricing/payment strategies; e) evidence-based health care delivery based on outcomes/pharmacoeconomic studies, f) quality of care and g) safe medicine use.

As a further proposal, this paper argues for close involvement of practitioners and patients throughout the overall process and urges for them a dominant role after registration. Specifically, it proposes a consortium of practitioners and patients to advance optimal health care, including pharmaceutical care, based on continually updated drug information. Independent, credible, authoritative practitioner and consumer experts would transform prospectively and retrospectively designed research studies and observational data into knowledge-based information monographs and wisdom-based brief summaries and alerts, following the paradigm of:
data → information → knowledge → wisdom.

An overarching theme is the need for action. With sufficient (but not exorbitant) resources, a collective effort based on this shifting duality of inputs (regulators to the community and community to regulators) may promote, as overarching strategic objectives, rational use of medicines and good, cost effective health care delivery practices. An overall structure is shown in Figure 2. The secretariat is imagined to operate in close cooperation with the World Health Organization, relying on frequent and continuing input from governmental and practitioner/consumer experts from all countries of the world and in particular from developing countries. This input would yield science and policy decisions that would be suitable for national adoption, based on local acceptance and modification if needed.

![Figure 2](image)

Such a secretariat could evolve over time into even stronger authorities and alliances, working to establish procedures that ensure transparency and trust and rely on advancing skills and shared values. Indeed, the vision perhaps leads to a world medicines agency with participants from experts from around the world, managed by a secretariat, and yielding scientific opinions on many topics suitable for national consideration and adoption. While not small, the expense of such a venture is almost certainly minimal compared to costs encountered today, which leave many if not all actors in civil societies at the mercy of fragmented, duplicative, and poorly coordinated approaches that are encumbered by inertia, misinformation, and perhaps even incompetence and corruption. A particular feature of the approach is that it consolidates and focuses the skills and wisdom of experts from developing countries themselves. Nonetheless, partnering with science and technical experts from developed countries is encouraged, so that skills and wisdom of all contributors are enthusiastically welcomed and shared.
ATTACHMENT 4

THE DRUG SITUATION IN THE SUB-SAHARAN AFRICA

EXECUTIVE SUMMARY

PREPARED FOR USP BY
THE USP AFRICAN HEALTH ADVISORY PANEL
MARCH 2008

CONTRIBUTORS
- USP African Health Advisory Panel
- USP Staff
- USP International Health Expert Committee
Since the United States Pharmacopeia (USP) is seeking to extend its activities to the sub-Saharan Africa, it was necessary to determine which activities within its ambit are most important to introduce into Africa. Therefore, the aim of this study was to identify the major health and pharmaceutical problems in a sample of African countries. This information was gathered by use of a questionnaire and literature search. It is hoped that this position paper will provide information that will be useful to the USP and all those who want to rescue Africa’s pharmaceutical situation.

1. From Table 1, it was observed that:
   - Most African countries have a District Referral Health Care System as well as a Centralized Medicines Distribution System with an open tender procurement policy for most drugs.
   - Although most countries have established drug regulatory authorities, pharmacy councils and drug control laboratories, most of these are inexperienced as they were established less than 10 years ago.

Table 1: The health system and pharmaceutical regulatory structures in some African countries.

<table>
<thead>
<tr>
<th>Region</th>
<th>SADC</th>
<th>ECOWAS</th>
<th>UEMOA CEMAC</th>
<th>EAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country</td>
<td>SA,</td>
<td>Ghana</td>
<td>Mali</td>
<td>Kenya</td>
</tr>
<tr>
<td>Pop. (millions)</td>
<td>42.6</td>
<td>22.9</td>
<td>13.5</td>
<td>32</td>
</tr>
<tr>
<td>Health system</td>
<td>DRS</td>
<td>DRS</td>
<td>DRS</td>
<td>DRS</td>
</tr>
<tr>
<td>Med. Distrib.</td>
<td>CDS</td>
<td>CDS</td>
<td>CDS</td>
<td>CDS</td>
</tr>
<tr>
<td>Regulatory Agency</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pharmacy Council</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Drug. Control Lab.</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

DRS = District Referral System; CDS = Centralized Distribution System

Regions: SADC = Southern Africa Development Community; ECOWAS = Economic Community West African States; UEMOA = West African Economic, Monetary Union; CEMAC = Economic and Monetary Community of Central Africa.; EAC = East African Community.

Countries: SA = South Africa; Zim. = Zimbabwe; Cam. = Cameroon; Tanz = Tanzania

2. From Table 2, it was observed that:
   a) The top 3 killer diseases were:
      - Malaria,
      - HIV/AIDS
      - TB
   b) The major drug quality issues are:
      - Counterfeits (CFT)
      - Lack of skilled personnel (LTP)
      - Inadequate regulatory mechanisms (IRM)
c) The major Medicines’ problems are:
   - Limited access
   - Inefficient distribution/drug supply systems
   - Weak monitoring of products on the market

Table 2: The top three health and pharmaceutical indicators in some African countries.

<table>
<thead>
<tr>
<th>Region</th>
<th>SADC</th>
<th>ECOWAS</th>
<th>UEMOA CEMAC</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Country</td>
<td>SA.</td>
<td>Zim</td>
<td>Ghana</td>
<td>Nigeria</td>
</tr>
</tbody>
</table>

a) Top 3 diseases
3. CVD TB URTI TB TB TB URTI

b) Top 3 on Quality & Product
1. CTF CTF LTP CTF LTP CTF CTF LTP
2. LTP LTP CTF LTP CTF LTP LTP CTF
3. IRM IRM IRM IRM IRM IRM IRM IRM

c) Top 3 Medicine Problems
2. Distrib Distrib Distrib Distrib Distrib Dist/Ac. Distrib

CTF = Counterfeit; LTP = Lack of trained personnel; IRM = Inadequate Regulatory Mechanism;
Access = Limited Access to Essential Drugs; Distrib = Ineffective distribution System; Monit. =
Inadequate monitoring of drug quality on a continuous basis.

Regions: SADC = Southern Africa Development Community; ECOWAS = Economic Community
West African States; UEMOA = West African Economic, Monetary Union; CEMAC = Economic
and Monetary Community of Central Africa.; EAC = East African Community.

Countries: SA = South Africa; Zim. = Zimbabwe; Cam. = Cameroon; Tanz = Tanzania

3. From Table 3, it was observed that the pharmaceutical market characteristics indicate that:
   - Foreign-based multinationals account for over 70% (median) of the market share, while
     about 30% is by domestically-based subsidiaries of the multinational companies and/or local
     manufacturers.
   - 80% of the products in all the countries studied are generics.
   - Counterfeits remain a big problem and it was estimated by WHO to range between 10 -30% of
     the products (UNICRI 2007).
   - There is wide inter-country variation in the number of products on the market.
### Table 3: Characteristics of the pharmaceutical market in some African countries.

<table>
<thead>
<tr>
<th>Region</th>
<th>SADC</th>
<th>ECOWAS</th>
<th>UEMOA</th>
<th>CEMAC</th>
<th>EAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country</td>
<td>SA.</td>
<td>Zim</td>
<td>Ghana</td>
<td>Nigeria</td>
<td>Mali</td>
</tr>
<tr>
<td>M-Nat. outside</td>
<td>73%</td>
<td>15%</td>
<td>70%</td>
<td>32%</td>
<td>98%</td>
</tr>
<tr>
<td>M-Nat. inside</td>
<td>27%</td>
<td>5%</td>
<td>30%</td>
<td>14%</td>
<td>2%</td>
</tr>
<tr>
<td>Generics</td>
<td>80%</td>
<td>70%</td>
<td>70%</td>
<td>80%</td>
<td>?</td>
</tr>
<tr>
<td>Counterfeits</td>
<td>10%</td>
<td>?</td>
<td>8%</td>
<td>16%</td>
<td>15%</td>
</tr>
<tr>
<td>No. products</td>
<td>25,000</td>
<td>1500</td>
<td>5200</td>
<td>13,632</td>
<td>3,027</td>
</tr>
<tr>
<td>Pharm. GDP ($)</td>
<td>10.0</td>
<td>&lt; 1</td>
<td>1.0</td>
<td>2.0</td>
<td>4</td>
</tr>
</tbody>
</table>

M-Nat. outside = Multinational from outside the country; M-Nat. inside = Multinational (%) based inside the country; No. products = Number of products in market (estimated); Pharm. GDP ($) = Per capita drug expenses on pharmaceuticals (US $).

Regions: SADC = Southern Africa Development Community; ECOWAS = Economic Community West African States; UEMOA = West African Economic, Monetary Union; CEMAC = Economic and Monetary Community of Central Africa.; EAC = East African Community.

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4. Conclusion (Tables 4a, 4b, & 4c)

Overall, African countries have put in place the necessary regulatory drug policies and agencies, distribution systems, and drug control laboratories, but these systems are in dire need of assistance to be effective. Such assistance should address counterfeits, lack of skilled personnel and strengthening of the regulatory mechanisms. It is advised that the USP establishes facilities by which it can support Quality Control Laboratories as well as undertake training for laboratory and drug regulatory staff in Africa, and that this should be in collaboration with the existing stake-holders and plans in the region.
Table 4a: USP questions—Where in sub-Saharan Africa should USP establish a facility?

<table>
<thead>
<tr>
<th>SADC</th>
<th>EAC</th>
<th>ECOWAS</th>
<th>CEMAC</th>
<th>UEMOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>Zimbabwe</td>
<td>Kenya</td>
<td>Tanzania</td>
<td>Nigeria</td>
</tr>
<tr>
<td>a) South Africa: well established and functioning regulatory system which has exemplary success. Also, has established marketing channels to the rest of Africa through its diverse business contacts. Indeed, 40% of the South African pharmaceutical exports are to the rest of Africa.</td>
<td>South Africa – They have a strong pharmaceutical manufacturing industry</td>
<td>In Tanzania due to conducive investment environment, political stability and strong government support to ensure availability of safe and efficacious medicines of acceptable quality.</td>
<td>It is best established in Nigeria. Any assistance given to Nigeria will permeate to all the other countries being the most populated Member State. Nigeria has about ¼ of the SSA population. We have been sharing strategies and carrying other countries along in the West African Drug Regulatory Authorities Network (WADRAN) which we sponsor and supervise. We have carried positive international advocacy campaigns against drug counterfeiting which have led to the establishment of the International Medical Products Anti-Counterfeiting Task Force (IMPACT). Prof. Akunyili is the Chairperson WADRAN and the Vice Chairperson of IMPACT.</td>
<td>Ghana</td>
</tr>
<tr>
<td>b) Nigeria/Ghana: well established and functioning regulatory system. The high population adds promise to growth in the pharmaceutical industry. Of note, the facility is not for one country, as such, there is a need to establish communication with the East African region, which is expensive.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SADC = Southern Africa Development Community; ECOWAS = Economic Community West African States; UEMOA = West African Economic, Monetary Union; CEMAC = Economic and Monetary Community of Central Africa; EAC = East African Community.
### Table 4b: USP questions continued—What should USP do in the following areas?

<table>
<thead>
<tr>
<th>SADC</th>
<th>EAC</th>
<th>ECOWAS</th>
<th>CEMAC</th>
<th>UEMOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>Zimbabwe</td>
<td>Kenya</td>
<td>Tanzania</td>
<td>Nigeria</td>
</tr>
<tr>
<td><strong>Quality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Establish a second quality control laboratory and this should add value to the current situation. Support government and relevant bodies to fight against counterfeit products.</td>
<td>Assist laboratories implement quality management systems.</td>
<td>Establish a regional Drug Quality Control reference laboratory.</td>
<td>Support in provision of laboratory reference standards and reagents and laboratory equipment and instruments.</td>
<td>1. Support the provision of adequate infrastructure, human resources and sufficient funds for Quality Control Laboratories. 2. USP should conduct an assessment of capacities and identify existing gaps in Quality Control Laboratories. 3. USP should put in place structured mechanisms to enable exchange of QC and regulatory officials to bring about better understanding of processes adopted in Sub Saharan Africa. 4. USP should support the documentation of best practices to be replicated in other member countries with Nigeria as a starting point;</td>
</tr>
<tr>
<td><strong>Access</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Support government departments in developing models by which to distribute drugs to the people.</td>
<td>Assist laboratories access competitively priced equipment and reagents so they can be empowered to improve access to quality medicines in their countries.</td>
<td>Support Drug regulatory authority in establishing and monitoring ethical distribution by qualified personnel through registered outlets.</td>
<td>Support government efforts to improve quality of pharmaceutical services in rural and peri-urban areas.</td>
<td>USP should support the establishment of a strong and operational drug distribution system based on the Drug Mart Strategy. Encourage the establishment of Public Private Partnership in the drug Procurement and Distribution programs of governments. Encourage the establishment of Pharmacy chains e.g CVS and Walgreen in USA to improve access to quality and affordable medicines. Support Government to expand the National Health Insurance Scheme (NHIS) to cover States and Local Governments. Currently only Federal Institutions and a few states have subscribed.</td>
</tr>
</tbody>
</table>

**SADC** = Southern Africa Development Community; **ECOWAS** = Economic Community West African States; **UEMOA** = West African Economic, Monetary Union; **CEMAC** = Economic and Monetary Community of Central Africa; **EAC** = East African Community.
Table 4c: USP questions continued—What should USP do in the following areas?

<table>
<thead>
<tr>
<th>SADC</th>
<th>EAC</th>
<th>ECOWAS</th>
<th>CEMAC</th>
<th>UEMOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>Zimbabwe</td>
<td>Kenya</td>
<td>Tanzania</td>
<td>Nigeria</td>
</tr>
<tr>
<td><strong>Surveillance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Support government in establishing and running the drug and poison information centers.</td>
<td>Establish a network of laboratories in the region who can share information on surveillance and quality issues.</td>
<td>Establish post – marketing and Post – registration surveillance in liaison with national drug regulatory authority.</td>
<td>Assist in developing surveillance strategies to ensure effective market control including pharmacovigilance.</td>
<td>• USP should support the institutionalization of a Post Marketing Strategy and a robust Pharmacovigilance (PVG) system in member countries. Nigeria is registered as the 74th member and have received up to 630 reports which has resulted in the ban and restriction the use of some drugs. • Enhance the establishment of self regulation by the industry and pharmaceutical associations.</td>
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<td><strong>Education &amp; Training</strong></td>
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<td>Establish a permanent training facility in Africa where different courses can be offered all year round. Such courses should aim at training of not only workers, but also producing new local trainers.</td>
<td>Assist personnel from laboratories to access appropriate graduate training programs to strengthen their own institutions. Consider working with a regional training institution to offer such graduate programs.</td>
<td>Train laboratory staff in modern analytical techniques, training of drug dossier evaluators on evaluation of new medicinal products with special focus to medicines for malaria, HIV/AIDS, vaccines and biologics, inspection techniques for suspect counterfeit products.</td>
<td>• USP should develop Training modules in common languages and should designate two training centers, one in Nigeria and the other in SADC or EAC for building capacity within the region; • The capability &amp; skill of staff should be continuously upgraded through adequate training in specific regulatory areas of quality control, inspection and investigation. • USP/WHO should coordinate the Technical Assistance to be provided in the region to avoid duplication and overburdening member countries.</td>
<td>It is recommended strongly that the ECOWAS framework is used for training. Expert groups in various areas of medicines regulations could be set up as the basis for creating training centers and faculty.</td>
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<td><strong>Other</strong></td>
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<td>USP should support the formation and/or functioning of regulatory authorities in the different countries or regions. USP should support the relevant government department in the managing and maintaining drug supply chains.</td>
<td>Provide reference materials, access to information, and technologies to improve the efficiency of the laboratories in the region.</td>
<td>To establish long term co-operation and collaboration in developing the capacity of medicines regulation in the EAC.</td>
<td>• USP should embark on an effective Advocacy towards harmonization of QC, Inspection and Drug regulatory control within the Sub-Saharan Africa. WADRAN can provide a supporting platform. • Advocacy and Public Enlightenment materials should be developed and harmonized for use within the SSA region.</td>
<td>Liaise with the West African Health Programme (ECOWAS/EU project) for maximum impact</td>
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SADC = Southern Africa Development Community; ECOWAS = Economic Community West African States; UEMOA = West African Economic, Monetary Union; CEMAC = Economic and Monetary Community of Central Africa; EAC = East African Community.
While this proposal focuses on the MENA region, the basis for such an alliance could be adapted for other regions throughout the world.

**BACKGROUND**

Based on increasing regional trade, the challenges of counterfeit and substandard medicines, advances in measurement science, economic integration and other factors, this proposal suggests establishing an alliance of official medicines control laboratories (OMCLs) in the Middle East North Africa (MENA) region.

**PROPOSAL**

1. **EMRO/AFRO/MINISTRIES**

   WHO’s EMRO works in 22 countries in the region. WHO’s AFRO works in 44 African countries – including Algeria and Sudan, which are usually classified as MENA countries. Both EMRO and AFRO’s governing bodies are based on representation from national Ministries of Health from these countries. The ministries in turn have departments/agencies that have regulatory responsibility for medicines (drug regulatory agencies/DRAs). DRAs usually have oversight for the OMCLs. Beyond the national institution, some countries may also have state or provincial drug laboratories that may be part of the Network. EMRO and AFRO, which serve as the WHO Regional Offices for the MENA region, function in a coordinating role for many activities.

2. **ALLIANCE STEERING COMMITTEE**

   Strategy for the proposed Alliance will be handled by a Steering Committee composed of representatives from the national drug laboratories in the MENA region, representatives from WHO Regional Office(s), involved pharmacopoeias, and industry stakeholders. The Steering Committee
will be responsible for developing the strategic direction for the Alliance and related governance activities, taking into account roles and responsibilities of participants. The Alliance will have no regulatory authority, which is reserved to parent drug regulatory agencies. Strategy and tactic implementation activities of the Alliance will be consonant with corresponding requirements of involved organizations.

3. PROCESSES

The Alliance members will meet every year at a frequency and a venue determined by the Steering Committee. Work plans to meet the strategic objectives will be considered at each meeting with updates on goals and achievement of goals. Working groups may be established to execute against specific goals.

**ACTIVITIES**

- Laboratory standards development
- Conformity assessments to applicable standards
- Ingredient and product quality standards
- Training, education, certification of staff
- Proficiency testing
- Marketplace surveillance
- Anti-counterfeiting activities
- Capacity-building (e.g., equipment)

**COSTS**

Costs of the Alliance activities will be funded through available mechanisms. Additional funding may be sought from NGOs and other donor bodies. Costs will cover: secretariat support, meetings, web support, other.
ATTACHMENT 6
ADVANCING OPPORTUNITIES FOR INTERNATIONAL TECHNICAL ASSISTANCE

BACKGROUND

1. MANUFACTURING QUALITY

Because people in developing countries often do not have access to quality medicines, attempts to remedy the situation have included the use of generics and a tiered-pricing scheme.\(^1\) Supporters hoped that generic competition would drive prices down and, where generics were not available, establishing a tiered-pricing scheme effectively positioned developed countries or private companies to subsidize drugs for developing countries. Both approaches, however, have been undermined by manufacturers that lack the technical capacity to comply with industry-standard Good Manufacturing Practices (GMP). A larger pool of manufacturers that are GMP-compliant would potentially result in the increased production and availability of essential medicines prequalified by the World Health Organization (WHO) Prequalification Programme. Currently, there are 16 WHO-prequalified antimalarial medicines, ten of which are Artemisinin-based Combination Therapies (ACTs).\(^2\) As developing countries have increasingly replaced monotherapies with ACTs as their first-line treatment, the availability of prequalified ACTs has become a point of concern. Each of the 18 antimalarial medicine dossiers now under WHO evaluation is awaiting additional data from the manufacturers to fulfill the quality review. The same is true for many other essential medicines.

2. MEDICINE REGULATION

Medicine regulation in developing countries falls on governments with limited resources and/or technical capacity. Failure to strengthen regulations and inadequate enforcement against noncompliance has allowed substandard medicines to be manufactured and distributed. Such poor quality medicines pose an immediate and long-lasting threat to public health. Currently, only 20% of WHO’s 191 member states have well-developed regulation, only 50% operate at varying levels of regulation and capacity, and 30% have weak regulation or none at all.\(^3\) The variation in the capacity of the regulatory framework can be attributed to the lack of enforcement of existing regulations, regulation that does not address drug registration, incorrect use and interpretation of the USP-NF, and the lack of standards and procedures to perform conformity assessments.

Medicine Regulatory Authorities (MRAs) must be provided with the capacity to conduct: medicine evaluation and registration; inspection and licensing of manufacturers; and postmarketing surveillance. Official Medicines Control Laboratories (OMCLs) often operate below internationally-recognized standards.


\(^2\) The six other antimalarial medicines are monotherapies, four of which, when combined, form an ACT.

standards (ISO/WHO) for analytical methodologies and interpretation of monographs to assess compliance, and they need access to monographs and reference standards for neglected diseases.

3. TRAINING

Ultimately, systems that can ensure access to quality medicines require skilled personnel to perform testing, dispensing, policymaking, and enforcement. Yet for developing countries with limited resources, training is often overlooked. The lack of appropriately-trained personnel leads to ineffective quality assurance systems for medicines. MRA and OMCL personnel require continuous training to sustain their ability to ensure drug quality, but the lack of resources to acquire such training further jeopardizes medicine quality in the region. In addition, there is a need to provide unbiased medicine information to healthcare practitioners for dissemination to patients. Gaps in patient and practitioner information need to be addressed to ensure proper and safe medication use.

DISCUSSION/PROPOSAL

With funding from others, USP could expand activities that advance the types of products and services that the current USP Drug Quality and Information (DQI) program offers, which could play a pivotal role in increasing access to quality medicines in developing countries. USP recognizes the work of others in developing countries and would seek to collaborate on the following:

1) Assisting in the preparation of manufacturers’ product dossiers for submission to the WHO Prequalification Programme in a manner that fulfills the specified requirements.

2) Guiding manufacturers on site to comply with WHO-qualified GMP standards and helping strengthen their GMP capabilities.

3) Training regulators in developing countries in GMP standards and building capacity in quality assurance systems.

4) Develop monographs for new antimalarial drugs, especially those utilizing active pharmaceutical ingredients (APIs) available from various plant sources or those resulting from different manufacturing processes. USP addresses this issue through its flexible monograph approach.


6) Providing verification programs to manufacturers in developing countries that would help to improve ingredient quality.

7) Evaluate the quality assurance capacity of MRAs to determine if at least minimal functions are being met in the essential operations of medicine evaluation and registration, inspection and licensing of manufacturers, and postmarketing surveillance.

8) Evaluate the quality assurance capacity of OMCLs. Depending upon results of the assessment, USP may provide the necessary laboratory resources to conduct medicine quality control testing. USP or DQI staff could conduct training on Good Laboratory Practices, sampling, and analytical methods to test antimalarial and other essential medicines for content, identification, purity, and dissolution. Training might also include interpretation of drug quality data, as needed.

9) Provide additional technical support as required via the USP Pharmacopeial Education program to address specific compendial education needs of MRAs and OMCLs.
10) Provide regional educational and training programs aimed at improving the ability of local chemists, scientists, and healthcare practitioners to implement standards and best practices for the development, manufacture, regulation, testing, storage, and dispensing of medicines and their appropriate use.

11) Establish centers of excellence for the training of regulators and other stakeholders.

12) Establish Medicine Information Centers (MICs), organized and led by specially-trained pharmacists, to provide comprehensive drug information services to patients and healthcare professionals. In developing countries, pharmacists more commonly play the role of patient-care providers, and MICs are now recognized as an integral part of a successful and functional health care service.