

Developing a Pharmaceutical Product Quality Assurance Program in Tanzania: Strategies for Enhancing Access to Medicines Program Final Report

Strategies for Enhancing Access to Medicines Program
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About SEAM

The Strategies for Enhancing Access to Medicines (SEAM) Program is funded by the Bill & Melinda Gates Foundation under contract D3601, and works to improve access to essential medicines and vaccines in the developing world by fostering partnerships between the public and private sectors.

Program Background

In 2000, Management Sciences for Health (MSH) received a grant from the Bill & Melinda Gates Foundation to identify and test innovative approaches for improving access to essential medicines in developing countries through greater participation of the private sector. To fulfill this mandate, MSH set out to implement programs to promote access, design a method to measure the nature and extent of the lack of access to essential medicines, and monitor the impact of these programs.

The Strategies for Enhancing Access to Medicines (SEAM) Program has four components—

1. Technical collaboration with other Gates-supported global drug/vaccine access initiatives
2. Implementation of country-level public-private initiatives to improve access to essential drugs and commodities in two or three countries
3. Determination of the feasibility of franchising as a mechanism to improve access
4. Development and deployment of information and communications tools to support technical interventions

SEAM Access Framework

The SEAM access framework was developed after a review of the published and unpublished literature on access to health care in general and to medicines in particular. This framework was later discussed at a consultative meeting jointly sponsored by MSH and the World Health Organization (WHO), in Ferney-Voltaire, France, held December 11–13, 2000. More than 40 experts from 15 countries participated in the discussions and concluded that, as with health services, the concept of access to essential medicines is a construct with several distinct dimensions that are distinguished by sets of specific relationships.

The following four dimensions of access emerged from the discussions—

- Physical availability, defined by the relationship between the type and quantity of product and service needed and the type and quantity of product and service available
- Affordability, defined by the relationship between the products and services and the user's ability to pay for them
- Geographic accessibility, defined by the relationship between the location of the product or service and the location of the potential user of the product or service
- Acceptability (or satisfaction), defined as the fit between the user's and provider's attitudes and expectations about the products and services and the actual characteristics of these products and services

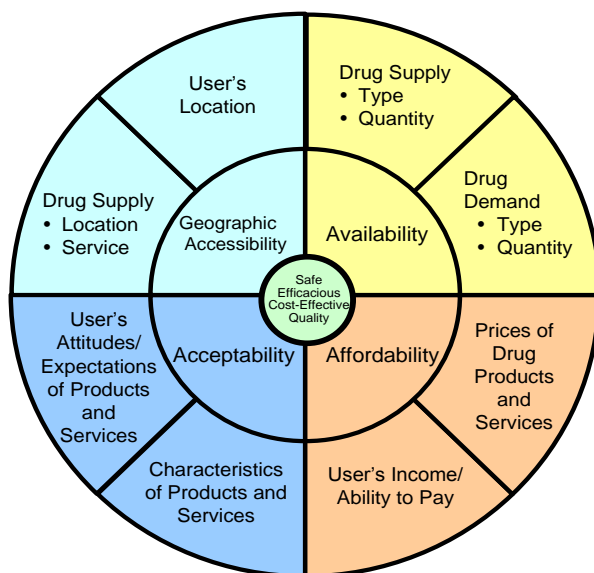


Figure 1. SEAM Access Framework

In addition, quality of products and services was defined as an essential component that cuts across all dimensions. Participants developed a set of 17 key indicators to represent the four dimensions of access and one crosscutting characteristic (see figure 1).

SEAM Country Assessments

After several rounds of internal discussions and consultations with experts from WHO and the World Bank and with contacts in developing countries, six countries—Ghana, Tanzania, Cambodia, India (state of Rajasthan), Brazil (state of Minas Gerais), and El Salvador—were identified in which to undertake assessments based on the conceptual framework, with the understanding that only two, or at most three, countries would eventually be selected for long-term SEAM projects. The initial selection criteria included perceived or known significant lack of access to essential medicines, perceived enabling environment for private sector initiatives, political and economic stability, and potential for collaboration with other MSH and Gates-funded local initiatives. The countries not selected for long-term assistance are expected to have benefited from the assessment exercise, in particular from a SEAM-supported analysis of potential public-private sector initiatives to enhance access to essential medicines. With such an analysis in hand, the country can approach donors and lenders to finance such work, as appropriate.

The assessments were carried out between February and May 2001. Local private, not-for-profit, and academic organizations collaborated in the adaptation of data collection instruments, sample selection, data collection, and analysis. The assessments included (1) determining the status of public and private sector access—in terms of geographical accessibility, availability, quality, affordability, acceptability—to essential public health medicines and health commodities; (2)

identifying opportunities for private sector participation in improving access to public health commodities; and (3) determining the feasibility of implementing public/private sector strategies to improve access.

Using feedback from the 2001 SEAM conference and input from the SEAM Advisory Committee, which held its first meeting on November 30, 2001, the MSH chief executive officer and Center for Pharmaceutical Management (CPM)/SEAM program managers elected to provide full support to country programs in Ghana and Tanzania and limited support for a country program in El Salvador. For both long-term and limited support, the results of the SEAM assessment surveys were critical in obtaining consensus among counterparts on the access problems that needed to be addressed, and in developing consensus around the interventions aimed at closing access gaps. The assessment results will also serve as a baseline, allowing both SEAM and country counterparts to measure change as progress is made in implementing the interventions.

Tanzania Country Background

The following section on health care in Tanzania was included as part of the 2001 SEAM assessment. This background provided part of the framework upon which the SEAM intervention in Tanzania was based. Though this information is dated, it presents the context to place SEAM's work in Tanzania.

Organization of Health Services

For almost 30 years, health services delivery has been largely a prerogative of the state; a limited number of private, for-profit health services were available only in major towns of the country. After independence, socialism was the guiding principle in the country, and free-market practices dwindled. Health care facilities were redirected toward rural areas, and free medical health services were introduced. However, the government could not afford the funds necessary to carry out essential health care, so it sought external financial aid starting in the late 1970s. By the late 1980s, donor funds made up a larger percentage of the health budget than government funds (GTZ 2001).

In 1977, private, for-profit health services were banned under the Private Hospitals (Regulation) Act and the practice of medicine and dentistry prohibited as a commercial service. This act had negative implications on health services in the country. After a series of major economic and social changes, however, the government developed and adopted new policies that looked favorably on the role of the private sector. The importance of the private sector in health care delivery was further recognized with an amendment to the 1977 Private Hospitals (Regulation) Act that resulted in the establishment of the Private Hospitals (Regulation) (Amendment) Act, 1991. Following this act, qualified individual medical practitioners and dentists could now manage private hospitals, with the approval of the Ministry of Health (MoH). Public-private partnerships are now actively encouraged as part of the Health Sector Reform policy pursued by the MoH.

According to government statistics, in 2000, Tanzania had almost 5,000 health facilities, of which 80 percent were classified as dispensaries.¹ Approximately 470 were health centers, which were primarily government run and served the rural areas of the country. Over 100 hospitals accounted for about 2 percent of all facilities. National government or parastatal organizations support most (66 percent) health facilities in Tanzania. Fifteen percent were run by nongovernmental organizations (NGOs) (i.e., religious organizations), and almost 20 percent were classified as private. Thirteen NGO hospitals operated as Designated District Hospitals in the districts without public hospitals. The role of for-profit private providers is still limited but has been growing rapidly, particularly in the urban areas, since the re-legalization of private practice in 1991. According to the government, the distribution of health facilities emphasizes rural areas where about 75 percent of the population lives.

The Pharmaceutical Sector

Pharmaceutical Policy, Laws, and Regulations

The Government of Tanzania's health reforms aim to improve health services through partnership between the public sector and private institutions has resulted in a number of legislative reforms and amendments. At the time of the 2001 assessment, pharmaceuticals were regulated through the Pharmaceuticals and Poisons Act No. 9 of 1978. The regulatory body overseeing pharmacy practice and medicine was the MoH's Pharmacy Board.

The Pharmaceutical and Poisons Act required that all pharmaceuticals be registered. However, enforcement of this provision was weak until 1999, when new management at the Pharmacy Board began to enforce registration requirements more vigorously. To carry out this work, the Pharmacy Board instituted a registration unit. Some of the pharmacists on staff had extensive experience in various areas of pharmacy, but limited experience in registration issues; however, some unit members attended training sessions. As of 2001, 4,800 products had been notified (entered the registration pipeline), and 1,408 human drugs and 64 veterinary drugs had been registered. Registration of human drugs increased by 123 percent in 2000 compared to 1999. Of the registered drugs, 60 percent were on the national essential drugs list. A lot of effort has been put into product registration and much was achieved within a relatively short time.

After the 2001 SEAM assessment, Parliament passed two acts that separate professional matters from the regulatory authority. The Pharmacy Act covers mainly professional norms and standards, educational standards, and registration of pharmacists, technicians, and assistants, and generally provides monitoring for good pharmacy practice. A Pharmacy Council oversees the implementation of the Pharmacy Act. The Tanzania Food, Drugs and Cosmetics Act establishes a food and medicine regulatory authority, the Tanzania Food and Drugs Authority (TFDA). In January 2003, Pharmacy Board's product-related responsibilities were assumed by the TFDA, and for the purpose of this report, TFDA will be referred to exclusively.

¹ National Bureau of Statistics (NBS), United Republic of Tanzania. 2002. Household Budget Survey 2000/01. <<http://www.tanzania.go.tz/hbs/>> (accessed No. 18, 2003).

The TFDA approves the registration of drugs if it considers that availability of the drug is in the public interest and it may authorize the sale of unregistered drugs for specified purposes. The TFDA grants licenses for importing, exporting, manufacturing, and selling medicines under specified conditions. Manufacturing licenses are subject to compliance with Good Manufacturing Practice (GMP).

The 1978 Pharmaceutical and Poisons Act governs the retail distribution of pharmaceuticals. The law labels prescription drugs as “Part I poisons” and over the counter drugs as “Part II poisons.” The sale of Part I pharmaceuticals is reserved for pharmacies in registered premises, conducted or supervised by a pharmacist. Part I pharmacies must be either owned by a pharmacist or the owner must enter into a legal partnership with a pharmacist to provide professional services. Exemptions are granted to dentists, veterinary surgeons, medical practitioners in the treatment of their patients, and staff members of a hospital, dispensary, or similar institution. In addition, as a result of the SEAM Program, new legislation created a different category of accredited drug dispensing outlets (ADDOS) that were given authority to sell select Part I drugs.

Duka la dawa baridi (DLDBs) literally means “Cold Drug Shops”—where “cold” drugs are nonprescription (over-the-counter). The law allows DLDBs to sell only nonprescription drugs (or Part II poisons), and thus these retail outlets, also known as Part II poison shops, are not legally required to be supervised by a pharmacist.

Pharmaceutical Distribution Structure

Manufacturers, wholesalers, sub-wholesalers, donors, and the medical stores department (MSD) are the main distributors of pharmaceuticals and medical supplies in Tanzania. The predominant single distributor of pharmaceuticals and medical supplies in Tanzania is the MSD. Since the government deposits funds for its health facilities with the MSD, it has a virtual monopoly for distributing pharmaceuticals and supplies to all public sector health facilities, including hospitals managed by church organizations. In addition to supplying government facilities, MSD has the country’s preeminent drug distribution system. The distribution structure is described as follows—

- Foreign manufactures sell products to the MSD, local manufacturers, importers/wholesalers, donors, NGOs/voluntary agencies, and private hospitals
- Local manufacturers sell products to the MSD, wholesalers, NGOs, and large private institutions (hospitals, retail pharmacies, etc.)
- Donors provide drugs to NGOs and voluntary agencies
- The MSD distributes products to government health facilities, NGOs/voluntary agencies, and parastatals from seven zonal stores
- Major importers/wholesalers sell primarily to sub-wholesalers/stockists, large private health facilities, and retail pharmacies; sales to the public sector and NGOs/voluntary agencies are generally minimal

- Sub wholesalers sell to smaller pharmacies, private health facilities, retail drug outlets (DLDBs), and smaller wholesalers
- Consumers obtain their products from public sector health facilities, private sector facilities, NGOs, pharmacies, and other drug outlets

Duka la Dawa Baridi

DLDBs constitute the largest network of formally licensed outlets for basic essential drugs in Tanzania. DLDBs are found in all 128 districts in the country. However, they are not evenly spread throughout each district and are usually found in the larger population and market centers. Although exact numbers are not available, it is estimated that there are more than 4,600 DLDBs in the country, about one for every 7,400 people. This is more than 80 percent higher than the equivalent figure for all public health facilities.

According to Guidelines for Dealing with Part II Poisons, the Regional Commissioner approves DLDBs for a TFDA permit after consultation with the Regional Technical Advisory Committee. After the Regional Commissioner approves the permit, and the Regional Trading Officer issues a business license, the owners are able to apply for a permit from the Regional Pharmacist, acting on behalf of the TFDA to sell Part II poisons. However, in some areas, Part II poison shops operate without a TFDA permit. Also, the responsibility for inspection of DLDBs lies with the TFDA; however, even after planned increases in personnel are taken into account, the financial and human resources available to the TFDA are insufficient for anything other than a limited number of inspections each year. From January 2000 to May 2001, for example, 159 Part II shops were inspected, which represents a small percentage of the shops in operation. Essentially, DLDBs have been able to operate outside of the regulatory framework.

DLDBs buy the drugs they sell from pharmacy shops, wholesalers, or unofficial supply sources. For those located in or close to a major urban center, finding these sources poses few problems compared with those located in distant areas. The latter group represents a significant proportion of DLDBs, and their operators often have to travel hundreds of miles to purchase stock from TFDA-registered suppliers. Sourcing is made all the more complicated because it is illegal for DLDBs to buy and sell Part I drugs. All of these factors may contribute to the high cost and uncertain quality of the drugs on sale.

Quality Assurance

National Quality Control Laboratory

The main tasks of the National Quality Control Laboratory (NQCL) are to—

- Assist with national drug registration and drug inspection
- Assist the medical stores department (MSD) in controlling the quality of its supplies
- Develop a quality assurance policy
- Supply testing resources for all regulated commodities

The NQCL started operations in 1999, but was formally inaugurated in March 2000. Staff members currently include drug and food analysts, technicians, microbiologists, and a secretary. Some of the analysts have postgraduate qualifications in pharmaceutical analysis and others are pharmacists. For tests it is unable to perform, the NQCL refers samples to other laboratories in the country.

As of 2001, quality testing is done predominantly on samples submitted by the inspection unit of the TFDA (48.6 percent), followed by requests from the registration unit (30.8 percent). About 20 percent of tests were done on request by other clients such as the MSD. In 2000, the laboratory received 354 samples, compared to 133 in 1999. Thirteen percent failed quality control tests in 2000. Of the total number of samples that failed quality control tests, 22 percent were locally manufactured. From January to May 2001, the laboratory received 64 samples; it analyzed 46 samples and 13 failed the tests. Of the submitted samples, 18 could not be analyzed properly for a variety of reasons (e.g., lack of reference standards, reagents). Of the tested samples, the reasons for failure were dissolution, counterfeiting, and low active ingredients.

Drug Inspectorate

The inspection unit is the TFDA's compliance monitoring and enforcement arm. Besides staff stationed at headquarters, it has inspectors who are located in regions and some POEs. This unit's functions include inspecting manufacturing premises for licensing purposes and compliance with GMP, monitoring of compliance with standards in all retail and public sector pharmacies and public and private wholesalers, inspecting narcotics and imported drugs at ports of entry, postmarketing surveillance of drugs, and conducting special inspections on any premises if mishandling is suspected. Inspectors have the power to enter any premises where medicines are handled and to seize illegal products when required.

The TFDA intends to extend the inspectorate presence to all 128 districts in the country and to cover all border posts. However, the inspectors' capacity may not be sufficient in terms of both numbers and expertise. They plan to do at least two routine inspections per registered site per year, but the number of pharmaceutical outlets is far more than they can cope with. Inspections ideally would include all 15 POEs (including Zanzibar), dispensing doctors, traditional medicine outlets, homeopaths, and DLDBs.

The two Dar es Salaam ports of entry have inspectors on site 12 hours a day. They inspected 942 consignments in 2000–2001. The consignments were generally found to conform to identification and labeling requirements approved by the board on the pro forma invoices. The other 13 official ports of entry had not yet been inspected. It is believed that there are several other unofficial entry points (e.g., Zanzibar, along borders with Kenya and Burundi).

Of 103 applications for new premises received in 2000, the inspectorate approved 56 (54 percent). One manufacturing plant was approved and one repackaging plant was approved. In 2000, 28 manufacturers were inspected for compliance to GMP (18 in Kenya and 10 local). Ten of the Kenyan facilities were approved. The inspectorate ordered 3 of the 10 local plants to stop production. It found three extemporaneous preparation plants to be manufacturing product and ordered them to stop. None of the local manufacturers met the GMP standards set by the TFDA.

From 2000 to May 2001, the inspectorate office monitored 102 Part I shops (private pharmacies that sell prescription medicines), 54 wholesalers, 159 Part II shops, 81 veterinary centers, and one MSD warehouse for good pharmacy practice in 2000 in the Dar es Salaam, Northern, and Lake Zone areas. The breakdown of the inspections during this period is tabulated in Table 13.

Table 13. Inspection of Premises Jan. 2000–May 2001

Type of Facility	Number of Registered Premises	Number of Premises Inspected	Coverage, %
Retail pharmacy	339	102	30
Wholesaler	155	54	35
Manufacturer (domestic)	10	10	100
Manufacturer (Kenya)	—	18	—
Prepackaging units	—	3	—
Government wholesaler/ importer MSD	10	1	10
Hospital stores	—	8	—
Agrovets	—	81	—
DLDBs	+/- 1,000 in Dar es Salaam alone; several thousand in other parts of the country	159	*

*The number of Part II shops is unknown, as they are not registered with the board. However, it is estimated that there are more than 4,600 in the country.

Defining the Need in Tanzania

The 2001 SEAM assessment revealed access gaps in drug availability, primarily in the public sector, and issues related to quality and affordability of products and services, especially in the private retail sector serving rural areas. The assessment made the following key findings: (1) geographical access to drugs does not appear to be a problem and is not perceived as a problem by the public; (2) availability of drugs is a problem at MSD, especially, but not exclusively, at zonal stores outside of Dar es Salaam Zone; (3) availability issues exist in public sector primary

health care facilities and also in many hospitals;² (4) availability does not seem to be a significant problem at NGO/mission health facilities; and (5) with respect to quality of drugs and services, SEAM data from districts surveyed revealed that the public cannot be assured of drug quality for a significant proportion of drugs in the Tanzanian market.³

These findings posed major challenges to the MoH, namely to seek the ways and means of improving the availability of drugs in the public sector, especially in hospitals and primary health care facilities, and the quality of products and services in the private sector. To address these challenges, SEAM developed strategies that were approved by the MoH for implementation. The strategies included (1) establishing a network of ADDOs in rural and peri-urban areas of the country to provide an increased range of products similar to those approved for primary health care facilities; (2) establishing a tiered pharmaceutical product quality assurance program; and (3) establishing an alternative, private sector supply system to augment the MSD supply system for the mission sector, other MSD clients, and possibly rural retail drug outlets by providing quality, competitively priced health commodities.

To address problems of availability, affordability, and quality of drug products and pharmaceutical services in Tanzania, SEAM implemented strategies to—

- Transform DLDBs into ADDOs that will provide a range of high-quality essential medicines and pharmaceutical services at reasonable prices. The network of outlets will be made up of independent entities that are not part of a centrally controlled franchise or organization that serves to ensure quality. Instead, quality of both products and services will be ensured through a combination of government accreditation (with the threat of losing licenses to sell drugs) and regulation mediated through routine monitoring by district and subdistrict local government and community structures.
- Help improve drug product quality by developing a national quality testing program that uses tiered testing to help ensure pharmaceutical product quality and that can also serve as a model for other resource-constrained countries.
- Foster improved access to affordable, high-quality pharmaceutical products for the public and mission health care sectors through the development of a system of alternative pharmaceutical suppliers from the commercial sector that can supplement the supply services provided by the medical stores department.

The SEAM Program has produced separate reports detailing the activities of the ADDO Program and the alternative distribution program for the mission sector. Those reports can be accessed at www.msh.org/SEAM

² Districts surveyed included Dar es Salaam-Temeke, Kinondoni, Masasi, Njombe, Karagwe, Kilimanjaro Rural, Tanga Urban, and Dodoma Urban.

³ Results obtained from pharmacies and *duka la dawa baridi* in study districts revealed that between 42 percent and 50 percent of drugs lacked TFDA registration or notification. In addition, 21–23 percent of drugs were classified as TFDA-notified drugs and thus quality was unknown.

Rationale and Objectives for the Quality Assurance Program

Substandard drugs circulating in the market are a problem in many countries. Based on studies in 10 countries, WHO reported that 10–20 percent of marketed drugs did not comply with accepted quality standards. In its 2001 assessment, SEAM took 110 samples of 10 different drugs from three categories of facilities (public, NGO/voluntary, and private pharmacies) in eight districts and the medical store department. Of these 110 samples, while none from NGO/mission facilities were found to be substandard, 6.5 percent of the samples from public facilities and 8.7 percent from private pharmacies were found to be substandard.

Postmarketing surveillance inspections conducted by TFDA in previous years revealed counterfeit products in the market. The production of high-quality counterfeit labels points to the possible sophistication of the counterfeit industry.

A further measure of the quality of drugs in the marketplace is the percentage registered with the TFDA. Only 26 percent of the drugs surveyed by SEAM in the 39 DLDBs were registered with the TFDA, while a further 24 percent were notified. The remaining 50 percent were therefore neither registered nor notified. The quality of notified and unregistered drugs cannot be assured, since they have not passed through the registration process, which would include almost three-quarters of drugs surveyed from DLDBs.

Not only do these pharmaceutical products pose threats to the health of the general public through ineffective treatment, they also waste scarce resources and undermine the confidence of the public in the health care system. More seriously, they can cause injury and even death. This situation is further complicated by the fact that prescribers and users of pharmaceutical products are not able to assess the safety and quality of medicines for themselves before use.

As discussed in an earlier section of this report, the TFDA has a drug inspectorate unit supported by a national laboratory to sample and test for quality assurance. However, the resources available limit the number of inspections and tests, although the goal of the government is to increase those capabilities. Box 1 shows the large number of areas and responsibilities that TFDA must regulate and monitor to assure quality pharmaceuticals in the Tanzanian marketplace.

Box I. TFDA Regulatory Universe: Areas of Responsibility

The TFDA has the responsibility for monitoring—

- 42 Countries of origin
- 264 Manufacturers
- 874 Active ingredients
- 2,833 Registered products
- 207 Wholesalers
- More than 380 retail pharmacies
- 149 ADDOs
- More than 4,000 DLDBs (Part II shops)

The TFDA must enforce numerous regulations related to—

- Compliance history of firm
- Information on importing country
- Status of WHO pre-qualification
- Safety and efficacy of ingredients
- History of suppliers
- Document examination at POEs
- Physical examination at POEs
- Screening at POEs
- Condition of facility storage
- Legality of products—registered, unexpired
- Legality of sales practices
- Prescribing/dispensing practices at drug outlets

Using data collected during the 2001 SEAM assessment, the situation in Tanzania before the SEAM intervention can be summarized as follows—

- Eighty percent of pharmaceutical products were imported (based on value)
- Fifteen official POEs existed
- Six POEs were approved for drug imports
- Two POEs had TFDA inspectors
- NQCL tested 354 pharmaceutical samples in 2000
- Thirteen percent (46) of samples failed these tests
- Ten percent of samples failed assay tests
- Of medicines surveyed at dispensing outlets, 48 percent were neither notified nor registered; 50 percent of those were imported

- Local production was not compliant with Good Manufacturing Practices (GMP)
- A general perception of quality problems existed

In addition, the data needed by inspectors for reference include a listing of approved products, manufacturers, and importers. Although the TFDA updates and revises this information frequently, distance, cost, and maintenance factors prevented the data from being readily available to inspectors in the field. The information collected was handwritten by the inspectors which was difficult to manage. Because of a shortage of staff, the pace of data compilation had been greatly limited, and the data collected had not been made available in a timely fashion for use in making important public health decisions.

The goal of SEAM's pharmaceutical product quality support to the TFDA was to help establish a comprehensive national quality assurance program with financial and technical assistance. The program contributed to the development of a system capable of better ensuring that both imported and locally manufactured drug products meet approved quality standards.

The projects objectives were to—

- Create an overall drug product quality assurance strategy
- Increase the number of drug samples tested
- Reduce substandard and counterfeit products entering and circulating in the country from both imports and local manufacture
- Establish a quality assurance program that, once established, could be taken over by the TFDA and provide a model that can be replicated by other countries

Quality Assurance Stakeholders and their Roles

Medical Stores Department

The parastatal nationwide medical supply system medical stores department (MSD), established in 1993 through the reorganization of the former Central Medical Store, is based in Dar es Salaam with seven zonal stores around the country. TFDA and MSD developed a cooperative inspection program because drug products are directly imported into MSD from the Dar es Salaam Harbor POE and directly procured from local manufacturers without inspection. TFDA inspectors now visit the MSD at regular intervals to examine and collect drug products for assuring compliance with the regulations and laws.

Muhimbili University College of Health Sciences

Staff members contributed to the development of a training manual and one-week training course for TFDA inspectors on thin-layer chromatography and Minilab[®] drug quality screening techniques.

Satellite

This nonprofit organization works to expand information technology in developing countries. SATELLIFE worked with TFDA and MSH to adapt the existing inspection process to incorporate the use of personal digital assistants (PDAs) by inspectors.

TFDA

The TFDA mandate is to ensure that pharmaceutical products conform to acceptable standards of quality, safety, and efficacy, and that premises for manufacturing, storing and distributing them comply with requirements. The TFDA is responsible for drug inspection, drug registration, and quality control. The TFDA worked closely with MSH/SEAM on the development and implementation of the quality assurance program. The TFDA is responsible for all aspects of the program, including policy/procedure setting, development and use of inspection tools, capacity building, data analysis, product testing, and enforcement of the quality assurance standards.

WHO

WHO provided technical equipment and training.

Other stakeholders include the pharmaceutical manufacturers, wholesalers, retail shop owners, physicians, dispensers, pharmacists, patients, and local and regional government officials.

Creating a Drug Inspection and Screening Program

Conceptual Overview of the Quality Assurance Program

A comprehensive strategy for assuring product quality comprises a range of components, including review and analysis of documentation, visual inspection, product testing, monitoring of products and manufacturers, effective enforcement of regulations, and drug defect and adverse reaction reporting. The primary focus of the SEAM intervention was on visual inspection and pharmaceutical testing at ports of entry and drug dispensing outlets.

To address concerns about drug quality in Tanzania, the Tanzania Ministry of Health and the TFDA, with SEAM support, developed a three-tiered product quality assurance inspection and testing program. This program emphasizes the timely testing of medicines as they enter the country and appear in the market, and involves developing capacity for three levels of screening—

1. *Tier-one (primary) screening*: Inspection of product documentation, physical examination of products, and visual thin-layer chromatography (TLC) screening methods
2. *Tier-two (secondary) testing*: Testing with the legal reference methods, which generally are based on high-performance liquid chromatography (HPLC), to test the products that are found to be potentially substandard during primary testing
3. *Tier-three (tertiary) testing*: Specialized testing with much higher levels of sensitivity and selectivity, such as HPLC coupled with mass spectrometry

The SEAM program supported the implementation of a structured physical inspection program of documents and products and TLC screening for a limited number of antimalarial, antibiotic, and antiretroviral (ARV) products.

This screening approach is used to assess the quality of selected essential pharmaceuticals and any suspicious products at three levels within Tanzania—

- POEs into the country
- MSD and private drug wholesalers/distributors
- Retail drug dispensing outlets

Ports of Entry

After drugs enter the supply chain in any market, it is difficult to monitor quality and to recall batches should a quality problem be identified. If timely and reliable data are available to regulators about products before they enter the market, then substandard products can be denied entry at POEs. In order to provide such data, regulators need to determine quickly if the product—

- Has market approval
- Is properly labeled and packaged
- Contains the correct (labeled) active ingredients in approximately the legally required amounts required to meet pharmacopeial standards

Determining the active ingredients promptly requires that the regulators have some analytical resources close to the major POE to help screen for products which are markedly substandard or counterfeit.

Post-Market Surveillance

Market surveillance requires the routine inspection of facilities and sampling of products in the marketplace, including distributors and retail outlets. Degradation during storage and transportation is of particular importance in tropical countries. Products being sold by retailers and distributors operating in the “gray” market also should be tested routinely. Such a surveillance program should also test suspected substandard and counterfeit products and follow up on reports of drug problems and adverse reactions.

This quality assurance strategy is dependent on the TFDA’s inspection and pharmaceutical testing capacity. To this end, the SEAM quality assurance program incorporated a number of tools and activities, among them—

- Quality assurance protocols and training based on a combination of visual inspection and non-laboratory-based testing using Minilab (see below)
- Standard operating procedures (SOPs) for inspection, including delineation of compliance actions.
- Expanded inspectional capability, including instrumentation, training, and other support for inspectors
- Electronic tools using personal digital assistants for inspectors to improve their recordkeeping, report preparation, and report submission.

Major Program Elements

Pharmaceutical Inspection Program

To expand its regulatory reach and capability, the TFDA has developed a six-zone administrative structure to coordinate and focus the activities in the 21 governmental regions into a more manageable configuration. The TFDA has organized zonal training of over 300 health workers who are employees of regional/district/local governmental authorities to serve as an auxiliary

cadre to perform food and pharmaceuticals product examinations and report the findings to the TFDA. Their training was based on the model and training materials developed by TFDA and SEAM.

For the pharmaceuticals segment, the training was focused on raising awareness of product quality, performing structured product physical examinations, and inspecting both public and private drug dispensing facilities. Stakeholder sensitization meetings also were held at the zones during the training sessions to alert them to the improved regulatory presence, and thereby enhance voluntary compliance to legal standards.

Personal Digital Assistant Inspection Data Logging System

The collection and availability of correct and timely drug product inspection and testing data are critical in drug regulation, allowing field staff to more efficiently monitor the flow of pharmaceuticals and enabling the larger governing body to identify and focus on trouble spots in the marketplace. To do their work, field inspectors must have easy access to the country's drug marketing authorization and registration databases and must be able to efficiently collect and submit inspection data.

To address the problems in the drug inspection data flow and preparation of reports, the TFDA, SEAM, and SATELLIFE adapted the existing inspection process to incorporate inspectors using PDAs. The continuing increase in PDA capability makes them a financially and technically reasonable option for addressing data collection and information sharing needs.

Expected benefits of the fully implemented program include tighter regulatory control of the marketplace, reduced error in data collection and transfer, greater availability of lists of approved products and marketers, more timely access to needed information, and lower personnel costs.

Minilab-Based Drugs Testing Program

Primary screening facilities should be available to test a significant percentage of imported finished dosage forms at POEs. Secondary level or legal reference methods, such as HPLC and gas-liquid chromatography, are not commonly found at POEs, even in developed countries. Furthermore, using these techniques for routine market surveillance could quickly overburden existing capacity. For monitoring drug quality at POEs and on the market, secondary level methods are too slow and expensive. Visual TLC—with its rapid setup, high throughput, and relatively low cost—is recommended for this work. Products failing TLC tests at POE could be denied entry into the country, and market samples passing primary TLC tests may not require further testing. TLC visual detection tests to assess pharmaceutical product quality have been included in a convenient kit concept developed by the German Pharma Health Fund⁴ called the Minilab.

⁴ The German Pharma Health Fund is a charitable organization supported by donations of research-based pharmaceutical companies in Germany.

SEAM proposed TLC as a component of both tier-one (primary) and tier-two (secondary) testing strategies. Tier-one TLC is semi-quantitative and relies on visual detection at POE and other noncentral sites. Tier-two TLC is quantitative, based on instrumented detection using densitometry, and is housed in a lab facility. The initial phase of the program focused on developing the tier-one TLC, while tier-two TLC would be included in a future phase of the program.

In addition to inspection training, a select group of Tanzanian health workers were trained on Minilab drug quality screening procedures to manage testing sites in the various zones. All of the inspectors who participated in this testing program are pharmaceutical technicians or pharmacists who have had prior laboratory training. On this basis and with the support of the WHO, which provided additional Minilabs, the TFDA expanded Minilab screening centers from six to ten sites (see figure 2) and increased the number of screened samples.



Figure 2. Tanzania Food and Drugs zonal structure and Minilab centers

The testing sites at Musoma and Mwanza are in the Lake Zone, Arusha, and Tanga in the Northern Zone; Kigoma and Dodoma in the Central Zone; Mbeya and Songea in the Western Zone; Dar es Salaam in the Dar es Salaam Zone; and Mtwara in the Southern Zone.

Box 2 lists the components that comprise the TFDA’s tier-one screening program.

Box 2. Components of Tier-One Inspection and Screening

The drug inspector verifies the following documentation—

- The consignee has an approved pro forma invoice.
- The Clean Report of Finding date is before the pro forma invoice expiration date.
- All consignment information matches the information on the approved pro forma invoice.
- Each batch of products has an approved Certificate of Analysis.
- At the time of arrival, products with shelf lives of more than 24 months have 60% of their shelf life remaining, and those with less than 24 months have 80% of their shelf life remaining. The inspector will perform a label examination for all products.
- Labels must bear the name and address of the manufacturer.
- There is no evidence of tampering; tamper-proof seals are intact.
- Labels and package inserts must be written in Swahili and/or English.
- Batch numbers and expiration dates on the samples must match the numbers on the Certificate of Analysis unit samples.

The inspector performs a physical examination—

Solid form: Odor, uniformity of size, shape, color, coating, and markings. Breakage, cracking, foreign particle contamination, splitting, pinholes, broken or open capsules, and stickiness

Liquid or semi-solid form: Evidence of cracking, breakage, tearing, leakage, particulate matter, clarity, fluidity, uniformity, and redispersability

The following antimalarials are sampled—

- Quinine tablets
- Injectable artesunate
- Sulfadoxine-pyrimethamine (S-P) tablets

The following antibiotics are sampled—

- Amoxicillin
- Ampicillin
- Co-trimoxazole
- Erythromycin
- Metronidazole

The following antiretroviral products are sampled—

- Didanosine
- Indinavir
- Lamivudine
- Nevirapine
- Stavudine
- Zidovudine

The samples are screened with the following tests—

- Color reaction if available.
- Disintegration
- TLC
- Dissolution test at the Central Laboratory (for each S-P sample)

QUALITY ASSURANCE PROGRAM ACTIVITIES, OUTCOMES, AND TOOLS

Tanzania QA Program Timeline November 2001–February 2005

	Nov. 2001	Oct. 2002	Apr. 2003	Oct. 2003	Jan. 2004	Apr. 2004	Oct. 2004	Feb. 2005
INSPECTION	Develop: • Flowchart • SOPS • Training inspection materials	Launch with stakeholders		Launch PDA initiative	Stop PDA initiative		Re-launch PDA initiative	
		Start new inspection program	Conduct 6-month program review	Conduct 6-month program review	Conduct 6-month program review	Conduct 6-month program review	Validate PDA data	
TESTING	Develop testing training materials							
	Develop inspector roles and procedures	Launch Minilab initiative	Present PDA initiative	Develop proficiency test protocol	Test Minilab proficiency round 1	Conduct performance qualification	Test Minilab proficiency round 2	
	Conduct training programs		Add antimalarials	Add antibiotics				Add ARVs

Quarter/ year	Activities	Responsible Parties	Outcomes/Resources/Tools
	Project Development		
	Drafted a framework for pharmaceutical product quality assurance for resource-constrained countries	TFDA, SEAM	TZ 2001 assessment
Q4-01 to Q4-02	Developed a Tanzania-specific tiered testing program to help ensure pharmaceutical product quality.	TFDA, SEAM, MUCHS	Marked increase in number of products examined and rejected
Q4-01	Prepared an ordered listing of the drug product quality regulations and requirements to help improve the efficiency of the inspection and testing programs	SEAM, TFDA	Marked increase in inspections of outlets and number of products confiscated and unlicensed premises closed
Q1-05	Finalized evaluation strategy for quality assurance initiative	TFDA, SEAM	Evaluation strategy document

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Quarter/ year	Activities	Responsible Parties	Outcomes/Resources/Tools
	Pharmaceutical Inspection Program		
Q4-01	Codified from the TFDA laws and regulations and the Tanzania Revenue Authority, a ranked inventory of requirements and policies. Drawing from this inventory, created a compliance decision tree to direct the inspection process. The decision tree outlines the procedures that drug inspectors at POEs must follow in inspecting and testing drugs entering the country.	MOH, TFDA, SEAM	POE compliance decision tree and flow chart
Q3-02	Held a workshop with wholesalers and importers to make them aware of changes in regulatory expectations.	TFDA, SEAM, Tanzania Association of Pharmaceutical Industries	Sensitization workshop report
August to October 2002	Developed SOPs and checklists to guide the inspection processes and improve the uniformity and consistency of the inspection process. The SOPs, which outline steps for conducting and recording inspections of products and premises for compliance with regulations, serve as a reference for manufacturers, importers, wholesalers, and retail distributors	SEAM, TFDA	Inspection SOPs
Q3-02	Prepared reporting forms to document decision points in the inspection process. The SOPs and forms were pilot tested by experienced inspectors for several months to improve the communication and smooth the order of the work.	TFDA, SEAM	
Q3-02	Compiled field-tested forms and SOPs into the Inspector's Handbook	TFDA, SEAM	Inspector's Handbook <ul style="list-style-type: none"> • Sample Receipt Form • Rejection-Detention Form • POE Screening Certificate • Facility Screening Certificate • Confiscation-Quarantine Form • POE Consignment Inspection Form • POE Product Physical Examination Form • Facility Product Physical Examination Form • Part I Shop Inspection Form-Retail Prescription Pharmacy

Quality Assurance Program Activities, Outcomes, and Tools

Quarter/ year	Activities	Responsible Parties	Outcomes/Resources/Tools
			<ul style="list-style-type: none"> • Abbrev Part I Inspection Form • Dispensary Inspection Form • Abbrev Dispensary Inspection Form • Part II Outlet Inspection Form—Baridi-Muhimu • Abbrev Part II Inspection Form
Q1-02	Prepared a facilitation guide with daily study guides and examination materials for a one-week training program on inspections of products and premises for conformity to laws and regulations.	MUCHS, SEAM, TFDA	<ul style="list-style-type: none"> • Training Facilitation Guide • Daily study guides • Examination materials
Q1-02	Developed a one-week training course on pharmaceutical testing using TLC, colorimetric procedures, and measuring disintegration.	MUCHS, TFDA, SEAM	Training Facilitation Guide
Q2-02 to Q1-05	Trained drug inspectors on structured approach to conducting inspection of drug dispensing outlets and pharmaceutical testing.	TFDA, SEAM	339 drug inspectors were trained in all six zones: 86 lake zone; 52 central zone; 66 southern highlands; 60 northern zone; 32 south zone; 43 eastern zone
Q1-03	Instituted premises inspections and routine surveillance programs in pharmacies and DLDB shops in the Lake Zone, Northern Zone, and Dar es Salaam to assess their compliance with the TFDA regulations and laws	TFDA, SEAM	In the course of premises inspections, numerous unregistered and unauthorized products were confiscated; shop owners were warned to comply with the laws and regulations
Q1-03 to Q4-04	Extended training program nationally through zones to expand coverage and strengthen compliance.	TFDA	Trained 17 trainers of trainers
Q3-03	Instituted a cooperative inspection program between the TFDA and the medical stores department (MSD) because drug products are directly imported into MSD from the Dar es Salaam Harbor POE and directly procured from local manufacturers without inspection.	TFDA, SEAM	TFDA inspectors now visit the MSD at regular intervals to examine and collect drug products for assuring compliance with the regulations and laws.
PDA Inspection Data Logging System			
Q3-03	Selected Pendragon Forms software (www.pendragon-software.com) for use with the Palm m130 PDA (www.palm.com) to bring the paper-based inspection forms into an electronic medium.	SATELLIFE, SEAM	
Q3-03	Reviewed inspection forms in order to develop master forms for POEs and premises inspections	TFDA, SEAM	Master forms for POE and premises inspections developed in PDAs

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Quarter/ year	Activities	Responsible Parties	Outcomes/Resources/Tools
Q3-03	Designed and implemented alpha-version PDA-based inspection reporting system based on menu-driven reporting forms and listing of approved products, consignees, and manufacturers.	SEAM	Data logging and transfer SOPS
Q3-03	Conducted training in the use of PDAs and the converted inspection forms for a majority of the current drug inspectors. Once the training was completed, the inspectors field-tested the PDAs and the forms at various inspection points around Dar es Salaam, reporting errors and making adjustments to the forms and process based on their experiences.	TFDA, MSH, SATELLIFE	Training materials
Q3-03	Installed inspection form into PDA	SATELLIFE, TFDA, SEAM	Twenty Palm Pilot model 130 PDAs installed with inspection forms for POEs and premises inspections
Q3-03	Trained inspectors on PDA usage and performed field testing of first version of PDA based forms	TFDA, SEAM, SATELLIFE	<ul style="list-style-type: none"> • Nine drug inspectors trained on PDAs applications/functions • Inspection is conducted using PDA in 3 centers • Problem occurred in synchronization of the program
Q2-04	Developed second version of PDA including validation of data	TFDA, SEAM, SATELLIFE	Total of 11 staff members were trained out which 9 were drug inspectors and 2 from information technology section
Q2-04	Reviewed inspection forms to develop master forms for POE and premise inspections based on second version of PDA	TFDA, SEAM	All inspection forms reviewed and PDAs updated to conform to the second version
Q3-04	Trained inspectors on second version of the PDA-based inspection forms and synchronization process on updating of dynamic field of the PDA inspection forms	SATELLIFE, SEAM, TFDA	Twelve drug inspectors trained and inspection is conducted using PDA in three centers which Dar Harbors, Dar International Airport and Northern zone (namely Namanga border)

Quality Assurance Program Activities, Outcomes, and Tools

Quarter/ Year	Minilab-Based Drug Testing Program		
Q3-02	Developed SOPs and decision trees for sampling and screening of target antimalarial drugs	TFDA, SEAM	<ul style="list-style-type: none"> • SOPs for sampling and screening of antimalarials • Drug inspection decision trees and flow chart • Antimalarials incorporated in the program were sulfadoxine-pyrimethamine, quinine and artesunate products
Q3-03	Developed a one-week training program on the use of the Minilab techniques for screening the quality of antimalarial products in non-laboratory facilities	SEAM, TFDA, MUCHS	<ul style="list-style-type: none"> • Training facilitation guide • Daily study guides • Examination materials
Q3-02	Conducted a sensitization workshop to increase stakeholder awareness in the program activities, set time limits, and explain the program objectives	TFDA	130 stakeholders (drug importers, wholesalers, drug manufacturing, and retailers) attended
Q3-03	Trained inspectors on GPHF Minilab techniques. After one-week training, each of the inspectors was sent with a Minilab to perform the product screening tests at various locations in the country including colorimetric identification, thin-layer chromatographic estimate of amount and identification confirmation, and measurement of disintegration time.	TFDA, SEAM, MUCHS	Nine inspectors completed the training program.
Q4-02	Officially launched the quality assurance program	Minister for Health Hon. Anna Abdallah (MP)	Gained political support for the program
Q4-04	Established 7 Minilab screening centers Oct 2002	TFDA	Dar-es-Salaam Harbors, Dar-es-Salaam International Airport, Mbeya, Musoma, Arusha, Mtwara, and Dodoma
Q1-03	Instituted pharmaceutical quality inspection and Minilab product screening programs immediately following the program launch, for the examination of imported products at the ports of entry (POEs) at Dar es Salaam International Airport, Dar es Salaam Harbor, Sirari (in the Lake Zone), and Namanga (in the Northern Zone). Phase I focused on antimalarial drug products.	TFDA, SEAM	
Q2-03 and ongoing	Conduct regular monitoring and evaluation	SEAM, TFDA	Monitoring is performed on six operating centers twice annually
Q3-02	Developed chain-of-custody SOPs in packing and shipping of samples and register log book	TFDA, SEAM	<ul style="list-style-type: none"> • SOPs • Register log book
Q4-03 and	Monitor sample flow from regional centers to the TFDA laboratory	TFDA, SEAM	No sample backlogs at the TFDA NQCL

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ongoing	for dissolution test and confirmatory test		
Q3-04	Developed proficiency test procedure to provide assurance that the Minilab screening tests were being competently performed. To reinforce the training on discerning these differences, a performance qualification test set was developed to improve their ability to discern the differences.	TFDA, SEAM	Proficiency Test I was conducted by 9 drug inspectors
Q4-04	Following the inspector's unsatisfactory performance of the qualification exercise, a second proficiency test was initiated Performed qualification of the TLC test methods.	TFDA, SEAM	<ul style="list-style-type: none"> • 12 inspectors participated in the performance qualification test exercise. • The performance of the inspectors in the second round of proficiency testing improved substantially
Continuous	Expanded the geographic reach of the program and include more target drugs	TFDA	10 centers countrywide have been established
Q4-03	Broadened product categories to include selected antibiotic drugs	TFDA, SEAM	Amoxicillin, ampicillin, co-trimoxazole, metronidazole, erythromycin and ciprofloxacin
Q4-03	Train inspectors in screening antibiotic drugs	TFDA, SEAM, MUCHS	12 inspectors trained in antibiotic drug screening
Q1-05	Broadened product categories to include six antiretroviral drugs used to treat HIV/AIDS	TFDA, SEAM, MUCHS	Didanosine, indinavir, lamivudine, nevirapine, stavudine, and zidovudine
Q1-05	Trained inspectors in screening of ARVs	TFDA, SEAM	15 inspectors were trained on ARV screening

Quality Assurance Program Evaluation

Evaluation Methodology

The program evaluation reviewed the results in terms of the various factors that influence access to medicines. The quality assurance program aims to improve the quality of products in the marketplace, by strengthening TFDA capacity to detect substandard products, prevent these products from entering the country, or remove them if they are already in the distribution channels.

Evaluation Design and Data Collection Techniques

The evaluation provided a detailed description of the product quality assurance program and the implementation process. Initial data gathering was conducted in 2001, which looked at the drug quality practices in place at the time. Quantitative outcome measures of the program's results largely reflect measurements gathered over the course of the program, using pre-post comparisons where available, and trend analysis to depict results.

The evaluation included the following components—

- In-depth interviews at the end of the program with project implementers and stakeholders (government, TFDA managers and staff, Muhimbili University College of Health Sciences, and professional associations) and review of project records to identify perceived benefits of the program, and enablers and constraints to establishment and sustainability of the program.
- Objective assessments of outcomes are based on measures of capacity for inspection, testing, and regulatory enforcement. There was not a before-after comparison for a sample of products. Results of inspection activity, Minilab, and NQCL testing were compiled and reported for 12-month periods.
- Data were provided on—
 - Number of inspections (by facility type)
 - Number of first-tier/screening (Minilab/TLC) and second-tier (legal reference/pharmacopoeial) tests conducted
 - Government of Tanzania/TFDA enforcement actions (for example, rejection of shipment entry, disposal of detected substandard or counterfeit products, product recalls, and confiscation of illegal or unregistered products)

The time period covered by this evaluation is as follows—

- 2001: Historical data collected during the initial SEAM Assessment in 2001
- October 2002-September 2003: First year of data gathering through SEAM program
- October 2003-September 2004: Second year of data gathering through SEAM program
- October 2004-April 2005: Third year of data gathering through SEAM program.

The table below describes the outcome indicators that were applied to evaluate the results of the quality assurance program. Each proposed indicator is listed along with the source of the data and the comparison periods.

Country	Tanzania
Introduction of inspection, screening, and primary product quality testing program Program Targets Ports of Entry Design for Performance and Impact Evaluation Inspection	Pharmaceutical Product Quality Assurance Program <ul style="list-style-type: none"> • Inspection program established at four ports of entry • Primary (screening) testing program established for antimalarials and antibiotics • Dar es Salaam International Airport • Dar es Salaam Harbor • Sirari (Lake Zone) • Namanga (Northern Zone, including Kilimanjaro International Airport) Pre/post launch trend analysis over time Time period: Pre-launch: 2001; Post-launch: October 2002-April 2005 <ul style="list-style-type: none"> • Number of POE pharmaceutical consignments inspected • Number of facilities inspected
Testing	<ul style="list-style-type: none"> • % of Minilab tested samples that failed tests • % of TFDA NDQC Laboratory samples that failed tests

Evaluation Results

Since the launch of the program in October 2002, the number of pharmaceutical consignments inspected at POEs has increased significantly. A total of 4,299 consignments—about 1,700 consignments per year—have been inspected since the program launch (figure 3). The efficiency of the inspection processes has been helped by uploading forms for product and premises registration data, as well as inspection forms, to PDAs; upon completion, the inspection forms may be automatically downloaded into an Access database.

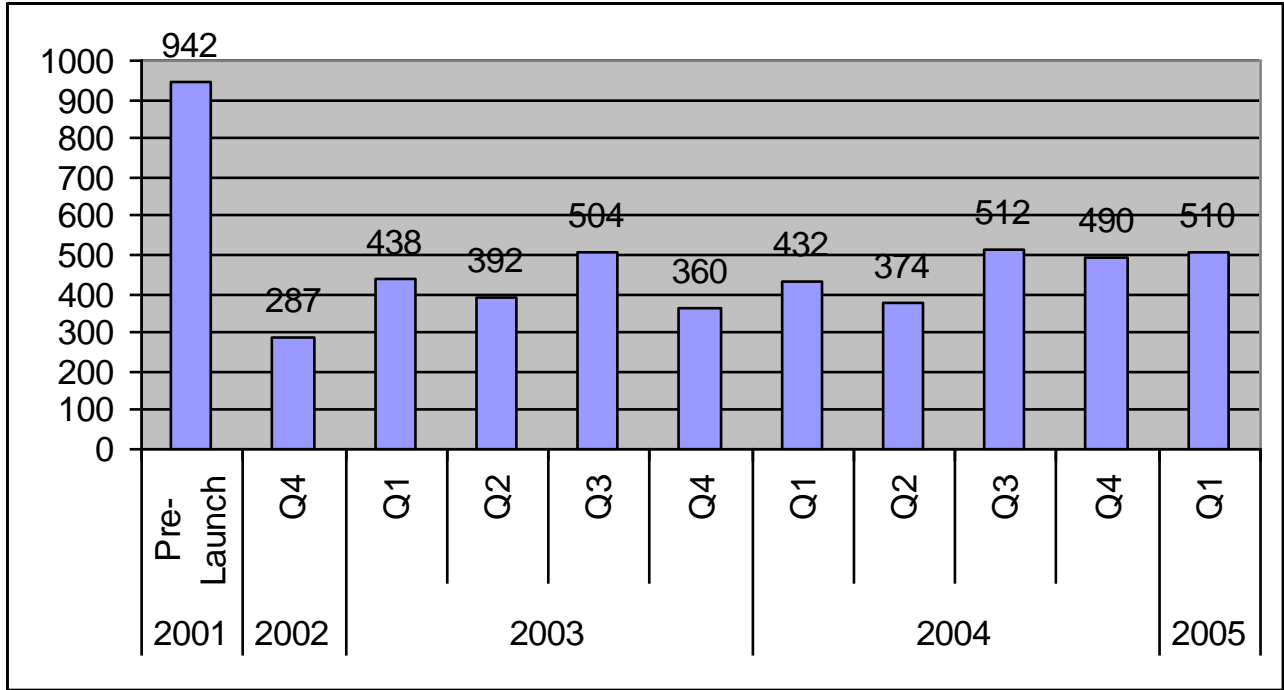


Figure 3. Number of pharmaceutical consignments inspected at POEs (Pre- and Post-Launch)

The number of drug dispensing outlets inspected has also increased significantly; the number of facilities inspected one year post-launch increased about five-fold (figure 4), and the trend has been maintained throughout the program implementation.

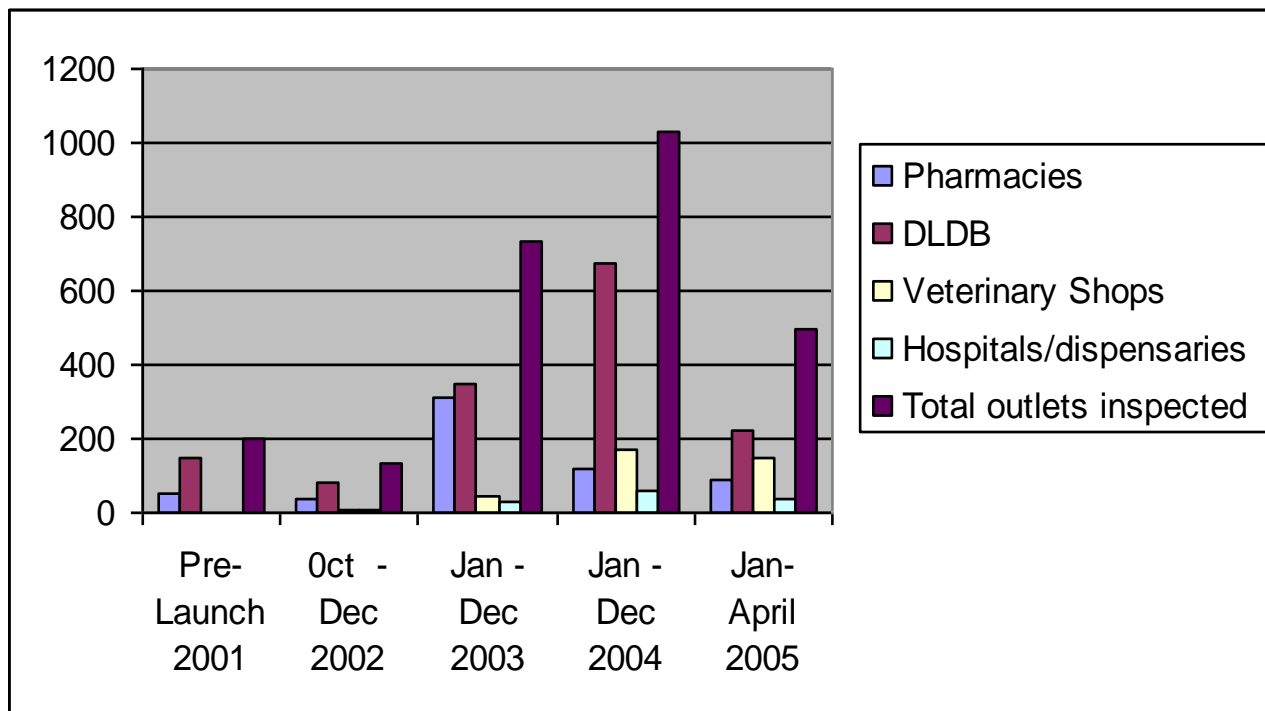


Figure 4. Dispensing outlet inspections (Pre- and Post-Launch)

Prior to the project’s implementation, the NQCL was the only means by which TFDA could monitor the quality of drugs on the market in Tanzania. But now, the NQCL is complemented by Minilab screening at the POEs and other TFDA Minilab centers. For example, in 2000–2001, the NQCL tested 354 samples from inspections and for registration. During the program evaluation period, a total of 1,257 batches of samples from inspections were screened of which 1,211 batches passed and 46 (3.7 percent) failed. Of the failed samples, only five batches failed the screening test, three quinine and two erythromycin, and all of these fake products were removed from the market. The majority of the failed drugs were sulfadoxine-pyrimethamine tablets that failed the dissolution test.

It is important to note that the screening program requires that all the screened sulfadoxine-pyrimethamine samples be sent to the NQCL for dissolution testing, regardless of whether they passed or failed the screening test. As a result, the quality assurance program has increased the number of products tested at the central laboratory.

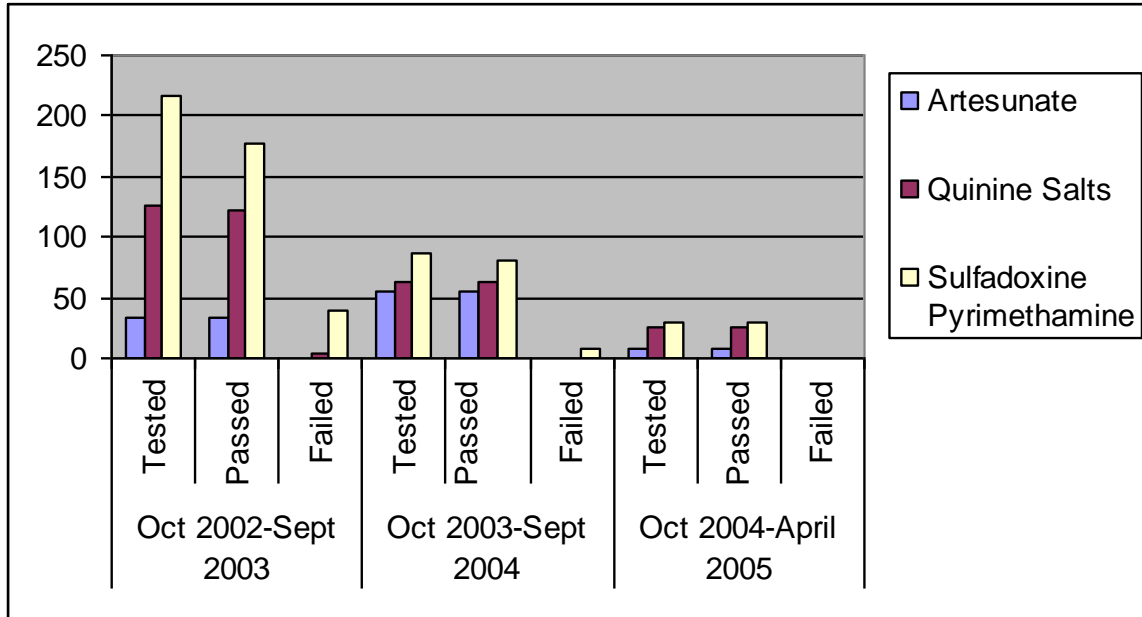


Figure 5. Antimalarial samples screened with the Minilab and tested at the NQCL (October 2002–April 2005)

In addition, the number of target drugs, which initially included only antimalarial medicines, has been expanded to include selected antibiotics and ARV drugs. These samples were screened with the Minilab. The number of batches of each drug category tested is shown in figures 5-7.

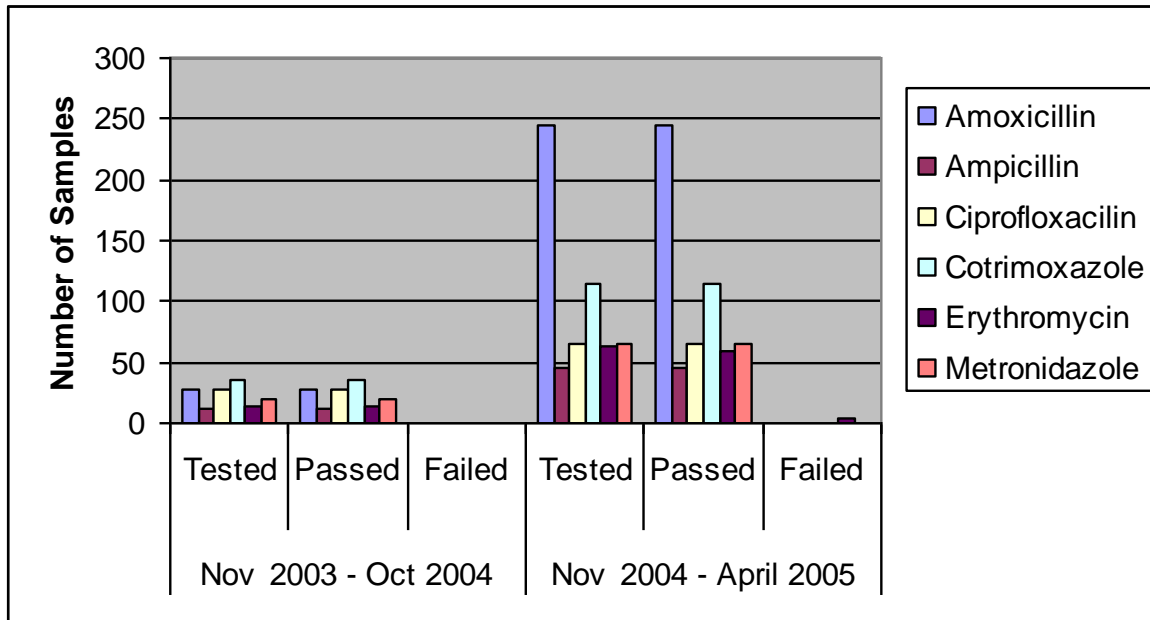


Figure 6. Antibiotic samples screened with the Minilab (November 2003–April 2005)

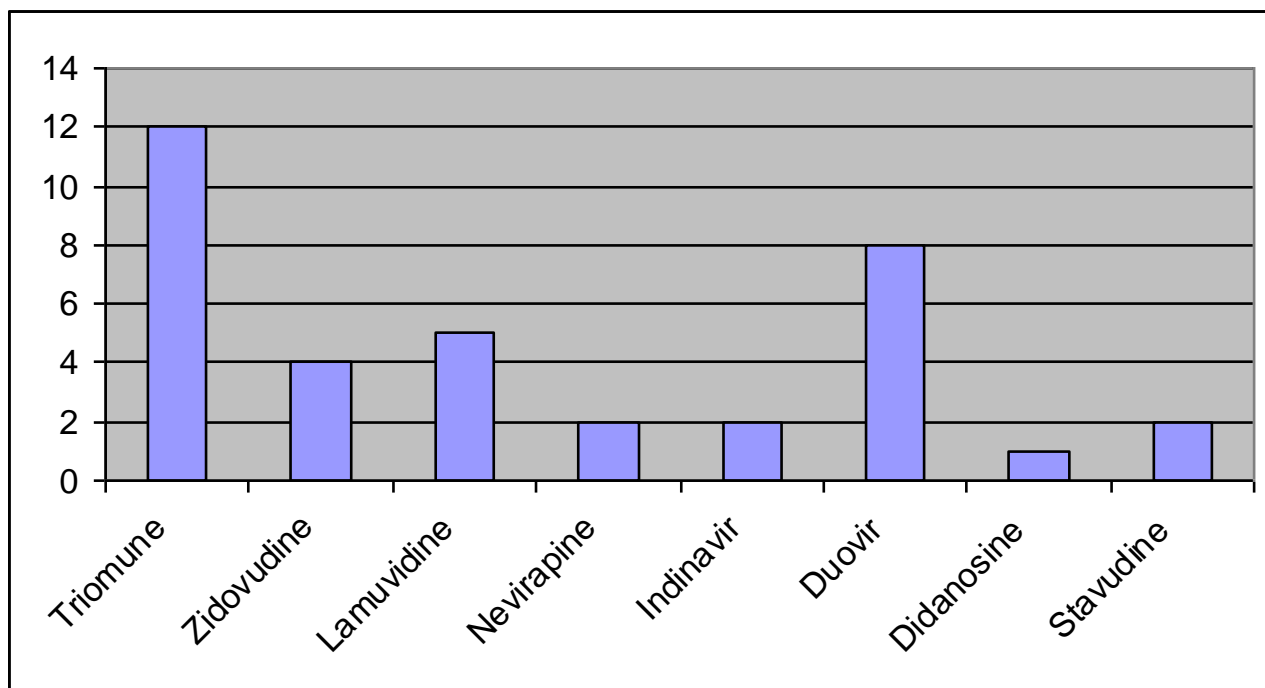


Figure 7. ARV Samples Screened with the Minilab (March 2005–April 2005)

Table 3 shows examples of enforcement actions that TFDA has taken as a result of the surveillance inspections.

Table 3. POE and Market Surveillance Inspections Result: Compliance Action

- A consignment of ciprofloxacin tablets failed physical examination and was re-exported.
- Nineteen small consignments illegally imported by unauthorized petty traders/individuals were confiscated.
- A consignment of magnesium trisilicate from an unregistered manufacturer was confiscated.
- Three donation consignments with expired drugs were confiscated.
- Osteocalcium tablets failed physical examination and were confiscated and destroyed.
- Unlicensed petty trader importing drugs illegally and storing them at unregistered premises resulted in confiscation.
- Unregistered drugs stocked in pharmacies and Part II drug shops were confiscated.
- Unauthorized products stocked in Part II drug shops were confiscated.
- Banned veterinary drugs stocked in Part II drug shops were confiscated.
- At least 10 batches of imported and locally manufactured antimalarial drugs worth millions of shillings were destroyed or refused entry into the country, while others were recalled from shelves because they were of poor quality

PDA Inspection Data Logging System

Because the data captured in the PDAs can be downloaded directly into a Microsoft Access database, report writing has been streamlined and data retrievals are much simpler to carry out. In addition, there are no transcription errors in transferring the inspectional data into the TFDA

databases. The primary determinant of the results of inspectors using PDAs is the inspectors themselves. Initially, some inspectors embraced the new technology and experienced remarkably improved efficiency; others have been hesitant to change from manual methods. However, with time and TFDA management encouragement, the hesitant inspectors who were slow learners have become more comfortable with PDA usage.

Regular PDA use for inspection has generally improved inspectors' efficiency—based on a review of records, inspection time has been reduced by 20–30 percent and has eliminated the need for inspectors to prepare weekly reports, resulting in a net time savings of 30–40 percent. The ability to download the data collected on the PDAs into the central database has reduced data entry time by over 90 percent, compared with manual entry of the data from written forms. In addition, data entry review has been reduced to occasional instances when the database administrator is prompted to check by the system.

Monthly report preparation time has also been reduced by over 90 percent; all of the data and statistics are compiled by the database, and the user needs only to print the correct report. As an additional benefit, all inspectors have up-to-date reference tables of all approved drug products, approved manufacturers, and approved importers. Future additional data will include the approved dispensary shops and their locations.

QA Program Lessons Learned

Pharmaceutical Inspection Program

- Obtaining political support, working closely with stakeholders, and sensitizing them to quality requirements helped establish the quality assurance program.
- Improving efficiencies in inspections and screening have allowed relatively few inspectors to conduct a large number of inspections.
- The QA program has given inspectors additional confidence in knowing what they are doing and how they are contributing.
- The quality assurance activities were conducted with relatively modest resources, but have markedly increased the visibility and presence of the TFDA in the marketplace, providing a significant deterrent to marketing substandard and counterfeit products.
- Pharmacies in zones where inspectors have been active had a better level of compliance.
- The inspection processes have improved standards, resulting in many product confiscations, importation refusals, and premises closures.

PDA Inspection Data Logging System

- Obtain buy-in from management so that they get involved with and ultimately own the project from the planning to the implementation stage.
- Assure that an adequate and dedicated central information technology resource is in place to—
 - Maintain the database
 - Manage upload/download of data
 - Create reports as needed by management
- A structured inspection process should already exist consisting of supporting laws and regulations, a regulatory decision tree, flow charts, and forms guiding the process.
- Carefully validate the electronic versus paper surveys results before rolling out the new electronic system.
- Limit the data included into the survey forms to what is necessary for inspectors to make a pass/fail decision and for what managers need for planning and compliance decision-making.
- Make the technology user friendly by including menu options that
 - Minimize the number of steps to enter data
 - Pop-up lists that display in order of frequency rather than alphabetically
 - Allow the maximum number of fields to appear on screen
- It is important for all inspectors to switch to the PDA system at the same time. Because some TFDA inspectors were reticent about adopting the PDAs at first, the information was split between paper and electronic systems until everyone caught up.

Minilab-Based Drugs Screening Program

- Through the Minilab screening tests of over 1,200 samples primarily from the POEs, three quinine and two erythromycin samples were found to be counterfeit with no active ingredient. It is of interest to note that no markedly substandard products have been observed in the screening of these legitimate market samples. These observations provide evidence that the upstream compliance activities of registration, record inspection, and physical examination are properly functioning and reflect the improved quality of marketed products when compared to SEAM baseline studies. The enforcement of this universe of activity including registration, inspection, physical examination, product screening, and laboratory testing provide a significant deterrent to marketing illegal products which improves the market for legitimate conscientious manufacturers and distributors.
- It is important to include proficiency testing in the Minilab implementation plan to provide an added measure of confidence in these screening tests and to identify additional training needs or other interventions to assure quality performance.

- The TFDA needs to ensure that they have procedures in place to give feedback on the results of the screening tests on sample drugs to the supplier/importer.
- Despite high volumes and pressure at ports of entry, introducing Minilab-based product screening has not caused unnecessary delays in clearing legitimate products for entry into the market.
- Using the Minilab to screen products in the field is cost-effective—needing an average of 1.5 hours per sample; 1,200 samples over a 2.5-year period required only about one person-year of work time.

	QA Initiative		<i>Question 1: What are the 5 (or less if you can't think of 5) key lessons learned from implementation of the QA initiative?</i>	<i>Question 2: What are the 5 (or less if you can't think of 5) most important contributions or impacts that the QA initiative has had on health care delivery and public health?</i>	<i>Question 3: What are the 5 (or less if you can't think of 5) most pressing continuing needs/problems in relation to the QA initiative that need to be addressed for roll-out and/or sustainability?</i>
Initiative Participants			Answers	Answers	Answers
I	Thomas Layloff	I	This initiative has had strong and continuing support from the MOH and CMO and thereby the TFDA. It has been their initiative with our support. The program development built around their laws and regulations and hammered out with headquarters management and field staff was very successful in gaining buy in on all sides. This kind of support is essential in building sustainable government organizations.	I believe the most important contribution was formalizing and ordering the inspection processes and building on that through training and sustained review a more robust, disciplined, and confident regulatory infrastructure. This includes the tightening of registration, inspection, physical examination, and screening-testing into an integrated structure to assure product quality.	There needs to be a major review of resource allocations and work planning. There are a lot of compliance activities which need to be addressed like keeping pressure on the part II shops. Having sales personnel in shops determining therapeutic options is probably a major hazard in the society.
		2	QA is critical in this business and the TFDA should have been encouraged sooner to launch the proficiency testing.	The formalized and structured inspection process has improved the compliance of importers to the proforma invoice requirements which has improved the TFDA income. At the QA session a rep from Shelys [a pharmaceutical company] noted that they had tightened their release testing to reduce the likelihood of inferior product moving out.	At the meeting I asked the lab technician how long it would take to analyze one paracetamol tablet at the lab. She noted perhaps several hours. I asked if that included standard calibration and she said no. I asked if the HPLC column was available and she said no. I asked how much one would cost and how long it would take to obtain one. She noted it would cost 100-400 USD for the column and one to three months to get it. I asked how long it would take to run the tablet by TLC with a standard and she noted about one hour and that all the supplies were readily available. Linking the current TLC screening methods to densitometric determination would be a very big help in the lab operations. That same technology could also be used to support other analytical needs in the TFDA. The field TLC screening operations processed over 1,200 samples at

Quality Assurance Program Activities, Outcomes, and Tools

				about 1.5 hrs per sample over the ten quarters since launch (one FTE). The personnel costs for that system is about 180 hours per quarter. The process caught five samples which were fake--three quinine and two erythromycin and reported no substandard products. The proficiency test showed in the first case that all inspectors could identify a sample with zero content and almost all failed to identify a 60% containing sample as being subpotent. There is a confidence visual discerning break between 0-60%; would they have caught 20, 30, 40, 50%? The performance qualification test needs more work also.	
		3	Product testing is the only definitive statement on quality and this needs some review. There are 14 people in the lab and only one operating HPLC which severely limits the analytical throughput. The lab resources probably should have been included in the building but there was reluctance in the TFDA to go through the lab.	The import firewall has improved, thus reducing the flow of inferior, outdated, or unregistered products entering the market.	I believe there is a significant amount of terminal sterilization being conducted in some hospitals and that the processes are not likely to be in control.
		4		The premises inspections has reduced the amount of unregistered, illegal (part 1 in part 2), and unregistered outlets.	The TFDA and WHO have committed to place minilabs in the 22 Regional Hospitals. This implementation will pose a large logistic and QA challenge which will require a build in the central QA efforts. This includes also continuing to build the zonal structures to manage this business.
		5		The aura of effective consumer protection has improved (at least subjectively). One person commented that people are coming from Malawi to purchase drugs in TZ because they feel the products are better. This reverses that person's previous observation. Also the Kenyans have come to look at the TFDA system as an emulation	The central and likely regional-district registration databases (goods and outlets) need to be updated and maintained so the domains of legal and illegal activities can be differentiated by inspectors in the field. Without the updated data the inspectors will lose confidence and commitment and the rollout momentum will be weakened.

Developing a Pharmaceutical Product Quality Assurance Program in Tanzania: Strategies for Enhancing Access to Medicines Program Final Report

				model.	
2	Peter Risha	1	A committed DRA with enabling and sound policy/regulations is need to be present	Structured inspection with clearly outlined decision trees, enabled inspectors and stakeholders know what is expected of them, thus improving voluntary compliance	Financial and manpower resources
		2	Need to build political will, involvement and sensitization of stakeholders is necessary for the success of the initiative	Inspection coupled to Minilab screening procedures provided a deterrent	Management commitment and involvement, providing supervisions
		3	Other components of the drug product quality dimensions (e.g., registration and reliable testing) need to be in place to augment the success of the program	Increased coverage and frequency of POE inspections, have contributed to increased revenue for the DRA from the import fees, enabling the TFDA to cover for the costs involved in the implementation of the program	Improvement in the IT resources
		4	Monitoring and evaluation and periodic reviews of progress should be build into the implementation plan		Provide for possibility of holding review meetings between management and field inspectors to review progress identify obstacles bring everyone involved to same page
		5	Build into the M&E, tools that can clearly be used to evaluate the impact		Avoid overstretching, consolidate, review resource capability before expanding
3	Olympia Mbatia	1	Political support is needed to implement a program like this one, and a well administrative structure (i.e., starting from the Ministry of Health, DRA, provinces/regions and districts).	Well-structured inspection system developed and Screening of the drugs to some extent assisted in reducing substandard drugs circulating in the market thus promoting public health	There is a need to establish a well structured proficiency testing protocol

Quality Assurance Program Activities, Outcomes, and Tools

		2	Involvement of stakeholders is very important in most stages starting in development of inspection tools and training material and launching of the program and even during the evaluation time their presence could give us the picture on how the program was accepted and what value have added in their business.	The well structured inspection activities at ports of entry have increased awareness of manufacturer in testing their products and sometimes retesting to be sure of the quality before exportation.	To establish or decide on what is the tolerable limit when discussing on failure rate of medicine screened or test
		3	The technical assistance and equipment (minilab) did assist a lot in taking short time in starting implementing the program initiatives	Postmarketing surveillance have made many wholesalers to adhere to good distribution practice of pharmaceutical products. for example item of documentation especially recording keeping of imports, purchases and sales have improved tremendously compare before the launching of QA program	Measurement of unregistered drugs in market should in number of the unregistered products not on number of premises storing unregistered drugs
		4	Training and re-training is a fundamental aspects in the program in general	Local manufacturers have change a lot as most are now manufacturing to the accepted standards even though not all have been issued with GMP certificates but testing is done before release of finished product to the market.	Under-utilization of the screening centers and the PDA's
		5	Stages developed of the various category of activities on implementing the program were careful planned and a lot of commitment was observed to some key members	Medical stores department are depending on the screening done through QA program before distribution imported and local manufactured drugs. This indicates that they depend on the QA for ascertaining quality their drugs.	There is need to review Thin layer chromatograph method and developing methods for screening other products which are not included in minilab kit (e.g., some antimalarial drugs—metakelfin and amodiaquine etc.
		6			Management information system need to be set up
4	Zera Msuya	1	Sensitization of stakeholders on legal requirements regarding dealing in drugs greatly improved voluntary compliance	Created awareness to pharmaceutical dealers on what is required out of them	Manpower
		2	Having structured inspection system improves compliance in the market	Introduced structured drug inspection system	Financial support

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		3	Use of TLC enables screening of large number of samples at low cost	Reduction of substandard drugs in the market	Improvement of infrastructure
		4	Stationing of drug inspectors at POE greatly reduce entrance of substandard drugs hence eliminate unscrupulous dealers	Established Minilab screening system of some drugs	Improve IMS
		5	Trained inspectors are confident on their daily activities	Training of substantial number of inspectors and analysts on inspection and screening	Sufficient equipment and supplies