

Trip Report: Pharmaceutical Quality Control System in Ethiopia

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About RPM Plus

The Rational Pharmaceutical Management Plus (RPM Plus) Program, funded by the U.S. Agency for International Development works in more than 20 developing countries to provide technical assistance to strengthen drug and health commodity management systems. The program offers technical guidance and assists in strategy development and program implementation both in improving the availability of health commodities—pharmaceuticals, vaccines, supplies, and basic medical equipment—of assured quality for maternal and child health, HIV/AIDS, infectious diseases, and family planning and in promoting the appropriate use of health commodities in the public and private sectors.

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Acronyms

AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
ARV	antiretroviral
CQCL	Central Quality Control Laboratory
CI	Cooperazione Italiana
DACA	Drug Administration and Control Authority
EHNRI	Ethiopian Health and Nutrition Research Institute
GMP	Good Manufacturing Practice
HIV	human immunodeficiency virus
ISO	International Organization for Standardization
MSH	Management Sciences for Health
PHARMID	Pharmaceuticals and Medical Supplies Import and Wholesale Share Company (parastatal import and distribution company)
PMTCT	prevention of mother-to-child transmission
QC	quality control
RPM Plus	Rational Pharmaceutical Management Plus Program
TB	tuberculosis
USAID	U.S. Agency for International Development

Background

Rational Pharmaceutical Management Plus (RPM Plus) Program/Management Sciences for Health (MSH) is collaborating with USAID/Ethiopia in the provision of technical assistance in drug and related commodities management and antiretroviral (ARV) procurement for President's Mother and Child HIV Prevention Initiative (PMTCT) and the President's Emergency Plan for AIDS Relief (The Emergency Plan) in Ethiopia.

Under this effort, RPM Plus will assist in national, regional, district, and health facility-level capacity development for delivery of PMTCT/ antiretroviral therapy (ART) services and ensuring access to and rational use of basic PMTCT/ART products through various interventions including training, development of standard operating procedures, strengthening of infrastructure and promoting improved commodities procurement, management and inventory control systems.

The Administration and Control Authority (DACA) had several discussions with RPM Plus and made requests for assistance in the area of quality control.

Executive Summary

The Central Quality Control (QC), EPHARM manufacturing and Pharmicure QC laboratories were visited during a three day preliminary visit to Addis Ababa, Ethiopia to conduct a preliminary assessment of the sector with a plan to conduct a future in-depth assessment and recommend further technical assistance. Except Pharmacure, the other two QC laboratories visited had some inoperable and/or unused equipment. Few in process test samples were observed. The resources available at any given site except Pharmacure were not sufficient to provide training and support a reasonable analytical program. The Instrument Maintenance and Training Section of the Science and Technology Commission appears to be very underutilized even though there is a glaring need for an operating resource of this type.

The School of Pharmacy appears to be making progress and expressed interest in developing and presenting certificate training programs to improve analytical discipline and proper use and care of analytical instruments. This needs further exploration. If it appears feasible an advisory panel of “consumer” stakeholders could be formed to help define the attributes required for the certificate program.

The relationship between the Regional Health Bureaus and the national Drug Administration Control Authority (DACA) needs clarification and perhaps a more federal coordination on pharmaceutical quality issues. It is likely that the Minilabs could assist in product quality assessments. Addis Ababa appears to be the center of most drug activities with little manufacturing or direct import activity outside the capitol.

Activities and Elements Specified in the Scope of Work

1. Conduct preliminary review of the overall pharmaceutical quality assurance capacity of the central quality laboratory of DACA located at the Ethiopian Health and Nutrition Research Institute (EHNRI)

The Central Quality Control Laboratory (CQCL) has been reassigned from the EHNRI to the DACA. The range of analyses expected to be performed at the CQCL is very broad with emphasis on those areas funded by donors and assignments from the DACA and/or Ministry of Health. The laboratory is attempting to keep a testing inventory of drugs (pre-registration, complaint, and suspicious drugs and is planning to add routine post-market surveillance sample testing next year), pesticides (industrial and household for toxicity), cosmetics (skin irritation), traditional medicines, condoms (pressure and leak tests) and surgical gloves (leak test). They, in addition, would like to add vaccine testing.

With the current staffing level of 10 pharmacists, two microbiologists, two chemists, one chemical technician, three laboratory aides, five paramedical assistants, and one veterinarian it is unlikely that the CQCL could mount a good effort along all of these lines. The Cooperazione Italiana (CI) has assigned Dr. Andria, a pharmacologist, to assist the laboratory but no work of that type is planned there at this time. The Head of the laboratories has requested for more pertinent technical assistance and CI is planning to send for several months two or three pharmaceutical-analysis competent individuals to do hands-on side-by-side work on method validation. The DACA Registration Department designates the methods to be used in the validation and testing assessments whether compendial or other depending on what the submitting firm declares.

In addition to the shortage of trained staff to undertake the proposed analytical support functions, the array and amount of equipment available could not support all of the areas simultaneously even if the CQCL had sufficient reagent resources and certified analysts for each of the categories. The CQCL staff noted that they had supply problem for chemicals and instrument parts and needed training.

The CQCL laboratory needs a good management planning system to include the development of time modules required to perform analytical functions so they could rationally plan and prioritize their work in concert with their stakeholders. In addition the equipment resource has no depth; if one unit fails the entire operation of that system comes to a halt. At a minimum the equipment resource inventory should be expanded to include TLC with computerized densitometry. Densitometry-TLC is more robust than other chromatographic techniques and has a equivalent or higher throughput. However the other chromatographic techniques have greater resolving power and lower variance which may be required for impurity assessments and analyses in the shadow of the legal limit.

Instruments in the DQCL				
Instrument	#	Brand	Age	Comment
HPLC	1	Shimadzu	5 mos	OK
GC	1	Thermo-Finnegan	1 mos	Qualified but not yet in use.
UV-Vis	2	Gensys	2 yrs	OK
IR	1		2 yrs	Inoperable
Dissolution	1		2 yrs	OK
Balances	5		3 yrs +	Most operational
TLC Viewing Box	1			OK
Condom Pressure Test	4	Swedish	0 mos	Being qualified during visit.
Condom-Glove Leak Detector	1	Swedish	0 mos	Being qualified during visit.

I was told that the Standards Authority of Ethiopia also performs some testing on an overlapping inventory but I did not have an opportunity to visit that site on this trip.

2. Assess the human resource and equipment capacity to monitor the quality of locally produced and imported drugs with focus on products related to HIV, TB and malaria

If the CQCL focused all resources on drug testing and if additional equipment were supplied at approximately one HPLC per pharmacist and they were properly trained in the operation and maintenance of the equipment the CQCL could conduct the method qualifications in the marketing authorization application submissions and pre-market routine testing of finished dosage in addition to routine surveillance of the HIV, TB and malaria products. If the testing resources were expanded to include TLC with computerized densitometry the analytical throughput for assay, content uniformity and dissolution testing could be markedly increased with ca three to five analysts supporting the program.

3. Assess the potential of introducing mini-labs at regional health bureau level

Although there was not sufficient time available to visit a regional health bureau our experience in Tanzania has shown that pharmacists and pharmaceutical technicians can be trained readily to successfully perform the product quality assessments in the Minilab.

4. Visit the central laboratory at EHNRI, the quality control unit of the School of Pharmacy, a couple of pharmaceutical plants in Addis Ababa and a regional health bureau

Because of scheduling problems visits to the quality control unit of the School of Pharmacy, and a regional health bureau could not be conducted.

Visit to the School of Pharmacy

The School of Pharmacy each year admits ca 80 students into their five-year BPharm program. They also have ca. 80 students in an evening diploma program which is equivalent to two-years full-time spread over five years (pharmaceutical technician program).

They are planning to expand their post-graduate programs to include Pharmaceutical Technology, Pharmaceutical Chemistry, Pharmacognosy, and Pharmaceutical Analysis.

The Dean would like to establish a sister-school relationship with a School of Pharmacy in the United States to exchange faculty and discuss program development. The establishment of the post-graduate and strengthening of their in-house programs is a defensive move since many students and faculty sent abroad to study frequently do not return to Ethiopia.

The Dean also has requested some senior Fulbright fellowships of three-four weeks duration for faculty visitors in Pharmaceutical Analysis, Clinical Pharmacology, Toxicology, etc.

Mr. Layloff discussed with the Dean his interest in establishing post-graduate certificate programs for laboratory analysts and laboratory supervisors—two programs which could include laboratory discipline, record-keeping, pharmaceutical analysis, ICH, International Organization for Standardization (ISO), care and maintenance of equipment and proper use, lab aspects of cGMPs, basic statistics, etc.

Visit to the Ethiopian Pharmaceutical Manufacturing Company (Epharm)

Dr. Negussu included a visit to the parastatal EPharm because it purportedly is known for its good QC and he serves on the Board of Directors. He is former Dean of the School of Pharmacy at AAU and is on the MSH staff. EPharm can produce eight dosage forms, has an inventory of 65 API (including two direct compressibles) and produces 42 finished formulations. Several of the lab instruments were inoperable because of bad installation, lack of repair parts or lack of manuals.

limited my visit to an informal walk-through and did not request to audit any of the records or probe their Good Manufacturing Practice (GMP) compliance status.

Visit to Pharmacure IV fluid Plant

This facility privately owned by Sheik Al-Amoudi¹, manufactures only terminally sterilized LVPs. The plant is a Swedish turn-key which was shipped in containerized modules. It is a two-year old state-of-the-art facility operating at 25% of capacity. They have been inspected by DACA and Zimbabwe regulatory officials. The firm has been approved by DACA and shortly will meet the compliance requirements of the Zimbabwe team—primarily challenge testing of air filtering systems. Pharmacure has had problems marketing in Ethiopia because tender limitations.

I limited my visit to an informal walk-through and did not request to audit any of the records or probe their GMP compliance status.

5. Brief USAID and DACA on findings and next steps

Because of major ARV meetings with AIDS concerned groups including CDC, Ministry of Health and MSH staff members in another city no briefing was conducted.

¹ Sheik Al Amoudi is an enterprising Yemeni-Ethiopian who made a large fortune working in Saudi Arabia and Sweden. He is revered in Ethiopia for his philanthropic activities and his numerous enterprises including also the five+ star Sheraton Hotel.

Other Related Activities and Elements

Visit to the “Instrument Maintenance and Training Section,” Science and Technical Commission

During the laboratory tours, visits and informal discussions exposed the lack of resources to maintain the laboratory equipment and provide training on the proper use on an ongoing basis. A facility already existed and arrangements were made for a visit.

It was explained that the staff level for the section was 124 persons but the staffing table (below) which was compiled from queries during the visit totals only 33 so there may be other significant operations underway or else there was a misunderstanding. The physical plant appeared to be large enough to have an operating staff level of 124 including the test equipment. They also are supposed to have a program underway to inventory all of the items used in the hospitals and health centers in Addis Ababa to build an inventory of repair manuals to help repair the instruments when they are down, but a copy of that inventory was not available. Little activity was observed at this relatively spacious site. Perhaps privatizing the organization or making it a parastatal function would invigorate the organization.

Department	Engineers	Technicians	Other
Electromechanical	5	3	
Chemical-Biomedical	6	2	
Nuclear and Radiation	4	1	
Glassblowing			4
Training*	8		
*The training department is divided into four units which correspond to the operating units			

Visit to the Drug Administration Control Authority

The Drug Authority Control Administration (DACA) has 129 staff-75% of whom have technical backgrounds, including Pharmacists, MDs, DVMs, Chemists, Biologists and Agronomists. Their authority includes regulation of drugs, medical supplies, medical instruments, cosmetics, pesticides, etc. They prepare standards and specifications for regulated products and premises from POE to outlets and license all premises and evaluate and register all regulated products. They also handle narcotics and psychotropic (licit) drugs and traditional medicines.

There are four technical departments in DACA:

- Drug Quality Control and Toxicology
- Drug Control and Abuse Prevention (includes inspection and licensing)
- Drug Evaluation and Registration
- Planning, Drug Information, Establishment and Distributor

It is estimated that 80% of drug products and API/excipients used in Ethiopia are imported from China, Egypt and India. Domestic imports are made primarily through Addis Ababa with some containers coming from the Port of Djibouti for trans-shipment to Addis. The drug industry is focused in Addis, except one in Tigrai.

Epharm supplies 10-15% of the Ethiopia drug market.

PHARMID, a government import and distribution parastatal handles 70-80% of the drugs used in Ethiopia.

It appears that following the overthrow of the socialist Derg controlled government in 1991 that the pharmaceutical market went into a free-expansion mode. The table below roughly outlines how the market has expanded.

	1994	2004
Retail Outlets	800	2500*
Importers	9	60
Wholesale Distributors		80
Manufacturers	1	13
Registered Drugs	80	150

The central office of DACA is planning to establish three regional DACA branches separate from the current regional structure. There currently are 11 semi-autonomous regions in Ethiopia with Regional Health Bureaus which independently conduct inspections, licensing of retail outlets, etc., and perform health inspections in their respective regions. They consist of nine ethnically-based states (kililoch, singular - kilil) and two self-governing administrations* (astedaderoch, singular - astedader); Adis Abeba* (Addis Ababa), Afar, Amara (Amhara), Binshangul Gumuz, Dire Dawa*, Gambela Hizboch (Gambela Peoples), Hareri Hizb (Harari People), Oromiya (Oromia), Sumale (Somali), Tigrai, Ye Debub Biheroch Bihereeseboch na Hizboch (Southern Nations, Nationalites and Peoples).