Global AIDS Program
International Laboratory Branch

Building Sustainable Integrated Laboratory Capacity In PEPFAR Countries

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention

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A personal Welcome From CDC Gap Director Dr. Deborah Birx

Dear Colleagues,

In 2006 the Centers for Disease Control and Prevention (CDC) Global AIDS Program formed the GAP International Laboratory Branch (ILB) with a recognition that laboratory capacity serves as a vital foundation not only for every activity we do to fight HIV/AIDS – prevention, care, and treatment – but also as a component of strong, sustainable global public health systems.

In 2007, the ILB achieved the prestigious College of American Pathologists (CAP) accreditation. The branch, which serves as an international reference and model for laboratory programs worldwide, went down in history as the first set of CDC laboratories to achieve CAP accreditation. The ILB is now setting the standard for laboratory quality, having joined the world's largest association composed exclusively of pathologists and widely considered the leader in laboratory quality assurance.

In January 2008, the ILB brought to bear its critical leadership in laboratory systems strengthening, gathering together a total of 120 experts and policy makers from 33 countries in Maputo, Mozambique to address building sustainable, integrated national laboratory strategic plans in order to deliver quality services for universal access to HIV/AIDS, TB and malaria prevention, care and treatment services.

As a part of the President's Emergency Plan for AIDS Relief (PEPFAR), the ILB is spearheading the development of these national plans, which address cross-cutting lab issues, including training, logistics and commodities management, and facility and equipment maintenance. These plans reduce parallel disease-specific lab systems, building efficiency and augmenting nations' ability to respond effectively to multiple life-threatening diseases.

In May 2009, President Obama announced a new Global Health Initiative, which aims to scale up U.S. global health programs over the next six years under a new comprehensive U.S. strategy that includes PEPFAR, but also addresses other critical global health issues, such as maternal and child health and neglected tropical diseases. As a part of this initiative, CDC will be able to leverage the work the ILB has done in supporting sustainable, integrated laboratory services and systems as an integral part of the overall health system, embracing an approach that focuses on strengthening recognized key elements that cut across diseases.

It is with pleasure that I offer you this overview of the ILB and its areas of expertise and offerings for technical assistance that are helping resource-poor nations build sustainable and integrated laboratory networks as a critical and core component of overall health systems.

I am sure that you will find the information useful as we work together to implement exciting new initiatives to build sustainable public health systems around the world.

Sincerely,

Deborah Birx, MD
Director, HHS/CDC Global AIDS Program

Introduction

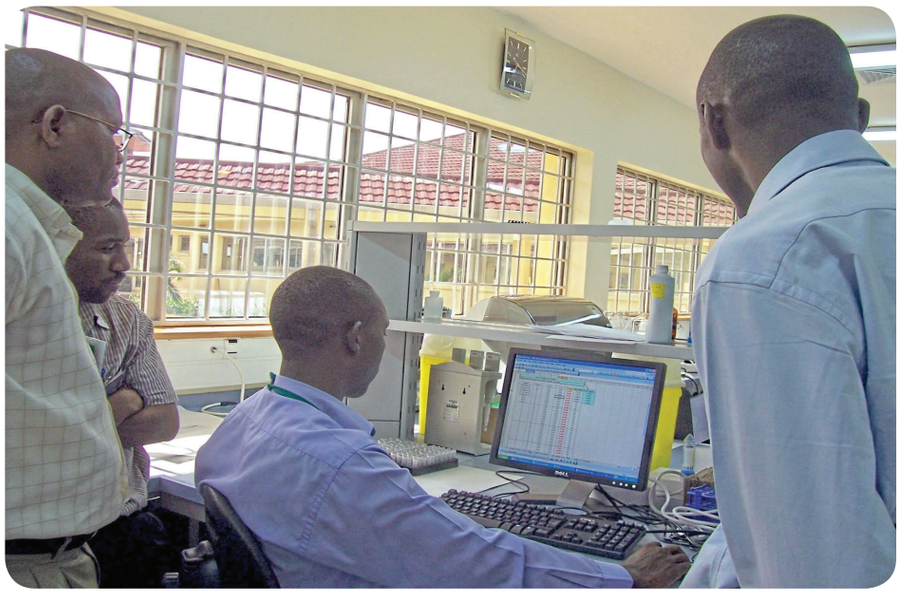
The CDC Global AIDS Program and the International Laboratory Branch

The Global AIDS Program (GAP), through the President's Emergency Plan for AIDS Relief (PEPFAR), supports over 70 countries, bringing to bear the technical expertise gained from CDC's more than 60 year history as the premier U.S. agency for disease control and prevention. CDC's long-standing partnerships with Ministries of Health (MoH) assist with improvement of critical infrastructure and services to build sustainable national public health capacity.

In 2003, the United States Government (USG) launched PEPFAR, an interagency initiative to provide $15 billion over five years to fund care, treatment and prevention services in 15 countries that were hardest hit by the HIV/AIDS epidemic. Emergency rapid scale-up of HIV/AIDS prevention, care and treatment programs and developing laboratory infrastructure to support the services became the intense focus in resource-limited settings. On July 30, 2008, PEPFAR was reauthorized with a budget of up to $48 billion over five years to combat HIV/AIDS, tuberculosis, and malaria, with a continued emphasis on laboratory system strengthening and improved diagnostic laboratory capabilities.

Accurate and reliable clinical laboratory testing is an important component of a public health approach to disease management in resource-limited settings. Laboratory data are essential for clinicians to accurately assess the status of patients' health, make accurate diagnoses, formulate treatment plans, and subsequently monitor the effects of treatment. Clinicians must be able to trust that the test results from the laboratory are accurate, reliable, and timely in order to use them for clinical diagnosis and treatment. The establishment of quality laboratory services is critical to building a strong and sustainable health system.

Prior to PEPFAR, CDC strengthened laboratory infrastructure in host countries by using a "top-down" approach which concentrated on strengthening the national reference laboratory, or main laboratory in the host nation, and establishing partnerships with regional laboratories. With the inception of PEPFAR, CDC broadened its scope and began activities to improve capacity at all levels of a tiered laboratory system: national, provincial, district, and primary care. The activities helped PEPFAR to reach its initial set of ambitious goals: treatment for 2 million HIV-infected people, prevention of 7 million new infections, and care for 10 million people infected with, or affected by, HIV/AIDS. The new 10-year goals aim to increase the number of those treated to 3 million, the number of infections prevented to 12 million, and the number of people receiving care to 12 million.



Kenya - Early Infant Diagnosis (EID) training

The Work of the International Laboratory Branch

GAP's International Laboratory Branch (ILB) was established in 2006 to take the leadership role in developing sustainable, integrated quality laboratory services for all PEPFAR countries by working closely with Ministries of Health, CDC's other international laboratory programs, WHO and The Clinton Foundation.

Staff consults with Supply Chain Management Systems (SCMS), the procurement consortium created by PEPFAR, on all technical aspects of laboratory supply purchasing and standardization. The branch also conducts operational research to enhance the implementation of PEPFAR programs in test evaluations, incidence testing validation, infant diagnostics by polymerase chain reaction (PCR) testing, and ART drug resistance testing.

The ILB staff works to build and strengthen laboratory capacity in PEPFAR countries by serving as liaisons to countries. The laboratory liaisons work directly with MoH and other relevant partners to provide advice, strategic planning, and technical support in the following areas:

- Laboratory management
- Staff training
- Supplies and equipment
- Infrastructure (buildings)
- New technology
- Quality and reliability of laboratory data/test results
- Strategic planning for national laboratory systems

The International Lab Branch consists of four teams: Serology/Diagnostic Incidence, Molecular Monitoring, Clinical and Opportunistic Infection (OI) Monitoring, and Systems Strengthening. The Office of the Branch Chief provides coordination and guidance for all four teams.

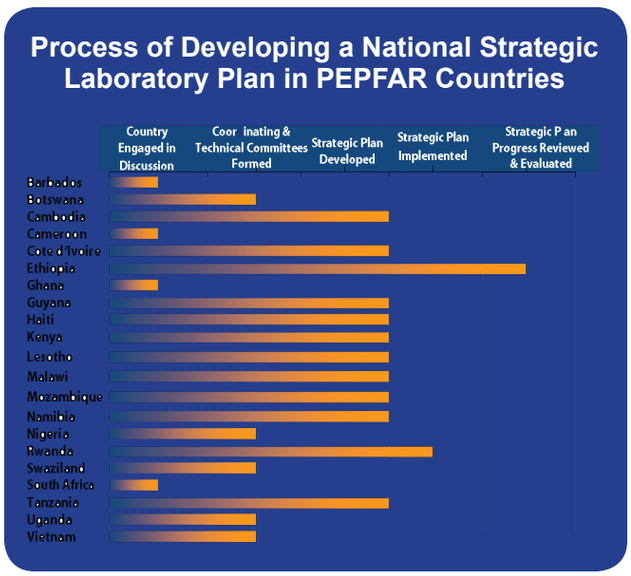
Building Laboratory Capacity

The conditions in the existing laboratory facilities in each PEPFAR country vary widely. The ILB brings expertise and resources to move each country along a continuum of quality improvement. A national laboratory assessment is performed in each country. The assessment includes site visits and preparation of a comprehensive report.

Individual laboratories are then prepared to be enrolled in an ongoing quality program.

Evaluation of the laboratory's capabilities includes retesting samples and troubleshooting the staff's methods. Improvements are scheduled, which may include building renovation (lighting, air flow, water, and electricity), equipment purchase, and staff training. Finally, each laboratory is enrolled in an external proficiency training program whereby an independent national body conducts retesting of specimens at regular intervals. At present, only South Africa has this type of national program, and the other countries look to CDC or laboratories in other countries to fulfill this need. Additional external proficiency training programs are under development on the African sub-continent.

CDC's vision for global health is that countries receiving support today will be able to stand on their own tomorrow. The ILB is working to improve laboratory services in the PEPFAR countries so that they can run independently. One of the most important planning exercises that the ILB conducts in partnership with local MoH is the development of National Strategic Laboratory Plans. The following chart shows the progress in this important area since 2006.



Office of the Branch Chief

The Office of the Branch Chief provides management oversight, administrative, budgetary, and supply procurement services to the GAP International Laboratory Branch. In addition, the office oversees relationships with a number of committees and partners that contribute to the advisory and leadership role that the branch performs for the PEPFAR countries.

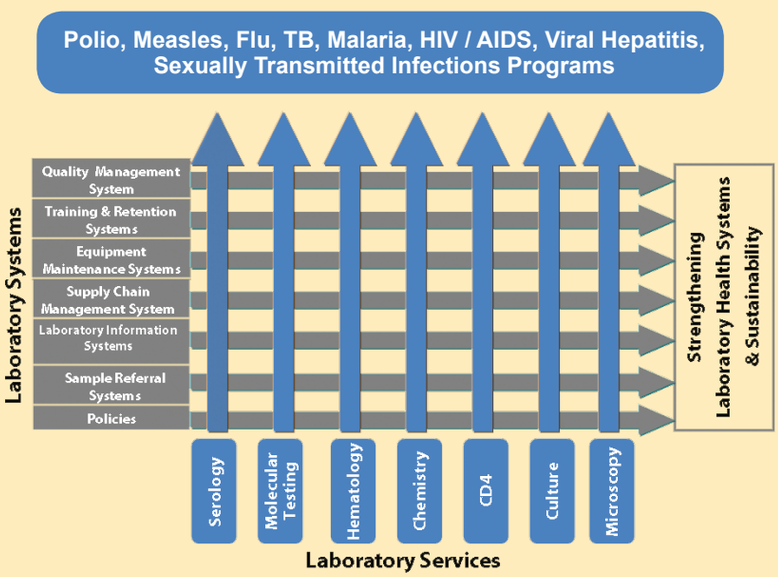
Branch Chief
John Nkengasong, PhD

The work of the International Laboratory Branch consists of improving the laboratory systems in PEPFAR - supported countries by training, inspecting, building, negotiating, advocating and organizing to move them along a continuum of steady improvement towards well-functioning, fully accredited laboratories. The establishment of these strong systems is a prerequisite to delivering quality services.

Seven Systems: Quality Management - Training & Retention - Equipment Maintenance Supply Chain Management - Laboratory Information - Sample Referral - Policies

The figure below illustrates the relationship between Laboratory Systems (left) and Laboratory Services (bottom). A solid base of well-functioning systems cuts across and impacts all laboratory services. The services, when properly supported, can attain the high quality level necessary to provide reliable testing to health care professionals who diagnose and treat multiple endemic, chronic, emerging, and re-emerging diseases.

It is the improvement of these seven systems in the PEPFAR - supported countries, in the national reference laboratories, at the provincial levels, and right down to district laboratories providing basic testing in rural communities, which is at the core of the ***mission*** of the International Laboratory Branch. As the team works to improve these laboratory systems, they are guided by the ***vision*** of creating sustainable systems which the host country can eventually manage on its own.



Laboratory Technical Working Group (LTWG)

The LTWG is a group of approximately 30 scientists and professionals drawn predominately from the staff of the International Laboratory Branch. The LTWG also includes members from USAID, Office of the Global AIDS Coordinator (OGAC), GAP Care and Treatment Branch, and the FDA. The group meets quarterly. Its main function is to **provide guidance on laboratory programs to PEPFAR programs.** The LTWG goals are:

- **One US Government (USG) response:** LTWG works with USG PEPFAR country teams to plan technical assistance activities in host countries.
- **Laboratory Quality Management System:** LTWG is the advocate for reliability and quality in testing practices, commodities, and equipment.
- **Integrated Response:** LTWG brings together laboratory experts, countries, and international organizations to discuss critical issues and establish consensus on practices and policies.
- **Strategic Direction:** LTWG provides guidance on strategies to implement quality standards, program implementation, and policy development.
- **Technical Assistance:** LTWG teams coordinate onsite in-country visits in accordance with work plans.
- **Technical Reviews:** LTWG members assess laboratory activities and plans in country operating plans (COP) and review laboratory-related technical documents, papers, and abstracts.

The group has organized subcommittees in the following areas:

- Accreditation
- HIV diagnostics
- Laboratory commodities
- Laboratory information systems
- Molecular diagnostics
- Patient monitoring
- Policy/strategic plans
- TB/opportunistic infections
- Training

LTWG Priority Areas for Fiscal Year '08–'09

- Development of national policies and strategic plans to create sustainable tiered laboratory services and integrated referral networks with uniform quality assurance measures.
- Establishment of a regional training center for Southern Africa.
- Implementation of best practices for quality systems management and development of standards for laboratory accreditation, focusing on quality assurance for HIV and TB and opportunistic infection diagnostics and monitoring.
- Coordination of laboratory training to support PEPFAR program goals.
- Support of a unified approach to manufacturers, vendors, and partners for procurement and distribution of laboratory commodities.

Laboratory Technical Liaisons

Members of the ILB are assigned to serve as liaisons to GAP country programs. Their mission is to improve coordination of laboratory activities within a country both across program areas and between the field and GAP headquarters in Atlanta. Each country has been assigned at least one liaison from the branch. In some cases, depending on country needs, a second CDC liaison has been assigned from a center other than GAP. [See Appendix for current assignments.]

The GAP laboratory liaisons are available to perform the following functions for their assigned countries:

- Provide laboratory technical assistance and work with the technical coordinator of the individual country management team to coordinate with the PEPFAR core teams.
- Promote integration of laboratory issues and activities into relevant prevention, care, treatment and strategic information programs.
- Provide regular updates to the branch chief about the country's progress and ongoing projects.

Expertise on Call—Cooperative Agreements (COAG) Managed by ILB

To assure that professional expertise is available to help build and improve laboratory infrastructure and operations in PEPFAR countries, the ILB has entered into multiple-year cooperative agreements (COAG) with the four leading American professional associations for laboratory science. The associations provide qualified consultants (physicians, pathologists, microbiologists, laboratorians) from their active membership base (total members for all four exceeds 129,000) to support PEPFAR goals and activities. These associations are a repository of expertise, information, and industry standards. The associations write and distribute guidelines for best practices in medical laboratory testing, convene international meetings on laboratory standards, and publish peer-reviewed journals for the life sciences. The ILB's COAG deliver well-qualified consultants and ongoing access to information to health officials in PEPFAR countries.

ILB Cooperative Agreement Partners

- **Association of Public Health Laboratories (APHL)**
- **American Society for Clinical Pathology (ASCP)**
- **Clinical Laboratory Standards Institute (CLSI)**
- **American Society for Microbiology (ASM)**

These are non-profit professional associations organized for educational, scientific and charitable purposes. Through them, ILB has access to top talent to advise the PEPFAR countries.

The consultants retained through the partners perform the following tasks in PEPFAR countries:

APHL Members—Specialized Expertise

- National strategic planning
- Improvement of the infrastructure for laboratory referral networks
- Laboratory management training
- Development of laboratory management systems
- Training of senior laboratory staff and the formation of local public health laboratory associations
- Formation of local public health laboratory associations.

ASM Members—Specialized Expertise

- Enhancement of services for TB and other opportunistic infections
- In-service training for basic microscopy
- Planning and procurement of laboratory equipment necessary for basic microscopy, TB culture, and drug resistance training
- Assistance with strategic planning for laboratory services
- Standardization of clinical microbiology protocols on a national scale
- Expansion of quality assurance measures (retesting of samples) at national, regional and local levels

ASCP Members—Specialized Expertise

- Service training for clinical hematology and chemistry tests
- Development of a Train-the-Trainer program to rapidly expand service training capabilities and ensure sustainability
- Strategic Planning for Public Health laboratory services
- Development of national standards for accreditation

CLSI Members—Specialized Expertise

- Alignment of countries' national practices with international standards for laboratory accreditation
- Development of standard operating procedures and written policies for laboratories
- Establishment of national norms at the local and regional levels by targeting necessary improvements in training, record keeping, specimen handling, and laboratory management

The Work of the Partners

The following table illustrates the breadth and scope of the work the consultants perform in PEPFAR countries.

	APHL	ASCP	ASM	CLSI
Laboratory Networks	◆	◆		
Laboratory Information Systems	◆			◆
Certification and Accreditation		◆	◆	◆
Pre-Service Training		◆	◆	◆
In-service Training	◆	◆	◆	
Microbiology and Opportunistic Infections		◆	◆	◆
Standardized Protocols		◆	◆	◆
Laboratory Management Training	◆	◆		
Chemistry and Hematology		◆	◆	
Molecular Diagnostics	◆		◆	◆
CD4 Monitoring	◆	◆		
Quality Assurance	◆	◆	◆	◆
Inventory Management	◆		◆	◆
Specimen Management and Transfer	◆		◆	◆
Drug Resistance	◆		◆	◆

Note: ◆ = Lead ◆ = Support

The funds awarded to the COAG partners are regarded as "seed money" provided by the ILB to allow the consultants to travel to the countries initially and establish relationships within host nation MoH and national laboratory systems. Once consultants begin working on a specific project for a country, money is generally set aside for them in the country's COP. An "Exit Plan" calls for the creation of a sustainable national laboratory system run by each host nation, and further consultant involvement would be only to provide technical assistance.

Associate Director for Science (ADS)

The ADS works with the Branch Chief to coordinate operational research within the branch, and collaborates with the GAP Science Office on review of laboratory protocols, abstracts, manuscripts and Public Health Evaluations (PHE's). In conjunction with colleagues in other GAP branches, the ADS creates or identifies the appropriate interface for PHE's between Laboratory and the Epidemiology, Care & Treatment and Prevention branches. The ADS also represents Laboratory in OGAC's PHE committee and works with lab directors in PEPFAR countries to coordinate operational research in field sites.

Conferences

The Office of the Branch Chief serves as the organizer or co-organizer of meetings and conferences related to the work of the branch.

Recent conferences included:

- Laboratory Harmonization and Standardization Conference, Maputo, Mozambique, January 21–25, 2008.
- Lab Advisors Meeting, March 29-31, 2009, Kampala, Uganda
- Early Infant Diagnosis Conference, Atlanta, Georgia, May 22–23, 2008
- Strengthening Laboratory Management: A Program to Accelerate PHL Capacity Building/ Accreditation, July 27-29, 2009, Kigali, Rwanda

ASCP staff conducting Basic Laboratory Operations Training in Lesotho.

(L to R) Mrs. Martha Papashane, Principal Laboratory Technologist at Queen Elizabeth II Hospital, Maseru, Lesotho; middle: Barbara McKinney, ASCP trainer; right: workshop participant

APHL members provide specialized expertise in national strategic planning and various laboratory training needs *Photo: APHL*

Serology/Incidence and Diagnostic Team

The Serology/Incidence and Diagnostic Team provides technical assistance and training in HIV diagnostic and incidence testing. The team evaluates rapid HIV test kits, performs rapid test kit training in the field, engages in HIV incidence testing, and carries out operational research on tests used to diagnose HIV or detect new HIV infections. The Serology/Incidence Team shares its members' knowledge and expertise by traveling to PEPFAR countries to advise governments or perform training. Team members also attend meetings, host visitors who stay from one week to three months in Atlanta, Georgia, for training in the labs, assist with in-country Country Operational Plan (COP) preparation and when invited, perform in-country lab assessments.

From August 1, 2007—August 1, 2008, the team logged 18 technical assistance visits, representing 225 person-days.

Team Lead-
Bharat Parekh,
PhD

The Team Supports GAP Activities

Expertise and technical assistance provided by the Serology/Incidence and Diagnostic Team is critical for the work of multiple program activities. There are many examples. Prevention efforts rely on accurate, rapid results so that clients can obtain test results and receive counseling and referrals on the day of their visit. Care and treatment programs count on accurate diagnosis to ensure that the right individuals are referred for treatment. Blood safety programs depend on accurate HIV testing to ensure that contaminated blood does not enter the blood supply. Surveillance of HIV provides valuable information about the state of the epidemic at the population level and the team's contributions in the areas of HIV serology and incidence testing are critically important to this effort. Data obtained from surveillance work assist PEPFAR country teams and host nation MoH in directing resources to appropriate populations to reduce the transmission of HIV-1.

Rapid Test Kits in the Diagnosis of HIV Infection

HIV diagnosis can be performed very efficiently using rapid test kits. The rapid tests provide results in 15–30 minutes and are ideal in resource-poor environments; most are stable at room temperature requiring no refrigeration. They are simple and easy to use and require no complex equipment. Tests can be performed by non-laboratory personnel with proper training; they use whole blood taken from a finger prick and are cost-effective. The use of rapid tests allows expansion of HIV testing and makes HIV diagnosis widely accessible. Rapid tests, in combination with appropriate counseling, are important in all PEPFAR countries for prevention and care and treatment.

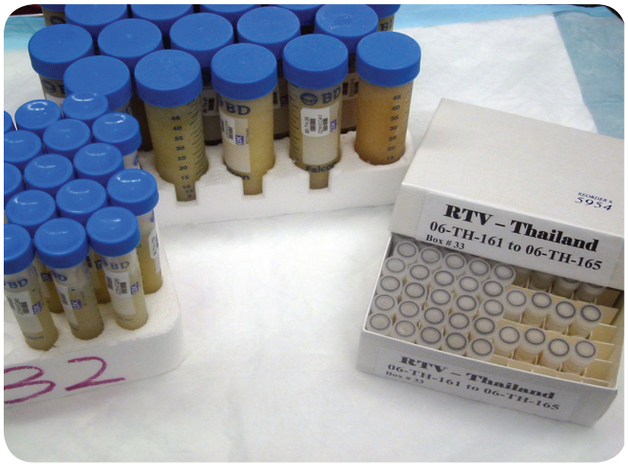
Evaluation of Rapid HIV Test Kits

As a first step to ensure the quality of HIV testing, the Serology/Incidence and Diagnostic Team evaluates new rapid HIV test kits using a standardized, molecularly diverse panel of HIV positive and negative specimens at CDC's laboratories in Atlanta. Only those tests which meet minimum requirements are recommended for possible use in PEPFAR countries. This activity, conducted in collaboration with USAID, ensures that the test kits of poor quality are not used in PEPFAR programs. In the past 2 years, the team has evaluated more than 25 test kits, and approved 12 of them.

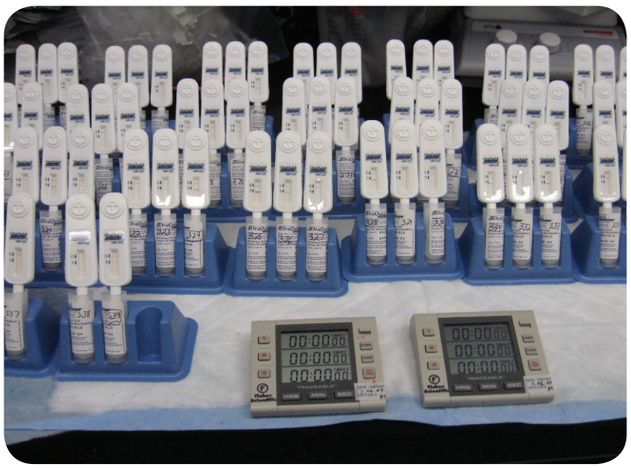
Instruction package developed by the Serology/Incidence and Diagnostic Team and the World Health Organization

Rapid HIV Test Training

While rapid HIV tests are simple to use, the counselors, nurses, or other lay professionals who do the testing in the field must take a training course to establish their proficiency. Training is designed to teach correct use of the test so that the result is accurate and that proper safety precautions are followed to protect counselor and patient.



The team evaluates rapid HIV test kits for use in PEPFAR countries

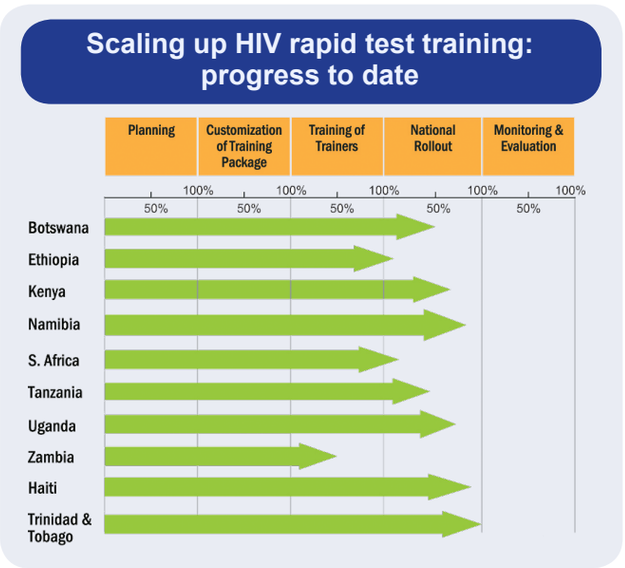


OraQuick Rapid Test Kits

Hetal Patel and Juliana Anyanwu check sample integrity and prepare to store them for later use

Dr. Xin Liu conducts rapid HIV test training for laboratorians

Members of the Serology/Incidence and Diagnostic Team, in partnership with the ILB training leader, provide training courses in PEPFAR countries. The courses are aimed at developing a cadre of competent trainers who train others and thus expand the testing program in each country. The team collaborated with the World Health Organization (WHO) in writing a comprehensive training package to standardize the course content. Team members customize the training package to meet the needs of each country where they work. The team also receives about 20–30 International Laboratorians per year in Atlanta for rapid HIV test training and other quality assurance needs.



Quality Assurance

Ensuring the quality of HIV testing is important and can be very challenging in resource-poor countries. The team provides training in good laboratory practices and has developed a number of simple but practical tools, such as standardized logbooks and dried tube specimens for proficiency testing programs, to help monitor and improve the quality of testing. These new concepts are being piloted and expanded in many countries with the goal of documenting and improving the testing quality.

Surveillance and Incidence Testing

A critical component in the effort to reduce HIV transmission rates is the ability to identify where the highest rates of new infections are occurring so that prevention programs can be deployed most effectively.

It is now possible to distinguish between recent and long-term HIV infection, using a test called the **HIV-1 BED enzyme immunoassay**, developed by Dr. Bharat Parekh of the Serology/Incidence and Diagnostic Team. The test can be used on a positive sample to determine if the infection occurred recently (within approximately 6 months). The HIV-1 BED enzyme immunoassay results are then used to derive the rate of new infections.

Performing this test requires a laboratorian well-trained in the technique. Team members are frequently invited by MoH to conduct the training, which is carried out in conjunction with members of GAP's Epidemiology and Strategic Information (ESI) Branch. The HIV-1 BED incidence assay is currently used in more than 35 laboratories worldwide. The team continually provides training and assistance to countries that use the incidence assay and has initiated a proficiency testing program to monitor and improve quality of incidence testing.

Operational Research

The Serology/Incidence and Diagnostic Team is engaged in operational research to improve the efficiency, quality, and portability of tests used in diagnosing HIV. Among the current projects are:

- Use of dried tube specimens to facilitate an external quality assurance for proficiency testing program (a technology invented by the team)
- Use of oral fluid based rapid HIV tests to help expand counseling and testing
- Validation of the BED assay for incidence estimates
- Development of new incidence tests, including a rapid incidence-prevalence test

Dr. Bharat Parekh and Dr. Andrea Kim of GAP's ESI Branch provide technical assistance and attend a Symposium on the application of the BED assay in China

Molecular Monitoring Team

The Molecular Monitoring Team is composed of two units. The Early Infant Diagnosis Unit performs training in Early Infant Diagnosis (EID) of HIV infection, provides quality assurance of EID programs for over 21 countries, and conducts operational research to meet the needs of EID testing in resource-limited settings. The Drug Resistance Unit engages in training and laboratory capacity building for HIV drug resistance testing in PEPFAR countries. The group's operational research is focused on the development of testing products for use in resource-limited settings. The Drug Resistance Unit's laboratory is one of six in the world accredited by WHO ResNet as a Specialized Drug Resistance Laboratory (SDRL).

From August 1, 2007–August 1, 2008, team members engaged in 16 missions, representing 200 person-days, to PEPFAR countries to share their knowledge and expertise.

Team Lead-
Dennis
Ellenberger, PhD

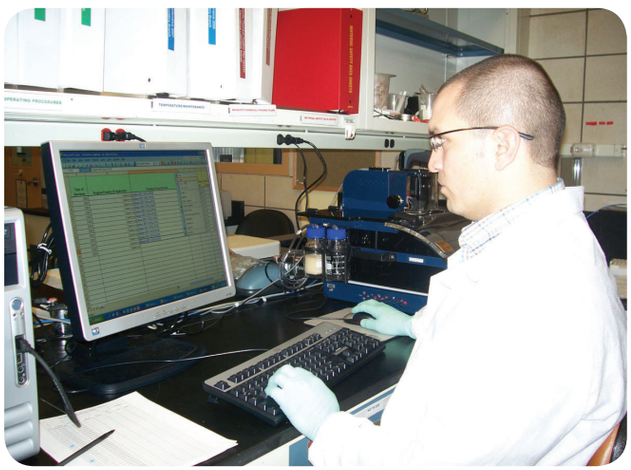
The Team Supports GAP Activities

The Molecular Monitoring Team supports the GAP Care and Treatment Branch's Prevention of Mother-to-Child HIV Transmission (PMTCT) program by making accurate, HIV diagnosis of infants available in PEPFAR countries. EID also provides essential data for PMTCT programs. This permits assessment of the program's impact and provides information for critical policy and program decisions. The Drug Resistance Unit monitors resistance to ART drug formulations, important both to the surveillance efforts of the GAP Epidemiology and Strategic Information Branch as well as the ART drug treatment programs of the Care and Treatment Branch.

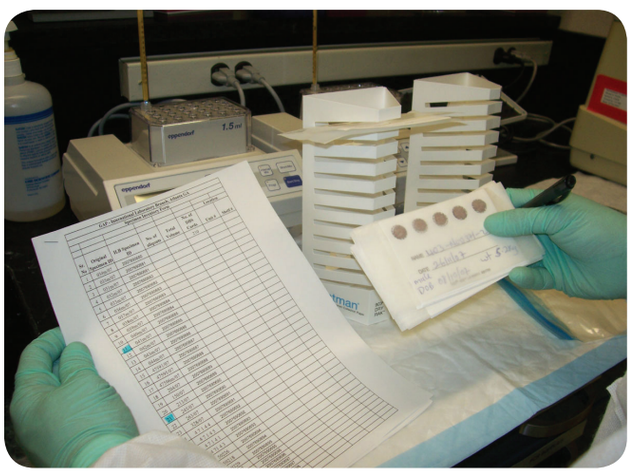
Early Infant Diagnosis and Viral Load Unit

Early diagnosis and treatment of HIV-infected infants are important goals of PEPFAR. The clinical course of HIV/AIDS is rapid in children, and early diagnosis is critical so that treatment can begin. If HIV infection is left unidentified and untreated, 50%–60% of HIV-infected infants die by age 2. Standard antibody tests (rapid HIV tests, ELISA) can only be used on children older than 15–18 months because the tests cannot distinguish between maternal and infant HIV antibodies in the child's blood. Nucleic acid (DNA) tests, however, can detect the viral nucleic acids indicating infection 4–6 weeks after exposure with nearly 100% accuracy, making nucleic acid tests the diagnostic tool of choice for infants more than 6 weeks of age.

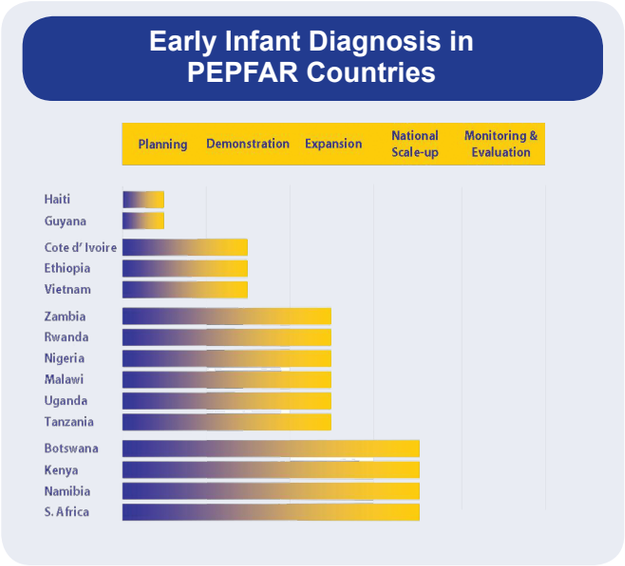
In an effort to expand access to infant testing, PEPFAR is promoting infant diagnosis through the use of dried blood spot (DBS) collection cards. A filter paper card is used for collection of a small amount of blood drawn



Albert Garcia processing DBS and recording data



Verification of DBS card with patient record



from the infant's heel. The card is then easily transported without the need for refrigeration to a laboratory for testing and storage. Use of the DBS eliminates the need for venipuncture to acquire the blood specimen, making it ideal for resource-limited areas. Additionally, DBS can be prepared in rural or remote areas and can be used wherever mothers are seen in clinics with their children for PMTCT counseling or well-child visits.

The EID Unit is working to make the PCR/DBS test available and accurate in all PEPFAR countries. To that end, team members are engaged in training, testing, and quality assurance (QA), as well as working with companies engaged in developing point-of-care technologies for HIV diagnosis.

- **Training:** The team conducts approximately six in-country training sessions each year. In addition, visiting scientists from PEPFAR countries are trained on the DBS-PCR protocol in CDC laboratories five to six times per year. By the end of 2008, laboratory staff in all PEPFAR countries had been trained to perform DBS-PCR. The team will continue to provide technical assistance on request.
- **Testing and external quality assurance:** To build quality assurance capacity in the PEPFAR countries, the team provides proficiency testing for 70 laboratories which are located in 21 countries. In-country laboratory staff is provided with panels to test for verification. Team members also perform laboratory site assessments that are combined with training workshops. The team also works with local MoH to bring regional reference laboratories up to speed with EID through DBS testing. Tanzania's National Quality Assurance and Training Center located in Dar es Salaam, Tanzania, and the African Centre for Integrated Laboratory Training located in South Africa have been strengthened by this activity.
- **Research:** The team's efforts are focused on bringing point-of-care testing to the patient. Research is focused on adapting tests for low-resource settings, assessing and validating new technologies, and finding ways to transport blood samples without refrigeration.

Drug Resistance Unit

A population-based public health approach and simplified, evidence-based standardized drug formulations appropriate for resource-limited settings have made antiretroviral therapy (ART) a reality for more than 2 million HIV-infected patients in PEPFAR countries. The simplified three-drug "cocktails" effectively suppress HIV viral replications in patients and delay development of HIV drug resistance. However, because HIV viruses mutate rapidly and continued medication is required throughout the patient's lifetime, HIV drug resistant viral strains emerge even if the best treatment practices are employed. Monitoring drug resistance in populations receiving ART and surveillance of those patients who are newly infected with drug-resistant viral strains are critical components in the prevention of the development of HIV drug resistance.

Dr. Karidia Diallo runs samples on the sequencer

Dr. Chunfu Yang demonstrates how to properly collect SampleTanker and dried blood spot specimens at a workshop held at the Gwagwalada Teaching Hospital in Nigeria.

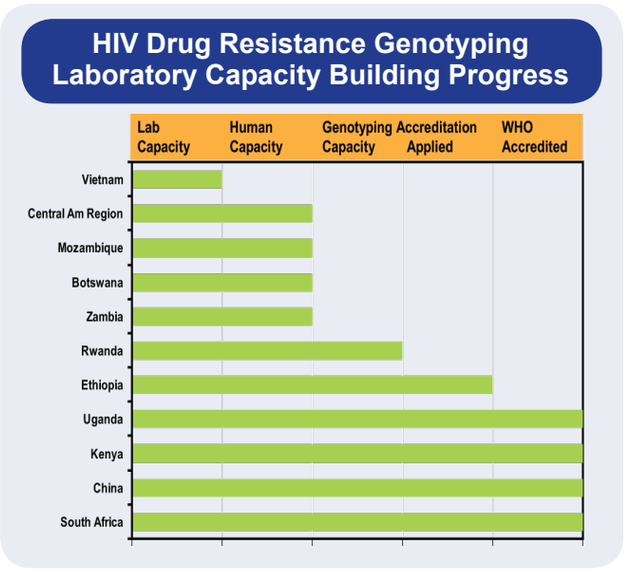
Resistance occurs at the viral genomic level. In order to identify mutations related to drug resistance, plasma, whole blood, or dried blood spot (DBS) specimens are collected from patients who are either receiving ART medication or are newly infected with HIV viruses. Viral RNA/DNA is extracted from the specimens, and the targeted fragment of HIV viral genome is amplified. The amplified product is sequenced in order to read its genetic code. Mutations related to drug resistance are identified by comparing the wild strain of HIV viral genome with the patient's HIV viral genome.

Local capacity building is a priority of the Drug Resistance Unit. The team works to implement the highly complex genotyping technologies available to PEPFAR countries and uses a quality system approach to make sure the test results are accurate. The team members have been engaged in the following activities:

- Training: Team members conduct drug resistance genotyping training upon request at the CDC in Atlanta or in the field. By year-end 2008, a total of 34 laboratory scientists from 11 PEPFAR countries had been trained using different genotyping platforms.
- Laboratory Accreditations: The team has worked closely with the WHO ResNet group to provide technical assistance to PEPFAR countries applying for WHO ResNet genotyping laboratory accreditation. HIV drug resistance genotyping laboratories in four PEPFAR countries (Kenya, Uganda, China and South Africa) have met the rigorous standards and been accredited; they now play a key role in HIV drug resistance surveillance and monitoring programs in their respective countries.
- Drug Resistance Training Package Development: The WHO ResNet Group and the Drug Resistance Unit are currently collaborating on the development of a training package designed to teach the selection of genotyping platforms, the use of a quality systems approach to ensure accuracy, the implementation of proper safety precautions and safe waste disposal.

The Drug Resistance Unit members actively conduct research to improve the genotyping quality of the tests and adapt them for use in resource-limited settings. The team has been engaged in:

- Development and application of a broadly-sensitive genotyping assay
- Evaluation of blood collection devices for use in the resource-limited settings found in PEPFAR countries
- Development of new drug resistance genotyping assays.



Clinical and Opportunistic Infections Monitoring Team

The Clinical and Opportunistic Infections Monitoring Team is composed of two units: the Clinical Monitoring Unit and the Tuberculosis (TB)/ Opportunistic Infections (OI) Unit. The Clinical Monitoring Unit improves the quality of hematology, clinical chemistry, and CD4 testing by evaluating laboratory equipment and providing training and technical assistance on quality improvements to laboratories in the PEPFAR countries. The TB/OI Unit provides training and technical assistance for TB smear microscopy, TB culture and drug susceptibility testing. The Clinical and Opportunistic Infections Monitoring Team members share their knowledge and expertise by frequently traveling to PEPFAR countries to advise governments, assess laboratories, and perform training.

From August 1, 2007 - August 1, 2008, team members engaged in 17 missions, representing 213 person-days.

Team Lead- Linda Parsons, PhD

The Team Supports GAP Activities

The Clinical and Opportunistic Infections Monitoring Team ensures the quality and availability of basic testing used for biomonitoring patients who are on antiretroviral therapy (ART) by working closely with the GAP Care and Treatment Branch. The team supports laboratories with technical assistance, training, and infrastructure improvements to diagnose TB and OI as well as drug-resistant strains of TB. The team collaborates with surveillance efforts by planning large-scale surveys for drug susceptibility testing in PEPFAR countries and aids in the surveillance of drug-resistant TB by performing molecular monitoring of drug-resistant TB strains. The Clinical and OI monitoring team specializes in the prevention of new cases of TB among laboratory workers by providing technical assistance on biosafety and infection control.

Before: Typical peripheral laboratory

After: Upgraded laboratory

Monitoring and ART

When ART is properly administered, it reduces the amount of HIV in a person's body. In addition to receiving appropriate treatment, HIV patients must be monitored to verify that the viral load in their blood stays low and to determine that the immune system is functioning well by measuring the CD4 count. Determining the approximate number of CD4 cells is also used to decide when an HIV-positive person should begin ART. Side effects from the medications are common, therefore hematologic, renal and hepatic functions are routinely monitored.

Clinical Monitoring Unit

In many PEPFAR countries, a substantial volume of blood testing is done for clinical monitoring of HIV-positive patients on ART. Samples of whole blood, serum, and plasma are collected and transported to laboratories where automated analyses can be performed on large quantities of samples, using specific instruments. Heat, humidity, power outages, water shortages, and poor building integrity are challenges to operating sensitive laboratory instruments in resource-poor environments. With PEPFAR support and technical assistance from the Clinical/OI Team, such challenges have been overcome in many locations.

CD4 Testing

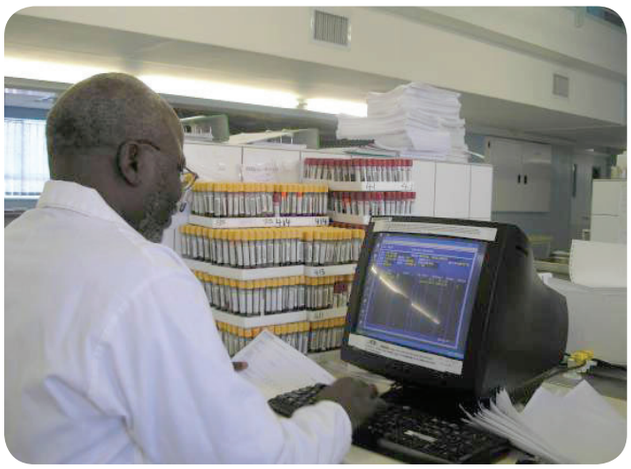
The CD4 test for patient monitoring is done on an instrument called a **flow cytometer.** The sample must be carefully prepared, and a trained laboratorian is required to perform the assay. The flow cytometer requires ongoing maintenance as well as daily calibration and use of controls each time tests are run. Before a new instrument can be placed into service, it must be validated by comparing results on the same samples tested on another instrument.

Team members travel to PEPFAR countries to assist with setup of new laboratories and are actively working with manufacturers at home and in the field to develop smaller CD4 testing machines for use in resource-poor conditions. At CDC laboratories in Atlanta, visitors receive training on use, calibration, and validation of these instruments.

Hematology and Clinical Chemistry

Blood tests performed on patient specimens to look for signs of toxicity during ART are run on a **blood chemistry analyzer,** which tests serum for signs of liver or kidney damage, and the **hematology analyzer,** which uses whole blood samples to check for anemia and signs of infection. These instruments also must be calibrated at installation and before each run and their results initially validated in the lab where they will be operated.

Checking CD4 count in blood samples



Entering test results into patient files

Tuberculosis/Opportunistic Infection (TB/OI) Unit

Tuberculosis and HIV

Mycobacterium tuberculosis (TB) causes one of the few HIV/AIDS-associated infections that can be spread to others just by breathing the same air. It is simple to acquire, as it is passed through the air in fine particles when an infected person coughs. A person who is infected with HIV is more susceptible to infection with TB than a person with a healthy immune response.

Of the roughly 38 million people infected worldwide with the HIV virus, as many as one-third are co-infected with TB. Over 85% of the worldwide HIV cases co-infected with TB are in sub-Saharan Africa. Without proper treatment, up to 10% of people who are HIV-infected die within months of contracting TB, making it the leading cause of death for people with HIV/AIDS in Africa.

Testing for TB

TB survives and multiplies primarily in the lungs. To test a patient for TB, a sputum sample must be collected, spread on a slide, stained, and checked under a microscope for the presence of the bacteria with

specific staining characteristics. This technique is called **acid-fast bacilli (AFB) smear microscopy** and it is the first step in diagnosis of TB.

Smear microscopy is inexpensive in terms of equipment required and is simple enough to be performed even in settings with rudimentary facilities. However, quality smear microscopy is still not readily available in areas of the world where the TB rate is high, and the distribution of microscopy facilities often does not match the distribution of the disease.

The TB/OI Unit provides training in smear microscopy, TB culture and drug susceptibility testing by presenting workshops using standardized training materials and procedures. The unit also plans for implementation of programs that will assure the quality of testing and provides technical assistance to laboratories that are upgrading their facilities.

In preparing laboratories to test for TB, the TB/OI Unit focuses on three main challenges:

- Creating a safe environment to protect the laboratory staff working with the specimens
- Ensuring that accurate and sensitive smear microscopy is performed at all sites throughout a country
- Training staff in the laboratory skills needed to safely and accurately culture TB in the laboratory to detect potential drug resistance: multi drug resistant (MDR TB) and extensively drug resistant (XDR TB).

Other diagnostic techniques for TB include tests at the molecular level to rapidly identify TB and ascertain if it is a drug-resistant strain. The Team's goal for each country is a fully functioning national laboratory system that can perform all of the tests reliably, quickly, and in proximity to the patients they are serving.

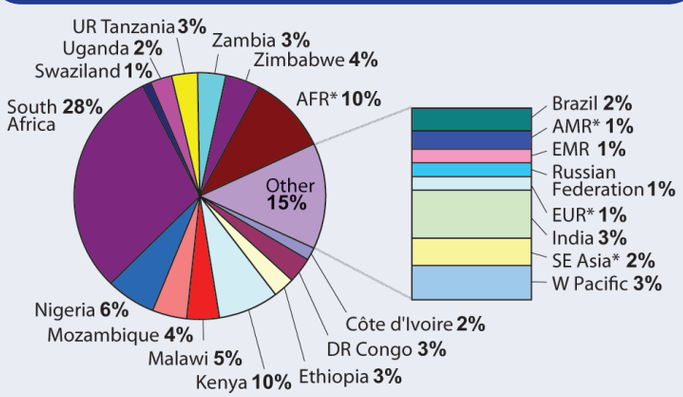
Opportunistic Infections

The many infections that the compromised immune system of an HIV/AIDS patient cannot fight effectively include meningitis, bacterial pneumonia, diarrheal diseases, malaria, and septicemia. Because laboratory assays to identify and differentiate these infections are varied and often not widely available, patients on ART are routinely treated with cotrimoxazole because it will eliminate most of the common opportunistic infections.

Operational Research

The Clinical and Opportunistic Infection Monitoring team works with instrument manufacturers to develop and validate new technology to improve the sensitivity of smear microscopy and molecular testing in CDC's Atlanta laboratories and in the field. The team also performs initial evaluation and validation of new technologies and reagents for CD4 testing useful in resource-poor environments, including field testing at appropriate sites in-country.

Geographical Distribution of Estimated HIV-Positive TB Cases, 2006



AFR* is all countries in the WHO African Region except those shown separately; AMR* excludes Brazil; EUR* excludes the Russian Federation; SEAR* excludes India.

Source: WHO Report 2008: Global TB Control

Systems Strengthening Team

A host of cross-cutting efforts support the work of all three teams within the International Laboratory Branch to provide systems-focused attention to strengthening PEPFAR laboratory activities. These activities cover quality assurance, training, equipment maintenance, laboratory information systems, the African Centre for Integrated Laboratory Training (ACILT), the public-private partnership, and in-country laboratory quality.

Team Lead- David Cross, MS

Quality Assurance

The branch runs five laboratories on CDC's Atlanta campus, all of which are involved in some level of external quality assurance and monitoring of laboratories in the PEPFAR countries in addition to conducting research. The quality assurance activity maintains and improves the quality management system that has been established at GAP headquarters and consults with in-country laboratories as invited.

Dr. Katy Yao concludes a week-long "Train-the-Trainer" workshop in Addis Ababa, Ethiopia.

Training

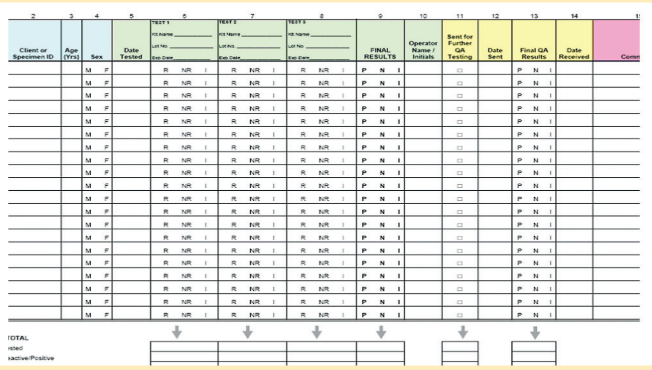
A training coordinator leads the branch, cooperative agreement partners, in-country partners, and MoH in their ongoing efforts to implement effective laboratory staff and counselor training programs. Advocacy, coaching, and consultation bring the partners effective, state-of-the-art methods that use recognized standards and processes for curriculum development, training rollout, and training of individuals who will train others. A successful, ongoing effort is rapid HIV testing training, which has benefited many PEPFAR countries by providing widespread access to fast and accurate diagnosis.

Equipment Maintenance

Robust, quality laboratory services depend upon both regular maintenance of equipment and timely delivery of supplies. Working through the logistical and climactic challenges inherent in providing these services in PEPFAR countries, ILB staff is currently exploring the use of modular and mobile labs for TB and HIV testing in the field, considering options for pilot partnerships to provide equipment maintenance, and working with SCMS (the procurement consortium created by PEPFAR) to improve and assure the purchase and distribution of lab supplies.

Laboratory Information Systems

A laboratory data coordinator works to develop standard methods of recording, organizing, and transmitting test result information for patient monitoring and population-based surveys and investigations for the PEPFAR countries. The technology method used is appropriate for each laboratory, whether it be on paper (log books) or in electronic formats.



Standardized log book for HIV testing.

African Centre for Integrated Laboratory Training

The training center located on the campus of the National Institute for Communicable Diseases (NICD) in Johannesburg, South Africa, started offering courses in 2008. It represents the fruitful collaboration between many institutions working to fight HIV/AIDS in sub-Saharan Africa. The African Centre for Integrated Laboratory Training (ACILT) provides hands-on training to laboratorians to build skills in diagnosis and monitoring of infectious diseases such as TB, HIV, and malaria.

The African Centre for Integrated Laboratory Training (ACILT) is located on the South Africa National Health Laboratory Service Campus in Johannesburg

Dr. Linda Parsons presents a certificate at the end of a training session

USG-PEPFAR Public Private Partnership with Becton Dickinson

This non-commercial venture is a five-year commitment, launched in 2007, between the Office of the Global AIDS Coordinator and Becton, Dickinson (BD) to strengthen laboratory systems in eight countries severely affected by the HIV/AIDS pandemic. With the ILB's guidance, BD has successfully developed partnerships with Ministries of Health and local and international organizations in Uganda, South Africa, Mozambique and Ethiopia; it has worked with 81 labs in Uganda to improve the quality of CD4 testing, used GPS technology to strengthen the specimen referral system for TB in Uganda, provided training for laboratorians from sub-saharan Africa in detection and idenfication of Mycobacterium Tuberculosis at the ACILT facility, consulted on phlebotomy and specimen management in Mozambique and initiated planning for pre-service capacity building and specimen referral in Ethopia.

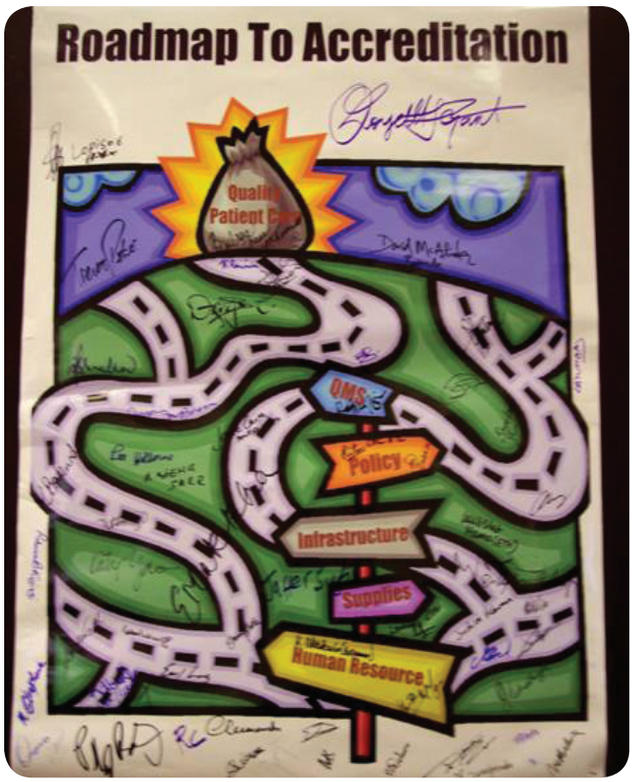
Becton Dickinson and ILB staff collaborate on training: workshop participants from Nigeria and Ethiopia watch as specimens are logged in before processing for TB culture.

In-Country Laboratory Quality

Country staff assist with planning, initiating, designing, coordinating, and conducting external quality assurance programs. The activity involves assessing laboratories in countries, training professionals at MoH to assess their own countries' laboratories, establishing standards, and arranging for external partners to provide ongoing quality assessment through retesting of samples. Staff is actively collaborating with WHO-AFRO to introduce a stepwise approach to laboratory accreditation in African countries.

The Kigali Launch targets PEPFAR II Laboratory Indicators

The July 2008 reauthorization of PEPFAR included a new requirement for reporting on specific indicators of progress related to Laboratory: number of labs supported and number of labs accredited. The number of laboratories accredited is a key indicator used to measure progress made in strengthening laboratory systems in developing countries. The successful Kigali meeting, attended by 120 experts and policy makers from twelve countries introduced a blueprint of the path toward accreditation, it obtained key stakeholders' support for accreditation and it showcased a task-based, training program designed to make accreditation a reality using a stepwise method.



Participants at the Kigali launch meeting pledged their support and commitment to moving their countries' laboratories toward accreditation by signing the poster "Roadmap to Accreditation"

L to R: Lady Elizabeth Okonkwo, Medical Laboratory Science Council, Nigeria; Dr Thérèse Nkoa, Cameroon MoH; Dr. Judith Shang, CDC-Cameroon; Dr. Mireille Kalou, GAP/ILB; Dr. John Nkengasong, GAP/ILB; Dr. Madeleine Mbangue, Hospital Laquintini, Cameroon; Henry Mbah, Laboratory Services, FHI/GHAIN Project, Nigeria and Dr. Patrick Njukeng, University of Dschang, Cameroon.

Participants from MoH, CDC and partners in-country eagerly pose for a photo with one of several themed posters developed for the meeting to launch the tools to support WHO-AFRO's lab accreditation scheme in Kigali, Rwanda (July 27-29, 2009) This meeting, organized by the ILB, was jointly hosted by WHO-AFRO and the ILB, in partnership with The American Society for Clinical Pathology and The Clinton Foundation.

Poster "Laboratory Professionals Make a Difference!" from the Kigali launch meeting, July 27-29, 2009