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Building Laboratory Capacity in Support of HIV/AIDS Care Programs in Resource-limited Countries

Report from a Global AIDS Program Meeting
December 16 and 17, 2003
Atlanta, Georgia

Centers for Disease Control and Prevention
Department of Health and Human Services

Abbreviations

AFB	Acid-fast bacteria
AIDS	Acquired Immunodeficiency Syndrome
ALT	Alanine Transaminase
AMREF	African Medical and Research Foundation
ANC	Antenatal Clinic
APHL	Association of Public Health Laboratories
ARV	Anti retroviral
ASCP	American Society for Clinical Pathology
ASM	American Society for Microbiology
BD	Becton-Dickinson
CAREC	Caribbean Regional Epidemiology Center
CBC	Complete Blood Count
CDC	Centers for Disease Control and Prevention
CT	Chlamydia trachomatis
DASTLR	Division of AIDS, STD, and TB Laboratory Research
DBS	Dried blood spot
DFID	Department for International Development (UK)
DLS	Division of Laboratory Systems
DST	Drug Susceptibility Testing
EIA	Enzyme Immunoassay
EQA	External Quality Assessment
FM	Fluorescent Microscopy
GAP	Global AIDS Program
GC	Gonococcus
GTZ	Gersellschaft für Technische Zusammenarbeit (German Technical Cooperation)
GUD	Genital Ulcer Disease
HgB	Hemoglobin
HHS	Department of Health and Human Services
HIV	Human immunodeficiency virus
HRSA	Health Services and Resources Administration
HSV	Herpes simplex virus
ID	Identification
I-Tech	International Training & Education Center on HIV
IUATLD	International Union against TB and Lung Diseases
JICA	Japan International Cooperation Agency
K+	Potassium
MIC	Minimum Inhibitory Concentration
MTB	Multi-drug resistant Tuberculosis
NCCLS	National Committee for Clinical Laboratory Standards
NCEH	National Center for Environmental Health
NCHSTP	National Center for HIV, STD, and TB Prevention
NGO	Non-governmental Organization
NHLS	National Health Laboratory Service
NICD	South African National Institute for Communicable Diseases
NIH	National Institutes of Health
NVP	Nevirapine
PCR	Polymerase Chain Reaction
PEPFAR	Presidents Emergency Plan for AIDS Relief
PHPPO	Public Health Practice Program Office
PMTCT	Prevention of Mother to Child Transmission
PMTCT+	Prevention of Mother to Child Transmission plus Care
QA	Quality Assurance

QC	Quality Control
RPR	Rapid Plasma Reagin
SOP	Standard Operating Procedure
STI	Sexually Transmitted Infection
TA	Technical Assistance
TB	Tuberculosis
TPHA	Treponema Pallidum Hemagglutination Assay
TPPA	Microhemaglutination Trep - Pallidum
TV	Trichomonas vaginalis
UNAIDS	The Joint United Nations Programme on HIV/AIDS
USAID	United States Agency for International Development
UTAP	Universities Technical Assistance Project
VCT	Voluntary Counseling and Testing
WHO	World Health Organization
WHO-AFRO	World Health Organization – Africa Regional Office
ZN	Ziehl-Neelsen

Building Laboratory Capacity in Support of HIV/AIDS Care Programs in Resource-limited Countries

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1. Background

The urgency of the need to respond to the global HIV/AIDS epidemic has resulted in a series of major initiatives to expand HIV care and prevention services to persons living in countries with limited resources. These initiatives include:

- The President's initiative for preventing mother-to-child transmission (PMTCT) of HIV. This initiative is intended to reach 1 million women annually, and to reduce by 40% mother-to-child HIV transmission among women treated.
- The President's Emergency Program for AIDS Relief (The Emergency Plan). This program has as a goal the prevention of 7 million new HIV infections. It also provides the means for HIV/AIDS treatment to 2 million HIV-infected people living in targeted countries.
- The WHO 3 X 5 Initiative. Under this plan anti-retroviral treatment will be provided to 3 million AIDS patients by 2005.
- The Global Fund aims at supporting national programs in the fight against HIV/AIDS.

The successful implementation of these initiatives will require a significant strengthening and expansion of laboratory services and infrastructure in targeted countries. Diagnostic services provided by laboratories are essential to most prevention, care, and treatment activities. The services must be accessible, provided in a timely fashion, and results must be accurate and reliable for programs to succeed. A considerable effort is needed to improve laboratory systems to meet immediate care and treatment program needs. Coordination of these efforts will require the focused attention of laboratory experts and their partners who provide care.

A vital step in strengthening the capacity of laboratories to adequately respond to these important initiatives is the development of comprehensive recommendations. This document is the report of a planning retreat held December 16-17, 2003 convened by the Department of Health and Human Services, Centers for Disease Control and Prevention. Participants included HHS/CDC-Global AIDS Program (GAP) personnel and those providing laboratory support to GAP country programs: the Division of Laboratory Systems (DLS), PHPPO; the Division of AIDS, STD, and TB Laboratory Research (DASTLR), NCHSTP; the Newborn Screening Program, NCEH; the Association of Public Health Laboratories (APHL); the Universities Technical Assistance Projects (UTAP) – represented by Harvard Medical School; University of North Carolina, Chapel Hill; University of Medicine and Dentistry New Jersey; and University of Maryland. Also participating were representatives from USAID, the WHO Regional Office for Africa, WHO headquarters in Geneva, and NIH.

Participants were charged with developing a detailed roadmap for providing quality laboratory support to meet the objectives of expanding HIV/AIDS prevention and care activities in resource-limited countries. In addition, the group was asked to formulate a strategy for sharing this strategic plan with relevant authorities, advocating the plan's adoption, and elaborating a strategy for timely and rational implementation of laboratory activities. Specific objectives were:

- to develop a clear strategy for introducing and supporting quality basic laboratory services to HIV/AIDS care and prevention programs in a timely manner, in resource-limited countries;
- to review and prioritize the spectrum of laboratory technologies available to adequately respond to the different components of HIV/AIDS care and prevention programs; and
- to develop a clear strategy for rapid scale-up of laboratory support to programs as they expand services.

Most of the work in the retreat was accomplished in five small workgroup sessions. Each group was asked to review and prioritize current technologies and make recommendations on critical activities that should be accomplished and products that need to be developed during the first year. They were then asked to provide guidance for the expansion of services beyond the first year. In addition, they were asked to identify partner organizations and institutions with comparative advantages to support the recommendations made. The small work groups were as follows:

- HIV Diagnostics: Expanding access to HIV testing, especially for ANC, VCT, pediatric diagnosis, PMTCT/PMTCT+, and blood safety

- Basic Laboratory Support for HIV Care and Prevention Services (Hematology, Chemistries) and Information Technologies

- Monitoring AIDS Patient Therapy – CD4, viral load, and drug resistance

- Laboratory-Based Diagnosis of Common Co-Infections, Including Malaria

- Laboratory Support to STI services; TB Diagnosis and Monitoring

2. Summary of the workgroup discussions and recommendations

The work groups began by describing the laboratory diagnostic services that are needed for the effective implementation of prevention, care, and treatment programs. Some of these services must be available at or near the point of care, while others can be referred to a central location in order to achieve efficiency and needed quality. The following is a list of minimum services needed in order to adequately support AIDS care and treatment programs, as well as prevention efforts. These are divided into central laboratories (national references laboratories, national public health laboratories, large teaching hospitals and other large centrally-located laboratories) intermediate laboratories

(regional hospitals, mid-sized care centers), and peripheral laboratories (district hospitals, primary hospitals, smaller care centers, more rural locations).

Central laboratories

HIV rapid testing and EIA	Creatinine
CD4 (high-end flow cytometer)	Potassium
Western blot	Full serum chemistries
Viral load	Culture and susceptibility testing
Hemoglobin	MTB culture
Pregnancy test	Microscopy: wet mount, stool,
Urinalysis	Gram stain, malaria, TB
CBC and differential	Quantitative RPR
Platelet count	GC culture
Coagulation tests	ALT

Intermediate laboratories

HIV rapid testing and EIA	ALT
CD4 (FACSCount)	Creatinine
Hemoglobin	Potassium
Pregnancy testing	Microscopy: wet mount, Gram stain,
Urinalysis	Tzanck, Giemsa, TB, malaria
CBC and differential	MTB culture
Platelet count	Syphilis rapid tests and
Coagulation tests	TPPA/TPHA

Peripheral laboratories

HIV rapid testing and EIA	Creatinine
CD4 manual counts*	Potassium
Hemoglobin	Syphilis serology - RPR
Urinalysis	Sputum collection
CBC and differential	Smear microscopy
ALT	

* Alternatively, transport specimen or patient to intermediate laboratory.

In many countries targeted by The Emergency Plan, current laboratory services fall short of these minimum needs. In order to provide the necessary level of laboratory testing, and to do so in a way that ensures accurate and reliable results, a number of actions were recommended. Each target country needs a national laboratory assessment and a carefully formulated strategic plan. This plan should address the specific situation and needs of the country and will be needed to promote in-country capacity building. The plan will provide an ongoing coordination of effort of all partners, and will provide a framework for advocacy and partnerships at the country level. Areas to address should include:

- **Personnel needs**. Lack of sufficient numbers of well-trained laboratory scientists is of major concern. Attention must be given to both pre-service and in-service training, and a plan for recruitment and retention, to include actions for long term is very important. Policies are needed to deal with issues such as certification, training requirements, and necessary qualifications for personnel performing tests (especially important for HIV rapid testing). Laboratory leadership must be both supported and developed.
- **Guidelines and consensus protocols.** Partners such as WHO and CDC need to work together to develop guidelines in all of the major technical areas. These guidelines are needed for preparation of standard operating procedures and to provide guidance for quality assurance practices. These should involve a consensus process.
- **Monitoring and evaluation** are essential to ensure ongoing accuracy and reliability. Checklists and assessment tools must be developed for in-country use.
- **Supply management.** This is often a difficult problem in the countries targeted in the HIV/AIDS initiatives. However, the timely availability of needed equipment, supplies, and reagents is critical to provision of laboratory support. Methods to provide and maintain necessary equipment must be improved. A system for dependable and sustainable acquisition of high quality reagents and supplies is needed.
- **Data management.** In targeted countries most data handling systems are manual and paper-based. If well organized and managed, these systems can be accurate and reliable, but standardized forms, reporting methods, and record keeping policies are needed in order to achieve this. Where possible, simple computerized systems that can be maintained should be considered.
- **Quality assurance**. Laboratory results must be reliable and accurate in order to be useful in prevention, care, and treatment programs. In order to reduce error and achieve accurate and reliable laboratory results, a plan that addresses all the areas of the laboratory where errors can occur, a quality system plan is needed. Implementation of the plan needs to occur at all laboratories, including central, intermediate, and peripheral locations.

3. Additional recommendations from the small group discussions:

- Multi-nation regional laboratory support is needed for the performance of more sophisticated or infrequently needed tests such as tests for the calibration of syndromic management of STIs and regional ARV drug resistance surveillance.
- A laboratory emergency response team composed of CDC and partners should be formed so that immediate technical assistance can be provided when needed.
- Promote a leadership role for the national reference laboratory. In many countries this laboratory (or laboratories) provides support and needed services to laboratories throughout the country.
- Consideration should be given to developing key components for a national laboratory plan at central or regional levels to avoid duplication of effort. These components might include standard operating procedures (SOP) formats, quality

assurance system design, external quality assurance services, training curricula, and bulk procurement schemes.

4. Issues raised in plenary session panel discussions
:

- Each country must develop a specific national plan for laboratory activities to be implemented. Coordination between all partners will be essential to use resources most efficiently and achieve critical laboratory improvements.

- There must be a designated national laboratory coordinator (advocate) in each country. Requests for laboratory staff should go to the national laboratory coordinator.

- CDC and its partners need to put more emphasis on pre-service training for all kinds of health-care workers, especially laboratory staff. Training systems need to be revised to prepare people for salaried careers as civil servant laboratorians. Certification of institutes that would train and certify laboratory technicians in core competencies can be provided by WHO.

- Generalist laboratorians such as medical technologists would be ideal choices to staff laboratories in GAP countries, especially small laboratories where one medical technologist could perform all the necessary tests.

5. Partners identified in plenary and small group sessions

Many current or potential partners were identified during the plenary and small group sessions. These included international health agencies such as WHO (especially headquarters, and the Regional Office for Africa) and UNAIDS; international NGOs, such as AMREF, the Bill and Melinda Gates Foundation, and the Clinton Foundation; regional health agencies, such as CAREC; international bi-lateral donors, such as DFID, JICO and GTZ; host country national centers of excellence, such as the National Institute of Communicable Diseases (NICD) in South Africa; and GAP Cooperative Agreement partners, such as the Association of Public Health Laboratories (APHL) and the institutions participating in the University Technical Assistance Program (UTAP).

There was some discussion of the appropriate roles or functions different partners might take. It was suggested that CDC should provide leadership, consultation, and partnership management. U.S. Government and international agency coordination should be provided by USAID, DOD, NIH, HRSA, the World Bank, UNAIDS, WHO, and the Global Fund for AIDS, Tuberculosis and Malaria. Technical assistance could be provided by all of the above, as well as APHL, UTAP, the American Society of Clinical Pathologists (ASCP), the University of Washington, the International Training & Education Center on HIV (I-Tech), and NCCLS.

Building Laboratory Capacity in Support of HIV/AIDS Care Programs in Resource-limited Countries

Summaries of Individual Work Group Sessions

Group A. HIV Diagnostics: expanding access to HIV testing, especially for ANC, VCT, pediatric diagnosis, PMTCT/PMTCT+, and blood safety

HIV diagnostics are essential for HIV prevention and care activities. In order to expand access to PMTCT, VCT and blood safety services proposed in The Emergency Plan, it is necessary to know which patients, clients, or donors are HIV-positive. This is not only important for making clinical decisions, and transitioning to appropriate care, it also creates an opportunity for delivery of prevention messages. Where high patient/client throughput prevails, as is the case with major hospital facilities and major blood transfusion services, EIA-based testing is desirable when it does not disrupt patient flow. Because of the difficulty of getting patients into clinics for testing and the resulting loss to follow-up when they must return for their results at a later date, rapid HIV testing with same day results are extremely necessary if the projected number of clients anticipated to receive services through The Emergency Plan are to be met. Programs will require a major commitment to improve HIV testing capability at both central and district levels. Because of the expansion of testing sites, the quality of test results becomes even more important. Achieving the goals of The Emergency Plan will therefore require a systems approach that would involve the development of general standards for laboratory testing, a strict adherence to the standards and a system to objectively document adherence to the standards.

General Recommendations:

- Each Emergency Plan country needs a national laboratory assessment and a 5-year strategic plan:
    - To address the specific situation and needs of that country
    - To provide a framework for advocacy and partnerships at the country level
    - To promote an ongoing coordination of effort
    - To promote in-country capacity building (e.g., laboratory management, resources, infrastructure, human capacity.
- Each laboratory needs sufficient laboratory personnel to support point-of-service rapid diagnostics.
- When laboratory resources are insufficient to support point-of-service rapid diagnostics, new laboratory staff, adjunct laboratory staff, and other health staff need to be hired and trained, under the supervision of senior laboratory staff
- WHO and CDC guidelines on rapid diagnostic tests and algorithms should be reviewed and updated
- Diagnostic algorithms at different levels of the health system need to be evaluated and monitored on an ongoing basis.
- Because laboratory issues and their implementation are fluid and constantly evolving, they require monitoring and evaluation as part of program support

Key Issues to address in a laboratory strategic plan:

- A plan for roll-out and support of both central and district level laboratories
- Equipment support

- Reagents and supply chain management
- Quality Assurance
- Certification of laboratory personnel
- Training of laboratory personnel, including:
    - Current
    - Pre-service
    - Development of new personnel
- Policy issues, including:
    - Who will be allowed to perform testing
    - What tests should be performed
    - At what laboratory level should key tests be performed
    - Necessity of adapting and updating laboratory guidelines as new technologies and resources become available
    - Necessity of responding to new issues

Essential laboratory tests needed for an HIV diagnostics program:

- General clinical diagnostics, i.e., rapid, same day testing using a 3-step sequential algorithm, for the following types of sites:
    - VCT centers
    - TB clinics
    - STI clinics
    - ANC clinics

  The specific rapid tests that make up the algorithm should be determined by a systematic national evaluation and consensus process.

- PMTCT/PMTCT+
    - Adult clinical
        - Rapid same-day HIV testing
        - CD4 testing to screen for appropriate care and treatment
    - Adult special program needs
        - Nevirapine (NVP) resistance monitoring
    - Pediatric testing:
        - Simplified early infant diagnosis (e.g., P-24 antigen testing) for clinical management and program impact evaluation
        - Evaluation and use of rapid enzyme immunoassay (EIA) testing beyond 15 months and post breastfeeding for final outcome evaluations
        - Continued need to have some polymerase chain reaction (PCR) capacity in-country as gold standard
        - Need to be able to do dried blood spot (DBS) testing

- Blood Banking and Blood Transfusion Services
    - Rapid testing for point of service blood transfusions
        - Discard blood based on one single positive

        - Refer patients with a positive test result for confirmatory testing and voluntary counseling and testing (VCT)

Levels of Laboratory System: Tests and Services Performed

- Central Laboratory
    - Rapid HIV-1 test
    - EIA
    - CD4 dual-platform
    - Western Blot
    - Nucleic Acid tests (NAT) for viral load
    - Specimen archiving
    - Reagent controls
    - Test confirmation and validation
    - National Quality Assurance program
- Intermediate (provincial) Laboratory
    - Secondary reference
    - Moderate Capabilities
    - Rapid HIV-1 test
    - EIA
    - CD4 simplified flow (FACSCount)
- Peripheral (district) Laboratory
    - Rapid HIV-1 test
    - EIA (if equipment already present)
    - Manual CD4 test
    - Provide quality assurance for point of care testing

First Year Plan

- Develop statement of purpose for rapid HIV-1 testing and CD4 testing
- Develop training plan and training curriculum for rapid HIV-1 testing and CD4 testing
- Develop assessment protocol
    - Checklists for each laboratory tier
    - Identify the person/team for assessment
    - Establish laboratory goals and indicators
- Identify and assess priority sites
- Determine plan for central test kit procurement (rapid HIV-1, EIA and CD4)
    - Bulk agreements
    - Distribution (with coordination of large donors)
- Procure laboratory equipment for central and district laboratories
- Identify and establish hierarchical “centers of excellence”
- Hire key expert personnel
    - National quality assurance leader
    - National quality assurance team members
- Hire in-country laboratory program advisor (US government-sponsored)
- Establish laboratory data management system

Second Year Plan

- Adopt statement of purpose at the national level
- Implement training at the national level
- Train and implement at least 50% of program sites
- Establish a system for monitoring and evaluating the program, completing the first report by the end of the second year

Critical tools and Products

- National guidelines for testing, including a menu of tests:
    - Rapid HIV-1 test
    - CD4 test
- National standard operating procedures for testing
- Training packages, including curriculum development
- National quality assurance and assessment plan
- Implementation plan
- Procurement, inventory, and distribution plan

Group B. Basic Laboratory Support for HIV Care and Prevention Services (Hematology, Chemistries) and Information Technologies

General Recommendations

- Advocate for resources to expand laboratory technical assistance staff
- Develop and implement national laboratory quality system plans (based on the recent Botswana Conference recommendation)
- Create a laboratory emergency response team to focus on trouble-shooting
- Develop a self-evaluation plan and an annual certification process
- Promote laboratorians as an integral part of the in-country HIV ARV team
- Procure necessary reagents
- Review basic hematology guidelines
- Identify possible analyzers:
    - SYSMEX (hematology)
    - ABX (chemistry)
    - Cobas Mira (chemistry)
- Identify basic hematology training courses
- Link with private companies for training
- Determine maintenance contracts
- Look at volume of tests that will be done; consider possibility of group testing and sample volume

Levels of Laboratory System: Tests and Services Performed

- Central (national reference) Laboratory
    - Hgb
    - Pregnancy Test
    - Urine Test
    - CBC and Differential
    - Platelet count
    - Coagulation
    - ALT
    - Creatinine
    - K+
    - Full Serum Chemistries
- Intermediate (regional) Laboratory
    - Hgb
    - Pregnancy Test
    - Urine Test
    - CBC and Differential
    - Platelet
    - Coagulation
    - ALT
    - Creatinine
    - K+
    - Full Serum Chemistries

- Peripheral (district) Laboratory
    - Hgb
    - Pregnancy Test
    - Urine Test
    - CBC and Differential
    - ALT
    - Creatinine
    - K+
- Remote peripheral (health center, point-of-service) laboratory
    - Hgb
    - Pregnancy Test
    - Urine

First Year Plan

- Target the major laboratories identified in the national plans where ARV treatment is ongoing or planned
- Ensure laboratory capacity for hematology and chemistry
    - Develop teams to support laboratory program activities
    - Review prior assessments
    - Develop checklists
        - Personal competencies
        - Infrastructure
- Create action plans
    - Streamline and strengthen logistic and supply systems
    - Identify equipment, supplies, etc.
    - Have each country develop a plan to transfer tests to the provincial laboratories and selected health centers within four years

Second Year+ Plan

- Evaluate what was done in the first year and expand plan to additional sites
- Work to transfer testing and technologies to the next lower level of laboratories, where possible
- Complete assessments in remaining laboratories
- Complete and implement the action plan from the first year

Critical tools and products

- Headquarters (available for Emergency Plan and other GAP countries)
    - Develop a list of recommended tests that CDC would provide TA to support
    - Determine list of equipment and supplies, including reagents with costing
    - Recommend standardized simple paper forms
    - Identify staff to provide TA
- Country level
    - Each country should develop a national laboratory quality system
        - Develop national guidelines for national laboratory practice and safety

        - Support capacity for evaluation of technologies and equipment to inform decision makers

Human Resources

- Establish and maintain laboratory leadership
    - Focus on keeping laboratory leadership intact at the national and provincial levels
        - Support key leaders to attend professional conferences and training courses
        - Improve working environment
        - Work with WHO to develop laboratory certification process
        - Promote laboratories as an integral part of the care team
- Determine appropriate working conditions that can help recruit and maintain/retain personnel
    - Look at TB and hematology models with low turnover rates
    - Strengthen laboratory consensus building and advocacy
- Develop fellowship programs to support US government capacity and provide additional laboratory pool to meet partner staffing

Training

- Identify/develop resources for training
    - Manufacturers who will go in-country and provide training
    - Training programs for quality assurance
    - Training programs for clinical practices
    - Training programs for other appropriate staff (e.g., engineers, maintenance, service)
- Strengthen in-service institutions in-country
- Provide training to trainers who will be working in GAP countries to familiarize them with THE EMERGENCY PLAN and recommended practices

Group C. Monitoring AIDS Patient Therapy – CD4, Viral Load, and Drug Resistance

General Recommendations:

- Each country should have the capability to provide relevant monitoring for both pediatric and adult patients.
- Each reference laboratory should have arrangements for backup capabilities.
- Although not ideal, other options include transporting specimens or referring patients. These options may be most useful in early years while laboratory infrastructure is being built.
- Each country should have a training program that will sustain the laboratory capability, not only for the first year, but also for subsequent years.
- Each reference laboratory should have both internal and external QA and QC.
- Each testing laboratory should develop SOPs (training, QA/QC, reagent acquisition, equipment maintenance).
- All prices on equipment and reagents should be negotiated.
- The experience in Brazil suggests that packages that include equipment, reagents, service, consumables, and training can be negotiated at a per test cost.

Levels of Laboratory System: Necessary equipment to perform CD4 testing

- Central Laboratory (laboratory with a patient volume >15,000/year)
    - Physical requirements
        - Reliable electricity
        - Laboratory management
        - Data management
        - Established QA program in place
        - Adequate sample processing capability
        - Air conditioning
        - Infrastructure
        - Reliable re-supply system
        - Human capital (supervisory and bench)
        - Biosafety, including adequate waste disposal
        - -70°C Freezer
        - Capability of performing CBC
        - Blood mixer and vortex mixer
        - Instrument service contract
        - Two refrigerators
        - Microscope
        - Class 2 Biological safety cabinet
        - Centrifuges
        - Laboratory quality water
    - Test equipment
        - High end flow cytometer (estimated cost--$150,000): possible choices:
            - BD FACSCalibur

- Beckman-Coulter XL with batch loader
- Backup, FACSCount

- Intermediate Laboratory (laboratory with a patient volume 2,001 – 15,000/year)
  - Physical Requirements: same as for Level One laboratory
  - Testing Equipment: dedicated flow cytometer (estimated $30-40K): possible choice – FACSCount (may need double shifts or second instrument)

- Peripheral Laboratory (laboratory with a patient volume up to 2,000/year)
  - Physical Requirements
    - Working microscope, including light source
    - Refrigerator
    - Reliable electricity
    - Laboratory grade water
  - Testing Equipment: manual CD4 tests (10 tests/technician/day, $4-$8 per test); choices include Dynabeads (Dynal) and Cytospheres (Coulter).

First Year and Beyond Plan for Viral Load Testing and HIV Drug Resistance Monitoring

- During the first year, the capacity for viral load testing and resistance monitoring should be developed in the central laboratory, primarily for program evaluation.
- Countries are encouraged to participate in the WHO HIV Drug Resistance Surveillance Network.
- To ensure long-term successful patient care, a funding mechanism should be established to support continuous program evaluation and program improvement, using virologic endpoints (viral load and HIV drug resistance testing). This goal can be accomplished through in-country partners and or regional/international partners and may be performed through periodic evaluation of the cost/benefit ratio of such technology.

Group D. Laboratory-based Diagnosis of Common Co-Infections, Including Malaria

Levels of Laboratory System: Tests and Services Performed

- Central Laboratory
    - Focus on the following tests:
        - TB
        - Malaria
        - Gram stain
        - Basic bacteriologies and sensitivities, including fungal culture for Cryptococcus
        - India Ink (CSF)
        - Stool microscopy
            - Iodine stain
            - Kinyoun stain
            - Trichrome stain
    - Assess current capacity of Central Laboratory (efforts by WHO-AFRO have already begun)
    - Have EQA performed by transnational regional laboratories

- Intermediate and Peripheral Laboratories
    - Focus on the following tests:
        - TB
        - Malaria
    - Have training performed by staff from Central Level Laboratory (train-the-trainer format)
    - Capacity: "laboratory in a box," including the following:
        - Teaching aids
        - Equipment
        - Reagents
    - Have EQA performed by sending a sampling of slides to the central reference laboratory

First Year Plan

- Develop train-the-trainer package
    - Develop train-the-trainer course
    - Use partner (WHO, CDC, AMREF) or contractor with country input
- Identify national trainers
- Develop a "laboratory-in-a-box" for TB and malaria
    - Use partner (WHO, AMREF, IUATLD, APHL) or contractor
- Develop EQA program
- Review assessments of national reference laboratories with WHO-AFRO, CDC laboratory teams (CDC laboratory GAP contact)
    - Identify current capacity and gaps
    - Focus on capacities in bacteriology, parasitology, and QA oversight

- Develop core materials for national reference laboratory (APHL, WHO)

Second Year+ Plan

- Central Level
    - Develop and implement plan to upgrade capacity
    - Develop and implement transnational EQA program (WHO-AFRO, NHLS program)
- Intermediate and Peripheral Levels
    - Implement training
    - Distribute "laboratory-in-a-box"
    - Implement EQA program
    - Add other tests (e.g., gram stain)

Group E (1). Laboratory Support to STI services

Syndromic case management of STIs is important because it allows investigators to know the patterns of disease in the target population and the antimicrobial resistance of the associated pathogens.

Monitoring conventional STIs in a population is important in HIV/AIDS control because STIs share common behavioral determinants with HIV and enhance the transmission of HIV. STI surveillance can act as a sensitive surrogate marker for changes in risk behavior. STI episodes are also a logical and convenient point at which to introduce voluntary counseling and testing (VCT) for HIV to a population that is at high risk. Serological testing for syphilis offers an opportunity for the introduction of prevention of mother to child transmission (PMTCT) activities for HIV.

Levels of Laboratory System: Tests and Services Performed

- Multi-country Regional Level
    - Provide training for central (national) level
        - Integrated training modules for existing workforce
        - Specialized training to support syndromic management, validation studies and antimicrobial susceptibility
    - Provide QA for activities at the central (national) level
        - Syphilis surveillance: general QA for central laboratory
            - Quantitative RPR
            - Rapid tests and TPPA/TPHA
            - Specimen panel for evaluation for proficiency
        - Analyses for treatment failures: QA for all testing performed at the central level
            - For GUD recurrence/etiology: Multiplex PCR GUD testing
            - Anti-microbial susceptibility testing
                - GC culture and MIC as gold standard + E-test, Disk diffusion
                - Amplified test for GC and CT
        - QA for syndromic management validation testing
- Central (national) Level
    - Provide training for district and peripheral levels
    - Procurement procedures
    - Capability to perform:
        - Syphilis surveillance: general QA for district and periphery
            - Quantitative RPR
            - Rapid tests and TPPA/TPHA
        - Analyses in cases of treatment failure
            - Wet mount
            - Gram stain
            - For GUD recurrence/etiology
                - Tzanck prep

        - Giemsa stain
        - GC culture
    - Syndromic management validation
        - Gram stain
        - Anti-microbial susceptibility testing:
            - GC culture
            - E-test
            - Disk diffusion of MIC
        - (Non)-amplified test for GC and CT

- District Level
    - Procurement of RPR/rapid tests and other laboratory needs for own testing and peripheral laboratories
    - Syphilis surveillance RPR/Rapid test for confirmation
    - Treatment failures:
        - Wet mount
        - Gram stain
        - For GUD recurrence/etiology:
            - Tzanck smear for HSV
            - Giemsa for Donovanosis
    - Syndromic management validation:
            - Gram stain
            - Specimen manipulation
            - GC culture
- Peripheral Level
    - Routine STI testing
        - Syphilis and HIV serology only
            - Screening with RPR or rapid test
                - All cases of genital ulceration
                - All cases of urethral discharge in men
                - All cases of vaginal discharge in women, when the rate of positive syphilis serology is <5% and the prevalence of GC/CT/TV is >20%
                - All cases of vaginal discharge in women, when the rate of positive syphilis serology is >5%
    - Laboratory functions
        - RPR surveillance
            - RPR if there is electricity and a refrigerator
            - Rapid treponemal tests if there is no electricity and a refrigerator
        - Algorithm validation specimen collection and storage

Training

- STI Laboratory training
    - Training for partners on SOP/CDC guidelines
    - Regional or National: Integrated training

        - QA: includes proficiency tests, specimen panel
        - Maintenance
        - Supervision and monitoring modules
    - National level: Specific training
        - Linked to implementation of programs nationwide performed by CDC/partners
    - School curriculum level: Medical, nurses, and technicians
    - Peripheral/District levels: specialized QA and program training courses performed by central partners
- Integrated training
    - Formations of a working group to investigate:
        - Integrated training at the district/peripheral levels, including:
            - Malaria
            - TB
            - Syphilis
            - HIV
        - Standardization of activities should include:
            - Record keeping
            - QA
            - SOP
            - Supervision, including EQA

Critical tools and products

- National standard operating procedures:
    - Screening guidelines
    - Antimicrobial susceptibility testing and syndromic management treatment guidelines
    - Treatment failure management guidelines
- Training package:
    - CD/Video modules adapted to each training
    - Checklist for QA
    - Curriculum development for STI syndromic case management for medical students, post-graduates and nurses; laboratory training for STI diagnostics for technologists and technicians

Group E (2). Laboratory Support TB Diagnosis and Monitoring

General Recommendations

- Strengthen TB microscopy centers by building on the existing infrastructure at the national, provincial, and district levels.
- Promote the leadership role for the National Reference Laboratory.
- Integrate the TB model with other laboratory tests through training, QA, EQA, supervision, and supply management.

Levels of Laboratory System: Tests and Services Performed

- National Reference Laboratory (located in the capital city)
    - Services to clinics
        - FM/ZN smear microscopy
        - Culture/ID of MTB, referral services
        - Drug susceptibility testing (DST)
    - Supports to intermediate laboratories
        - Supply of reagents/materials for smear microscopy
        - Training
        - Supervision
        - EQA of smear microscopy
        - Culture
        - Drug susceptibility testing
    - Manpower: 5-6 laboratorians (for TB work only)
    - Covering population: entire country

- Intermediate Laboratory (located in regional TB health institutions, including hospitals)
    - Services to clinics
        - FM/ZN smear microscopy
        - Culture and identification (ID) of MTB, referral services
    - Supports to peripheral laboratories
        - Supply of reagents/materials for smear microscopy
        - Training
        - Supervision
        - EQA of smear microscopy
    - Manpower: 2-3 laboratorians (for TB work only)
    - Covering population: 500,000-1,500,000
- Peripheral Laboratory (located in peripheral TB dispensaries/centers, health centers, district hospitals, 1st referral hospitals)
    - Services
        - Sputum collection
        - FM/ZN smear microscopy
    - Managerial
        - Recording/reporting
        - Slide keeping for EQA

- Manpower: < or equal to 1(2) laboratorian(s) (for TB work only); >2-3 laboratorians/<20 smears per day
- Covering population: 100,000-200,000

First Year Plan (General)

- Develop AFB training materials on the following areas for in-country use:
  - Basic microscopy
  - Implementation of EQA
  - Laboratory safety issues
- Implement training courses and mentoring for expert TB laboratory consultants
- Market and distribute existing TB guidelines and training materials
- Develop training strategy within each country
- Assess and upgrade equipment
- Ensure adequate supplies and inventory
- Examine fluorescence microscopy utility in anticipation of increases workload and to increase sensitivity of case detection

First Year Plan (Integrated Laboratory Network)

- Develop standards for the set of essential testing services to support The Emergency Plan
- Develop a model to implement and support this integrated testing model
- Establish a regional working group to address laboratory service integration at every level (National, Regional, District, Peripheral)
  - Develop checklist for supervision/EQA/QA
  - Develop integrated training curriculum
  - Documents, records, information system
  - Supply and inventory
  - Procurement
  - Procedures, technologies
- **Human resources**
  - Strengthening professional/in-service curriculum
  - Address workforce incentives/retention
  - Training, monitoring, supervision, QA of community-based (lay) worker testing