

INNOVATIVE TEST DEVELOPMENT AND EXPERT EVALUATIONS

OVERVIEW

The U.S. Centers for Disease Control and Prevention (CDC) International Laboratory Branch (ILB) provides critical technical expertise to PEPFAR-supported and CDC Global Tuberculosis priority countries to effectively reach UNAIDS' "90-90-90" targets, WHO's "End TB Strategy", and the Stop TB Partnership's "Global Plan to End TB" targets. ILB develops, evaluates and advises country laboratory programs on their performance characteristics, and the appropriate placement and utilization of HIV and TB diagnostics to ensure the quality of their assays. The evaluations include assays that are performed both in the clinical laboratory and at point-of-care testing sites. ILB provides guidance on these HIV and TB tests to support maximum impact of diagnostic testing on patient care and promote universal quality monitoring and assurance.

HIV INCIDENCE TESTING

It is critical to identify where the highest rates of new HIV infections occur so that prevention efforts can be aligned accordingly and assessed for effectiveness. ILB is at the forefront of research to develop unique assays to detect recent HIV infections. We have developed two incidence assays, tools that will play important roles in understanding the success of HIV prevention programs and the spread of HIV as we strive to reach zero new infections. The first is a low-cost assay (LAG-Avidity EIA) that distinguishes between recent and long-term HIV infections and can be used to estimate HIV-1 incidence in cross-sectional surveys measuring the impact of our programs. This commercially available, field-evaluated assay performs similarly across HIV-1 subtypes and has been shown to accurately estimate HIV incidence in cross-sectional populations without expensive longitudinal follow-up. The assay will be critical to monitor the epidemic, identify high-incidence populations, and assess the impact of prevention programs. ILB has also developed a simple rapid recency test that can simultaneously diagnose HIV infection and identify recent infection.

HIV DRUG RESISTANCE TESTING

Lifelong treatment for HIV infection can lead to the emergence of drug-resistant strains of HIV. The development of drug resistance can be mitigated by testing populations receiving ART and by following-up with those who are newly-infected with drug-resistant strains. A low-cost, broadly sensitive genotyping assay developed by ILB has reduced the reagent cost for HIV drug-resistance testing by 70 percent and has made HIV drug-resistance testing more accessible in remote areas of resource-limited settings. The technology was transferred to Thermo Fisher Scientific, which developed HIV-1 Drug Resistance Genotyping Kits. The standardized kit has greatly simplified the procurement process as well as streamlined and reduced technical hands-on testing time. The assay's ability to genotype diverse HIV-1 group M viral strains and dried blood spot specimens has made nationwide HIV drug resistance genotyping surveys a reality in many developing countries.

TB DIAGNOSTIC TESTS

TB is responsible for one third of HIV-related deaths worldwide, and people living with HIV are 20 to 30 times more likely to develop TB disease than those without HIV. However, traditional TB diagnostic tests have had long turnaround times and poor sensitivity in HIV-positive individuals and children, making TB detection a challenge that can lead to delays in treatment, particularly for drug-resistant forms of the disease. To strengthen rapid TB diagnostic services, ILB works with Ministries of Health to introduce and evaluate the impact of new TB detection and drug susceptibility testing technologies, such as the near-POC Xpert MTB/RIF assay. By providing customized technical assistance and guidance to more than 30 countries, ILB works to collaboratively assess: (i) new test placement, quality, and utilization, (ii) diagnostic sensitivity of novel specimen types, such as stool and nasopharyngeal aspirates, for HIV-positive and pediatric patient populations, and (iii) national TB diagnostic algorithms and strategic policies to improve TB diagnostic networks.

SPOTLIGHT: HIV VIRAL LOAD TESTING

As more people are identified as HIV-positive and receive antiretroviral treatment, there is an urgent need to monitor patients on treatment. Viral-load (VL) testing measures the amount of HIV virus in the blood and can be used to monitor the effectiveness of treatment.

VL testing typically requires fresh whole blood plasma specimens, which can be challenging in many resource-limited settings. ILB is leading research to use dried blood spot technology for VL testing and is investigating the use of point-of-care VL test technologies in these same settings.

HIV DIAGNOSTICS, RAPID TESTING, AND EVALUATIONS

ILB evaluates and approves new rapid HIV test kits for potential use in PEPFAR-supported countries using a unique program established by CDC. HIV rapid tests make diagnoses widely accessible by having test results available on the same day – typically within 30 minutes – using blood from a small finger prick. The tests do not require refrigeration, are easy to transport, and can be performed by non-laboratory personnel with proper training. As a result, HIV testing has expanded from about two million tests in 2004 to more than 68 million tests in 2015. In the last ten years, ILB received requests from various biotech manufacturers to evaluate 53 unique HIV rapid test kits. Of the 45 test kits that were subjected to the ILB evaluation process, which includes a dossier review and technical evaluation, 22 kits met the rigorous performance requirements (sensitivity >99 percent and specificity >98 percent) to qualify for inclusion in USAID’s procurement waiver list and potential use in PEPFAR programs. ILB evaluated novel test kits including the Geenius HIV-1/2 assay – a rapid confirmatory test that uses either serum, plasma or dried blood spot specimens – and three HIV-syphilis dual tests. The Geenius HIV-1/2 assay has the potential to improve the accuracy of HIV diagnostics, especially in the context of the HIV surveillance activities. Two of the three HIV/syphilis dual tests approved by ILB would be suitable for use in national HIV testing algorithms, particularly in preventing HIV transmission from mothers to their children, in STI clinics or in settings where syphilis screening is limited due to resource constraints.

EARLY INFANT DIAGNOSIS FOR EARLY ACCESS TO CARE AND TREATMENT

ILB is a leader in expanding relatively low-cost early infant diagnosis dried blood spot testing procedures and supports the development of training tools and quality assurance programs to advance the accurate and early diagnosis of infants born to HIV-positive mothers. Infants can be diagnosed as early as four to six weeks after HIV exposure with nearly 100 percent accuracy using this polymerase chain reaction test. ILB has evaluated two point of care (POC) or near-POC devices, Alere™ q HIV-1/2 Detect and Xpert® HIV-1 Qual, and these devices provided precise and accurate results that were comparable to current laboratory-based technologies.

CD4 TESTING

CD4 testing, used to determine eligibility for antiretroviral treatment and patient monitoring, has expanded outside the traditional laboratory setting with portable instruments for POC testing. ILB is a leader in evaluating these new CD4 assays and has helped to implement them in most PEPFAR-supported countries. ILB has evaluated four platforms including two POC, Alere Pima™ CD4 and BD FACSPresto™ Near-Patient CD4 Counter, and two laboratory: Beckman Coulter AQUIOS™ CL with Tetra-1 and EMD Millipore Muse® Auto CD4/CD4%. All four instruments were found to be suitable for use in field settings.