WHO Working Group on HIV Incidence Assays statement on the use of HIV-1 incidence assays for surveillance or epidemic monitoring

Background

In December 2005 the Joint United Nations Programme on HIV/AIDS (UNAIDS) Reference Group issued a statement recommending that the BED IgG Capture Enzyme Immunoassay (hereafter referred to as the BED assay) not be used for routine surveillance applications due to overestimation of HIV incidence caused by the misclassification of some individuals with long-standing HIV infections as recent HIV infection. The UNAIDS reference group for HIV estimates and projections called for further research on these issues\(^1\). The reference group also recommended use of alternative approaches to estimate HIV incidence.

The new UNAIDS and World Health Organization (WHO) five-year strategies aim to reduce HIV incidence, and although there is not clear consensus on how to measure incidence in all countries, HIV incidence assays can provide a good tool, especially for high burden countries. The most recent report (2010) by the Institute of Medicine that advises PEPFAR programs (Preparing for the future of HIV/AIDS in Africa) includes the following key recommendation: Measure incidence: African countries, with the support of donors, should develop and implement cost-effective methods for accurately measuring the level of and change in HIV/AIDS incidence to enable better planning and evaluation of HIV/AIDS prevention programs. Furthermore, a resolution was drafted at the June 2011 High Level Meeting (HLM) Political Declaration on HIV/AIDS: Intensifying our Efforts to Eliminate HIV/AIDS. Measuring HIV incidence in the future, jointly with other indicators, will be paramount to monitoring progress towards 2015 goals and the HLM declaration approved by the United Nations General Assembly in its sixty-fifth session.

HIV Incidence Working Group

At the 2008 International AIDS Conference in Mexico City, WHO established a Working Group on HIV Incidence Assays to provide normative guidance and support for developers and users of HIV incidence assays to estimate HIV incidence in the population. This group is made up of epidemiologists, laboratory specialists, biostatisticians and public health officials, and has worked to standardize terminology in the areas of assay calibration and validation and produce normative guidance on the development, validation, and use of incidence assays.

Several meetings were organized (2009, 2010 and 2011) to advance this agenda. These meetings have been successful in bringing a wider group of assay users, in particular from countries affected by the epidemic who may consider using HIV incidence assays in the future, together with key experts in the field of applying laboratory-based methods for estimates of HIV incidence. These activities have been achieved with the financial support of the Bill & Melinda Gates Foundation and in collaboration with the US Centers for Disease Control and Prevention (CDC) and other partners. Copies of reports are available on the HIV Incidence Working Group web page: http://www.who.int/diagnostics_laboratory/links/hiv_incidence_assay/en/.

**Update on HIV incidence assays: from a single assay to a testing algorithm**

The importance of HIV incidence as a key indicator of national program success or failure has been acknowledged and promoted by various organizations, but Ministries of Health and their partners should be aware of the complexities of producing valid incidence estimates based solely on data generated by surveys using the currently available assays that assess whether or not a specimen is from a persons who was recently HIV infected.

Although several HIV incidence assays have been developed to measure HIV incidence, only one (the BED assay) has been commercially available and applied widely across the globe. Several promising assays are under development and will be evaluated in a critical pathway prior to be considered for public health and surveillance use. It is expected that at least one assay (or algorithm) will be fully validated and publicly available by the end of 2013.

All antibody-based HIV incidence assays are challenged by the variability in the immune response to HIV infection. Specifically, individual differences in the early immune response among people with HIV-1 infection can be readily observed, such as individual variation of anti-HIV antibody titer, or the rate of antibody production and maturation. Moreover, the use of antiretroviral therapy and the advanced stages of acquired immunodeficiency syndrome (AIDS) are both associated with a reduction in anti-HIV antibody titer, which can be confused with an early immune response resulting in misclassification of some of these individuals as recently infected on these assays.

However, progress has been made over the past several years to address these challenges. Instead of relying on a single assay to measure HIV incidence, an integrated HIV incidence testing algorithm consisting of assay systems measuring different biological properties of antibody maturation (e.g., antibody proportion, antibody avidity, etc.) in combination with additional clinical information (e.g., HIV viral load, antiretroviral therapy, CD4 cell count) has been demonstrated to substantially improve the validity and accuracy of test results.

The WHO Working Group on HIV Incidence Assays published in 2011 guidelines on when and how to use assays for recent infections to estimate HIV incidence at a population level. This guidance document provides the framework and directions on using current HIV incidence assays to estimate HIV incidence in cross sectional surveys. It provides possible algorithms, sample size requirements, and the formulas to estimate HIV incidence and 95% confidence intervals.
There is an ongoing international, collaborative effort to create a repository of epidemiologically appropriate and globally representative specimen. This repository will be used to validate the existing and novel HIV incidence assays and to explore different algorithms, which should provide solid recommendations for the use of HIV incidence assays and algorithms. In the meantime we believe that the currently available guidelines provide the necessary framework to estimate HIV incidence at the population level using the available technologies, as well as limitations that must be considered prior to embarking on or in interpretation of data from assays and algorithms for recent infection and incidence estimation. HIV incidence determination is challenging and all available data sources should be explored to best estimate HIV incidence.