Technical Update: Use of the Determine HIV 1/2 Ag/Ab Combo Test with Serum or Plasma in the Laboratory Algorithm for HIV Diagnosis

In 2014 the Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories (APHL) published recommendations for the laboratory diagnosis of HIV infection.[1] This technical update provides information on the use of the Alere Determine HIV 1/2 Ag/Ab Combo single use rapid test (Determine) in laboratories where it is not feasible to conduct an instrumented antigen/antibody test as the initial test in the algorithm. In 2014, sufficient data were only available to recommend instrumented antigen/antibody tests. Since then, data describing Determine's performance using specimens typically used for laboratory testing (plasma and serum) have become available. We are writing to share this new information and to describe its implications for the recommendations for laboratory diagnosis of HIV infection.

The CDC and APHL continue to recommend that laboratories use an instrumented, laboratory-based antigen/antibody HIV screening immunoassay, followed, when reactive, by an HIV-1/HIV-2 antibody differentiation immunoassay. When the differentiation assay interpretation is negative or indeterminate for HIV-1, perform an HIV-1 nucleic acid test (NAT). Instrumented antigen/antibody tests are preferred over Determine because the former are more sensitive for HIV during acute infection.[2,3] However, Determine can detect infection earlier than IgM/IgG sensitive (antibody-only) immunoassays when used with plasma.[2,3,4] For laboratories in which instrumented antigen/antibody testing is not feasible, Determine can be used with serum/plasma as the first step in the laboratory algorithm. It may not detect infection as early as the instrumented tests. Laboratories using Determine are advised to acknowledge the limitations of the testing procedure when reporting results.

Determine separately reports detection of antigen and antibody, but there are limited data on the performance of the antigen component of the test when performed on plasma and serum. When Determine only detects antigen, some laboratories perform a supplemental antibody test and an HIV-1 NAT in parallel to expedite the identification of persons with acute HIV infection. We are seeking data on how this modified testing strategy works to inform future HIV testing guidance. Additional data on the specificity of the antigen component of Determine is required to evaluate the number of potentially expensive NATs that would be conducted for persons who are truly uninfected.

This technical update pertains only to the performance of Determine on plasma or serum for use in the laboratory algorithm for HIV diagnosis. Data are needed to fully characterize the performance of this test on whole blood. In accordance with current guidance, when a laboratory receives serum or plasma after a preliminary positive rapid test conducted in a CLIA-waived setting,[a] it should begin testing with an antigen/antibody test and not go directly to the HIV-1/HIV-2 antibody differentiation test.

In summary, in situations where instrumented antigen/antibody tests are available, these tests are preferred over Determine due to their superior sensitivity for detecting HIV during acute infection.[2,3] However, for laboratories that wish to use Determine as the screening test in the laboratory algorithm for HIV diagnosis, performing the single use Determine rapid test with serum or plasma may be a useful option, particularly for smaller labs that perform a low volume of HIV tests.

As additional data become available, CDC and APHL may make additional clarifications to the 2014 recommendations for the laboratory diagnosis of HIV infection. Thank you for your commitment to accurate laboratory testing for HIV. Please send any comments or questions to www.cdc.gov/info or 1-800-CDC-INFO.

[a]When Determine is conducted in CLIA-waived settings, it should still be followed with Determine on serum or plasma in the laboratory if that is the antigen/antibody test the laboratory uses. If the Determine on serum or plasma is non-reactive, testing stops, and the result is reported according to The Suggested Reporting Language for the HIV Laboratory Diagnostic Testing Algorithm (www.aphl.org/HIV).

1. Centers for Disease Control and Prevention and Association of Public Health Laboratories. Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations. 2014. http://stacks.cdc.gov/view/cdc/23447. Accessed June 27, 2016.
2. Delaney KP, Hanson DL, Masciotra S, Ethridge SF, Wesolowski L, Owen SM. Time Until Emergence of HIV Test Reactivity Following Infection With HIV-1: Implications for Interpreting Test Results and Retesting After Exposure. *Clinical Infectious Diseases : an official publication of the Infectious Diseases Society of America.* 2017;64(1):53-59.
3. Masciotra S, Luo W, Westheimer E, et al. Performance evaluation of the FDA-approved Determine HIV-1/2 Ag/Ab Combo assay using plasma and whole blood specimens. *Journal of Clinical Virology : the official publication of the Pan American Society for Clinical Virology.* 2017;91:95-100.
4. Masciotra S, Luo W, Youngpairoj AS, et al. Performance of the Alere Determine HIV-1/2 Ag/Ab Combo Rapid Test with specimens from HIV-1 seroconverters from the US and HIV-2 infected individuals from Ivory Coast. *Journal of Clinical Virology : the official publication of the Pan American Society for Clinical Virology.* 2013.