Memorandum

To: Arizona Clinicians and HIV Testing Programs
From: Alyssa Guido, MPH
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Ann Gardner
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Office of HIV Prevention
Arizona Department of Health Services

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Date: July 20, 2016
Re: Information for Clinicians and HIV Testing Programs about the Alere Determine™ HIV-1/2 Ag/Ab Combo Rapid Test

Dear Colleague:

This memo is intended to update Arizona clinicians and HIV testers on the accuracy of the Alere Determine™ HIV-1/2 Ag/Ab Combo Rapid Test. The Determine Combo received its FDA approval in August 2013 and CLIA (Clinical Laboratory Improvement Amendments) waiver in December 2014, making it suitable for use as a point-of-care (POC) rapid HIV test in clinics and outreach testing sites. The Determine Combo is designed to separately detect HIV-1 p24 antigen and HIV-1/2 antibodies and can be used with plasma, serum or whole blood specimens (including fingerstick). However, recent studies demonstrate that Determine Combo is less sensitive during early HIV infection than laboratory-based Ag/Ab combo tests, and rarely detects p24 antigen when used with whole blood specimens. Therefore, the Determine Combo does not reliably screen for acute HIV-1 infection when used with whole blood. Please review the attached fact sheet for more information. If you have questions or would like to request HIV training, please contact Alyssa Guido at alyssa1@deptofmed.arizona.edu or (520) 626-0723.

Sincerely,

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Arizona Department of Health Services
Alere Determine™ HIV-1/2 Ag/Ab Combo: Information for Clinicians and HIV Testing Programs

- Alere Determine™ HIV-1/2 Ag/Ab Combo is intended as a point-of-care rapid HIV test and is CLIA-waived. The Determine Combo has separate indicators for identifying reactivity to p24 antigen and HIV 1/2 antibodies.
- The package insert specifies:
  - Determine Combo is designed to detect HIV-1 p24 antigen and HIV-1/2 antibodies in serum, plasma and capillary (fingerstick) or venipuncture (venous) whole blood.
  - Determine Combo sensitivity\(^{a}\) is 99.9% (95% confidence interval 99.4 to 100.0%) in serum, plasma and whole blood specimens from persons known to be infected with HIV-1.
  - Determine Combo specificity\(^{b}\) is 100% (95% confidence interval 99.6 to 100%) in serum, plasma and whole blood specimens from low-risk\(^{c}\) subjects.
  - In specimens from high-risk\(^{d}\) subjects, the sensitivity ranged from 98.9% in serum to 99.7% in whole blood (95% confidence interval 97.7 to 99.8%).
- CDC studies\(^{1}\) using plasma specimens collected from 20 individuals in the process of seroconverting found that Determine Combo detects HIV infection approximately:
  - One to two weeks before other rapid HIV antibody tests;
  - One to three days before 3\(^{rd}\) generation laboratory-based HIV antibody tests;
  - Three to four days after 4\(^{th}\) generation laboratory-based Ag/Ab combo HIV tests.
- CDC studies\(^{2}\) using whole blood specimens from these same 20 seroconverters found a marked reduction of p24 antigen detection in early HIV-1 infections using whole blood compared with plasma:
  - Overall, Determine Combo reactivity in early\(^{e}\) HIV-1 infections was 56.4% using whole blood compared with 91.1% using plasma.
  - Eight seroconverters showed a median delay of 6 days between reactivity with plasma and reactivity with whole blood.
  - One seroconverter exhibited a second negative phase with whole blood of 7 days duration before Determine Combo antibody reactivity developed, after the initial p24 antigen reactivity reverted to negative.
- CDC studies\(^{2}\) using plasma specimens from high-risk persons that were HIV antibody negative but positive for HIV-1 RNA showed lower sensitivity with Determine Combo than with laboratory-based Ag/Ab combo tests:
  - Determine Combo detected 46 (54%) of 85 early HIV-1 infections detected by laboratory-based Ag/Ab combo tests.
  - Both Determine Combo and laboratory-based Ag/Ab combo tests detected 100% of established HIV-1 infections.
• In six studies\textsuperscript{3,4} that tested \textit{whole blood} specimens from more than 26,000 persons, the Determine Combo failed to detect any of the 26 acute HIV infections that were detected by pooled HIV RNA testing, a 0\% sensitivity for the HIV-1 p-24 antigen component of the Determine Combo.

In the 2014 updated recommendations for HIV testing, CDC indicated that data were insufficient to recommend use of the FDA-approved single-use rapid HIV-1/HIV-2 antigen/antibody combination immunoassay [Determine Combo] as the initial assay in the 4\textsuperscript{th} generation HIV testing algorithm.

Based on more recent data:
• Determine combo should not be used to screen for acute HIV infection using fingerstick whole blood given its poor sensitivity for HIV p24 antigen with whole blood in field studies.
• The updated CDC 4\textsuperscript{th} generation HIV testing algorithm with initial laboratory-based Ag/Ab combo tests should be used to screen for acute HIV infection and for testing after a reactive Determine Combo test.
• The Determine Combo detects HIV antibody in plasma specimens one to two weeks earlier than other rapid HIV antibody tests and might be preferred for use by laboratories that are able to perform HIV testing on serum or plasma only with rapid HIV tests.
• In cases where acute HIV is suspected and Determine is non-reactive, blood should be drawn and sent for laboratory-based 4\textsuperscript{th} generation assay or HIV RNA testing.

a. Sensitivity: Probability that the test will be reactive if infection is present
b. Specificity Probability that the test will be nonreactive if infection is not present
c. Low risk: population with prevalence of HIV infection <1%
d. High risk: population with prevalence of HIV infection >1%
e. Early HIV infection: includes both acute and recent HIV infection (up to 6 months after HIV acquisition)
References


