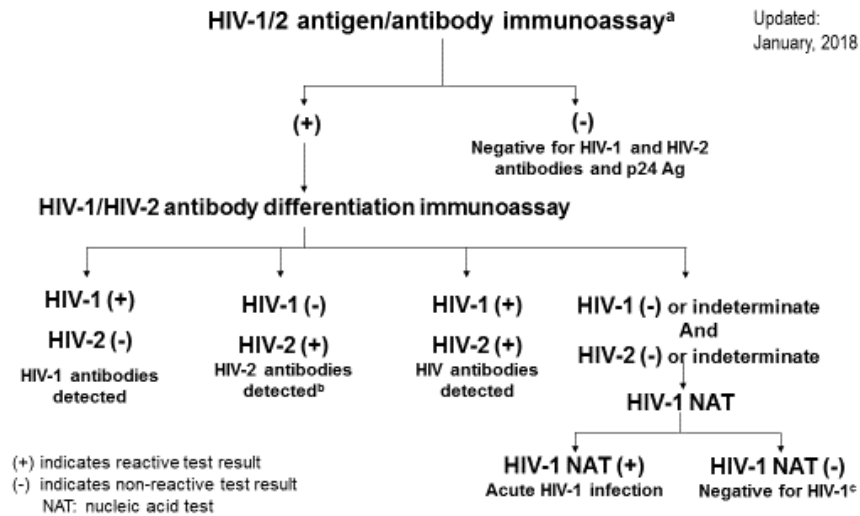


## Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens



- Laboratories should conduct initial testing for HIV with an FDA-approved antigen/antibody immunoassay<sup>a</sup> that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen to test for established HIV-1 and HIV-2 infection and for acute HIV-1 infection, respectively. No further testing is required for specimens that are non-reactive on the initial immunoassay. However, if there is a possibility of very early infection leading to a non-reactive initial antigen/antibody immunoassay, such as when recent HIV exposure is suspected or reported, then conduct an HIV-1 nucleic acid test (NAT), or request a new specimen and repeat the algorithm according to CDC guidance (1,4,5,6).
- Specimens with a reactive antigen/antibody immunoassay result (or repeatedly reactive, if repeat testing is recommended by the manufacturer or required by regulatory authorities) should be tested with an FDA-approved supplemental antibody immunoassay that differentiates HIV-1 antibodies from HIV-2 antibodies. Reactive results on the initial antigen/antibody immunoassay and the HIV-1/HIV-2 antibody differentiation immunoassay should be interpreted as positive for HIV-1 antibodies, HIV-2 antibodies<sup>b</sup>, or HIV antibodies, untypable (undifferentiated).
- Specimens that are reactive on the initial antigen/antibody immunoassay and non-reactive or indeterminate on the HIV-1/HIV-2 antibody differentiation immunoassay should be tested with an FDA-approved HIV-1 NAT.
  - A reactive HIV-1 NAT result and non-reactive or indeterminate HIV-1/HIV-2 antibody differentiation immunoassay result indicates laboratory evidence of acute HIV-1 infection.
  - A negative HIV-1 NAT result and non-reactive or HIV-1 indeterminate antibody differentiation immunoassay result indicates an HIV-1 false-positive result on the initial immunoassay.
  - A negative HIV-1 NAT result and repeatedly HIV-2 indeterminate or HIV indeterminate antibody differentiation immunoassay result should be referred for testing with a different validated supplemental HIV-2 test (antibody test or NAT) or repeat the algorithm in 2 to 4 weeks, starting with an antigen/antibody immunoassay (3).
- Laboratories should use this same testing algorithm, beginning with an antigen/antibody immunoassay on all serum or plasma specimens submitted for testing after a preliminary positive result from any rapid HIV test conducted in a CLIA-waived setting (7).

<sup>a</sup>The FDA-approved single-use rapid HIV-1/HIV-2 antigen/antibody immunoassay can be used as the initial assay in the laboratory HIV testing algorithm for serum or plasma. If any instrumented antigen/antibody test is available, it is preferred due to its superior sensitivity for detecting HIV during acute infection (1,2).

<sup>b</sup>This includes specimens reported as HIV-2 positive with HIV-1 cross-reactivity (3).

<sup>c</sup>Refer to last bullet, item 3 above.

Guidance for reporting results from the HIV laboratory diagnostic algorithm for use with serum and plasma specimens (4)

Guidance for Reporting Results from the HIV Laboratory Diagnostic Testing Algorithm for Serum and Plasma Specimens<sup>a</sup>

Test Outcomes	Test Sequence			Final Algorithm Interpretation <sup>d</sup>	Interpretation for Provider <sup>e</sup> (Sample should be reported as:)	Further Actions <sup>f</sup>
	Step 1	Step 2	Step 3			
	HIV-1/HIV-2 Ag/Ab IA <sup>b</sup>	HIV-1/HIV-2 Antibody Differentiation IA <sup>c</sup>	HIV-1 NAT			
Nonreactive	n/a	n/a	HIV-1 antigen and HIV-1/HIV-2 antibodies were not detected. No laboratory evidence of HIV infection.	HIV negative	If recent HIV exposure is suspected or reported, conduct HIV-1 NAT or request a new specimen and repeat the algorithm according to CDC guidance. <sup>g</sup>	
Reactive	HIV-1 Positive	n/a	Positive for HIV-1 antibodies. Laboratory evidence of HIV-1 infection is present.	HIV-1 Positive	Link patient to HIV medical care and provide appropriate prevention counseling. <sup>h</sup>	
Reactive	HIV-2 Positive	n/a	Positive for HIV-2 antibodies. Laboratory evidence of HIV-2 infection is present.	HIV-2 Positive	Link patient to HIV medical care and provide appropriate prevention counseling. <sup>h</sup>	
Reactive	HIV-2 Positive with HIV-1 Cross reactivity	n/a	Positive for HIV-2 antibodies. Laboratory evidence of HIV-2 infection is present.	HIV-2 Positive. This result is distinct from HIV positive untypable (undifferentiated).	Link patient to HIV medical care and provide appropriate prevention counseling. <sup>h</sup>	
Reactive	HIV Positive untypable (undifferentiated)	n/a	Positive for HIV-1 and HIV-2 antibodies. Laboratory evidence of HIV-1 and/or HIV-2 infection is present.	HIV Positive	Link patient to HIV medical care and provide appropriate prevention counseling. <sup>h</sup> Provider may consider additional testing for HIV-1 RNA or DNA and HIV-2 RNA or DNA to verify or rule out HIV-1/HIV-2 dual infection. Request additional specimen if original specimen volume is insufficient.	
Reactive	HIV-1 indeterminate, HIV-2 indeterminate <sup>i</sup> , HIV indeterminate	Detected	Positive for HIV-1. Laboratory evidence of HIV-1 infection consistent with an <b>acute</b> HIV-1 infection.	<b>Acute</b> HIV-1 Positive	Link patient to HIV medical care and provide appropriate prevention counseling immediately <sup>h</sup> to expedite prevention practices.	
Reactive	HIV-1 indeterminate	Not detected	HIV-1 antibodies were not confirmed and HIV-1 RNA was not detected.	HIV Negative	If recent HIV exposure is suspected or reported, request a new specimen and repeat the algorithm according to CDC guidance. <sup>g</sup>	
Reactive	HIV-2 indeterminate <sup>i</sup>	Not detected	HIV antibodies were not confirmed and HIV-1 RNA was not detected. HIV-2 inconclusive.	HIV-1 Negative, HIV-2 inconclusive	Refer sample for testing with a different validated supplemental HIV-2 test (antibody test or NAT) if available. Alternatively, redraw and repeat algorithm in 2-4 weeks to assess HIV-2 infection.	
Reactive	HIV Indeterminate	Not detected	HIV-1 antibodies were not confirmed and HIV-1 RNA was not detected. HIV-2 inconclusive.	HIV-1 Negative, HIV-2 inconclusive	Refer sample for testing with a different validated supplemental HIV-2 test (antibody test or NAT) if available. Alternatively, redraw and repeat algorithm in 2-4 weeks to assess HIV-2 infection.	
Reactive	Negative	Detected	Positive for HIV-1. Laboratory evidence of HIV-1 infection consistent with an <b>acute</b> HIV-1 infection.	<b>Acute</b> HIV-1 Positive	Link patient to HIV medical care and provide appropriate prevention counseling immediately <sup>h</sup> to expedite prevention practices.	
Reactive	Negative	Not detected	HIV antibodies were not confirmed and HIV-1 RNA was not detected.	HIV Negative	If recent HIV exposure is suspected or reported, request a new specimen and repeat the algorithm according to CDC guidance. <sup>g</sup>	
Reactive	Negative or Indeterminate	Invalid or not performed	Inconclusive	Inconclusive	Request an additional specimen and repeat the algorithm. Ensure HIV-1 NAT is performed, if indicated by results of HIV-1/HIV-2 Ag/Ab IA and HIV-1/HIV-2 Ab differentiation IA.	

a. The tests outlined in this table are not FDA approved for oral fluid or dried blood spots. b. The need for repeating screening IA on an initial reactive test is assay dependent, refer to product package insert. c. This column contains the Final Assay interpretation per the Geenius package insert, the only FDA approved test for this step. We recommend excluding the individual HIV-1 and HIV-2 results on the laboratory report. If they are used, the final assay interpretation or final assay result should also be included. d. This column contains suggested language to be used for the laboratory report and it can be directly used for reporting from LIMS systems. e. This column contains simplified language of the previous column, "Final Algorithm Interpretation," and is included here for healthcare providers or other non-laboratorians that may also use this table as a reference document. This does not need to be included on the laboratory report. f. Comments under "Further Action" can be included as language in the laboratory report or can be used as guidance for laboratorians to discuss test results with healthcare providers or health department staff. g. Please refer to Centers for Disease Control and Prevention guidance. Available at: <https://www.cdc.gov/hiv/testing/laboratorytests.html>, <https://stacks.cdc.gov/view/cdc/38856> and <https://www.cdc.gov/hiv/testing/clinical/index.html> h. Please refer to the Centers for Disease Control and Prevention HIV Guidelines and Recommendations to find the most appropriate information by age and risk group for the patient in question. Available at: <http://www.cdc.gov/hiv/guidelines/> i. Follow Geenius package insert and refer to the CDC Technical Update. Available at: <https://stacks.cdc.gov/view/cdc/40790>