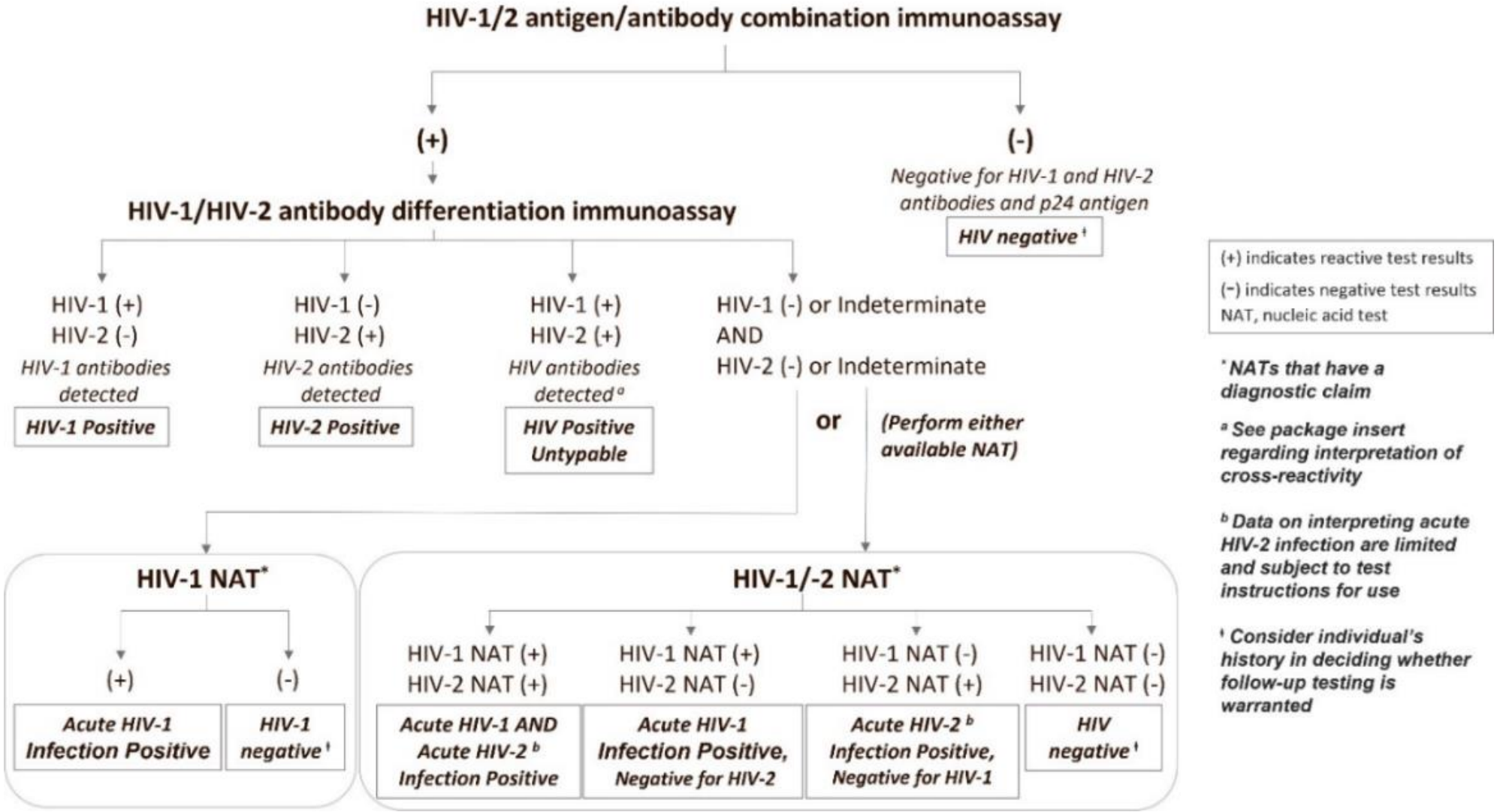
Recommended Laboratory Human Immunodeficiency Virus (HIV) Diagnostic Testing Algorithm



This figure shows the current recommended laboratory *HIV diagnostic testing algorithm* (1). The algorithm was updated to include approved HIV-1 and HIV-1/-2 nucleic acid tests with a diagnostic claim for step 3. See (1) for information on alternate, but not recommended, algorithms.

1. Laboratories should conduct initial testing for HIV with a U.S. Food and Drug Administration (FDA)-approved antigen/antibody immunoassay[a] 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 or HIV-1/-2 Nucleic Acid Test (NAT) or request a new specimen and repeat the algorithm according to CDC guidance (2, 3, 4, 5).
2. 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[b], or HIV antibodies, untypable (undifferentiated).
3. 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 or HIV-1/-2 NAT.
    - A reactive HIV-1 or HIV-2 NAT result and non-reactive or indeterminate HIV-1/HIV-2 antibody differentiation immunoassay result indicates laboratory evidence of acute HIV-1 or HIV-2 infection, respectively.
    - A negative HIV-1 or HIV-1/-2 NAT result and non-reactive or indeterminate HIV-1/HIV-2 antibody differentiation immunoassay result could indicate a false-positive result on the initial immunoassay or could occur in individuals using pre-exposure prophylaxis (PrEP), or who were treated early in infection with antiretroviral therapy, which can lead to low virus levels and delay or inhibit seroconversion.
    - 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 (6). Samples with a negative HIV-1/-2 NAT result do not need additional HIV-2 testing.
4. Laboratories should use the 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).

[a] 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 (2, 8).
[b] This includes specimens reported as HIV-2 positive with HIV-1 cross-reactivity (6).

(1) Technical Update for HIV Nucleic Acid Tests Approved for Diagnostic Purposes. https://stacks.cdc.gov/view/cdc/129018
(2) Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations https://stacks.cdc.gov/view/cdc/23447
(3) APHL Suggested Reporting Language for the HIV Laboratory Diagnostic Testing Algorithm https://stacks.cdc.gov/view/cdc/79272
(4) Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV-United States, 2016 https://stacks.cdc.gov/view/cdc/38856
(5) HIV Testing https://www.cdc.gov/hiv/testing/
(6) Technical Update on HIV-1/2 Differentiation Assays https://stacks.cdc.gov/view/cdc/40790
(7) Clinical Laboratory Improvement Amendments https://www.cdc.gov/clia/
(8) Use of the Determine HIV 1/2 Ag/Ab Combo Test with Serum or Plasma in the Laboratory Algorithm for HIV Diagnosis https://stacks.cdc.gov/view/cdc/48472

Food and Drug Administration-Approved Test Methods, Applicable to the HIV Diagnostic Testing Algorithm for Laboratories

As of January 1, 2024, the following United States Food and Drug Administration (FDA)-approved tests are available for use in the HIV Diagnostic Testing Algorithm for laboratories. The New York State Department of Health's preferred Logical Observation Identifiers Name and Codes (LOINC) for public health reporting in the Electronic Clinical Laboratory Reporting System (ECLRS) are listed.

Test Kit Name	Instrument Platform(s)	Test Manufacturer	Preferred LOINC and Result for ECLRS Reporting
Step 1. HIV-1/HIV-2 Ag/Ab combo immunoassay (screening assay)[1,2]			
HIV Ag/Ab Combo	Architect, Alinity	Abbott Laboratories	56888-1; Report Reactive results
Determine HIV-1/2 Ag/Ab Combo (Serum or plasma use only)	Not Applicable	Abbott Laboratories	75666-8; Report Antibody Reactive results or Antigen Reactive results or Antibody Reactive and Antigen Reactive results
Access HIV Ag/Ab Combo	DxI 9000	Beckman Coulter	56888-1; Report Reactive results
GS HIV Ag/Ab Combo EIA	Open, Evolis	Bio-Rad Laboratories	56888-1; Report Reactive results
BioPlex 2200 HIV Ag-Ab	BioPlex 2200	Bio-Rad Laboratories	56888-1 for HIV Ag-Ab; Report Reactive results[3] and 18396-2 for HIV-1 Ag; Report results and 29893-5 for HIV-1 Ab; Report results and 30361-0 for HIV-2 Ab; Report results
LIAISON XL Murex HIV Ab/Ag HT	LIAISON XL	DiaSorin	56888-1; Report Reactive results
HIV Combo	Vitros, ECi/ECiQ, 3600, 5600, XT 7600	Ortho Clinical Diagnostics	56888-1; Report Reactive results
Elecsys HIV combi PT	cobas e602	Roche Diagnostics	56888-1; Report Reactive results
Elecsys HIV Duo	cobas e801	Roche Diagnostics	56888-1 Report Reactive for HIV Ab and HIV-1 Ag[4] OR
	cobas e402		56888-1 Report Reactive for HIV Ab and HIV-1 Ag[4] and 31201-7 for HIV1+2 Ab; Report results and 18396-2 for HIV-1 p24 Ag; Report results
HIV Ag/Ab Combo (CHIV)	ADVIA Centaur, Atellica	Siemens Medical Solutions	56888-1; Report Reactive results

Test Kit Name	Instrument Platform(s)	Test Manufacturer	Preferred LOINC and Result for ECLRS Reporting
Step 2. HIV-1/HIV-2 antibody differentiation immunoassay (supplemental antibody assay)			
VioOne HIV Profile Supplemental Assay	Open	Avioq	95524-5 Report all result interpretations If individual HIV-1 and HIV-2 results are also reported, use: 29893-5 for all HIV-1 Ab results 30361-0 for all HIV-2 Ab results
Geenius HIV 1/2 Supplemental Assay	Geenius Reader	Bio-Rad Laboratories	80203-3 Report all final assay interpretations If individual HIV-1 and HIV-2 results are also reported, use: 68961-2 for all HIV-1 results 81641-3 for all HIV-2 results
Step 3. HIV nucleic acid test (supplemental RNA assay)			
Aptima HIV-1 Quant Dx Assay (Quantitative results: Plasma only) (Qualitative results: Plasma & serum)	Panther	Hologic	25835-0 Report all qualitative results 20447-9 Report all quantitative HIV-1 RNA copies/mL results 29541-0 Report all quantitative HIV 1 RNA Log_{10} results
Alinity m HIV-1 Assay (Quantitative results: Plasma only) (Qualitative results: Plasma & serum)	Alinity m	Abbott Molecular	25835-0 Report all qualitative results 20447-9 Report all quantitative HIV-1 RNA copies/mL results 29541-0 Report all quantitative HIV 1 RNA Log_{10} results
cobas HIV-1/HIV-2 Qualitative Assay	cobas 5800	Roche Diagnostics	25835-0 Report all HIV-1 RNA results 69353-1 Report all HIV-2 RNA results OR 96556-6 Report all results
	cobas 6800, 8800		25835-0 Report all HIV-1 RNA results 69353-1 Report all HIV-2 RNA results

[1] **Recommended Screening Immunoassays.** The CDC recommends that laboratories conduct initial testing with an FDA-approved HIV antigen/antibody (Ag/Ab) immunoassay. Less sensitive antibody-only assays are available but are not recommended**. Laboratories that use an antibody-only assay should include the following statement when reporting a negative screening result, "This screening assay may not detect acute HIV-1 infections."**

[2] **Determine HIV-1/2 Ag/Ab Combo.** The CDC's Technical Update: Use of the Determine HIV 1/2 Ag/Ab combo test with serum or plasma in the laboratory algorithm for HIV diagnosis (https://stacks.cdc.gov/view/cdc/48472) recommends that laboratories use an instrumented, laboratory-based HIV Ag/Ab screening immunoassay in Step 1 of the algorithm. However, for laboratories in which an instrumented Ag/Ab test is not feasible or practical, the Determine HIV-1/2 Ag/Ab Combo assay may be used with serum or plasma for Step 1 in the laboratory algorithm.

[3] **BioPlex 2200 HIV Ag-Ab Assay.** When the BioPlex overall result (HIV Ag-Ab) is reactive, report the overall result as well as all results, reactive and nonreactive, for the individual analytes (HIV-1 p24 Ag, HIV-1 Ab and HIV-2 Ab).

[4] **Elecsys HIV Duo.** When the Elecsys Duo overall result (HIV Ab and HIV-1 Ag) is reactive, report all available results i.e., overall result and (if possible) reactive and nonreactive results for the individual analytes (HIV1+2 Ab and HIV-1 p24 Ag).

Guidance for Interpretation of HIV RNA Test Results for Diagnostic Purposes (Step 3)

Three HIV nucleic acid tests (NATs) are approved by the United States Food and Drug Administration (FDA) for diagnostic use. This document provides guidance on the use of these HIV NATs in the third step of the current HIV Diagnostic Testing Algorithm. See https://www.cdc.gov/hiv/guidelines/recommendations/technical-update-for-hiv.html for additional guidance on the results and interpretations of the nucleic acid tests used for diagnostic purposes.

A. cobas HIV-1/HIV-2 Qualitative Test (Serum and Plasma)

The HIV-1/HIV-2 Qualitative test is presently the only FDA-approved qualitative NAT that provides and differentiates results for HIV-1 and HIV-2; this includes an overall result, individual results for HIV-1 and HIV-2, and a result interpretation for serum and plasma. Possible valid result combinations for the HIV-1/HIV-2 Qualitative test and interpretation are represented in the following table:

Target Results	Overall Result*	Interpretation
HIV-1 reactive and HIV-2 reactive.	Reactive	Target signal detected for HIV-1 and HIV-2.
HIV-1 reactive and HIV-2 non-reactive.	Reactive	Target signal detected for HIV-1. No target signal detected for HIV-2.
HIV-1 non-reactive and HIV-2 reactive.	Reactive	No target signal detected for HIV-1. Target signal detected for HIV-2.
HIV-1 non-reactive and HIV-2 non-reactive.	Non-Reactive	No target signal detected for HIV-1 or HIV-2.

*The reporting of overall result is not required from the cobas 5800 analyzer.

B. Aptima HIV-1 Quant Dx Assay (Serum and Plasma)

Result (copies/mL)*	Interpretation	Confirmatory Interpretation
Not detected**	Target not detected	Non-reactive for HIV-1 RNA
<30	Detected <30	Reactive for HIV-1 RNA
30 to 10,000,000	Detected and quantified	Reactive for HIV-1 RNA
>10,000,000	>10,000,000	Reactive for HIV-1 RNA

*Quantitative results can be reported on plasma samples only.
** A "Not detected" result should not be reported with a numerical value (*e.g.*, <30) to avoid confusion in conveying the absence or presence of detectable HIV-1 RNA.

C. Alinity m HIV-1 Assay

C.1.Plasma

For plasma samples, laboratories should interpret the HIV-1 RNA concentration as a qualitative result by following the 'User's Diagnostic Qualitative Interpretation' in the instructions for use, summarized in the below table.

Result (copies/mL)	Interpretation	Confirmatory Interpretation
Not detected*	Target not detected	Negative
<20	Detected <20	Positive
20 to 10,000,000	Detected and quantified	Positive
>10,000,000	>10,000,000	Positive

* A "Not detected" result should not be reported with a numerical value (*e.g.*, <20) to avoid confusion in conveying the absence or presence of detectable HIV-1 RNA.

C.2. Serum

For serum samples, quantitative results are not reported. Instead, only the qualitative results are reported as summarized in the table below.

Result	Interpretation
HIV-1 RNA not detected	Negative
HIV-1 RNA detected	Positive