

DRAFT Recommendations: Diagnostic Laboratory Testing for HIV Infection in the United States

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Definitions

Immunoassay generations:

- 1st – viral lysate antigens, designed for IgG detection (includes Western blot, IFA)
- 2nd – synthetic peptide or recombinant protein antigens, designed for IgG antibody detection
- 3rd – synthetic peptide or recombinant protein antigens, designed for IgM and IgG antibody detection
- 4th – synthetic peptide or recombinant protein antigens, p24 antibody, designed to detect IgM and IgG antibodies and p24 antigen

Acute HIV infection, for the purpose of these recommendations, is defined as the interval between the appearance of detectable HIV RNA and development of detectable IgG antibody.

Recommended Testing Algorithm

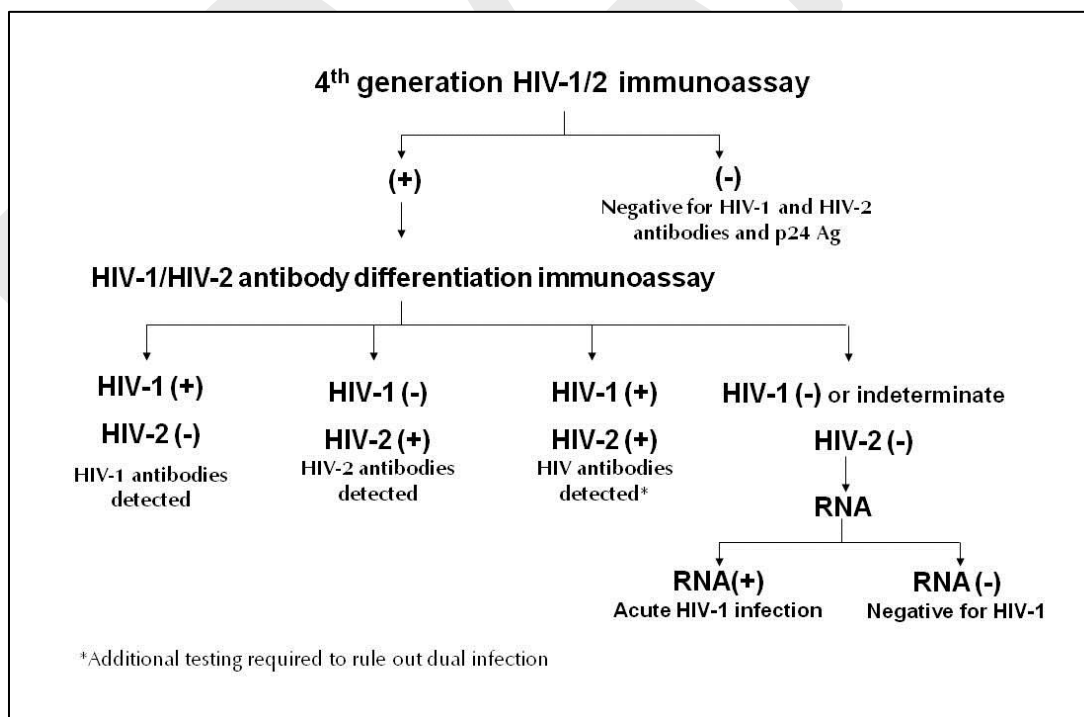


Figure 1: Recommended Testing Algorithm

1. An FDA-approved 4th generation HIV-1/2 immunoassay (IA) should be used as the initial test, to screen for acute HIV-1 infection and for established infections with HIV-1 or HIV-2.



2. Specimens with a reactive 4th generation IA (or repeatedly reactive, if repeat testing is recommended by the manufacturer) should be tested with an FDA-approved 2nd generation antibody IA that differentiates HIV-1 antibodies from HIV-2 antibodies.
3. Persons whose specimens give positive results on the initial IA and HIV-1/HIV-2 antibody differentiation IA should be considered positive for HIV-1 or HIV-2 antibodies and should initiate medical care that includes laboratory tests (such as viral load, CD4 determinations, and antiretroviral resistance assays) to confirm the presence of HIV infection, to stage HIV disease, and to assist in the selection of an initial antiretroviral drug regimen. *[DHHS Guidelines]*
4. Specimens that are reactive on the initial assay and negative on the HIV-1/HIV-2 antibody differentiation IA should be tested with an FDA-approved nucleic acid test (NAT) for HIV-1 RNA. Under these circumstances, a reactive NAT result indicates the presence of acute HIV-1 infection. A negative result indicates the absence of HIV-1 infection, either a false-positive result on the initial IA or rarely, recent HIV-2 infection. If HIV-2 infection is a possibility, a NAT for HIV-2 DNA can be considered. However, HIV-2 infection is rare in the United States, and there is no FDA-approved NAT for HIV-2.
5. This same testing algorithm beginning with a 4th generation immunoassay should be followed for specimens from persons with a preliminary positive rapid HIV test result.

Alternatives for use with other FDA-approved HIV tests

1. 3rd generation HIV-1/2 IA used as the initial test: perform subsequent testing as specified in the recommended algorithm. This alternative will miss some acute HIV infections in antibody-negative persons.
2. Alternative FDA-approved supplemental antibody test (e.g., HIV-1 Western blot or indirect immunofluorescence assay) used as the second test instead of an HIV-1/HIV-2 antibody differentiation IA: If negative or indeterminate, perform HIV-1 NAT; if HIV-1 NAT is negative, perform HIV-2 antibody IA. This alternative might misclassify HIV-2 infections as HIV-1, and incur additional costs, and increases turnaround time for test results.
3. HIV-1 NAT as second test instead of the HIV-1/HIV-2 antibody differentiation IA: If HIV-1 NAT result is negative, perform an HIV-1/HIV-2 antibody differentiation IA or other FDA-approved supplemental antibody test. If result of this antibody test is negative or indeterminate, perform an HIV-2 antibody test. This alternative fails to distinguish acute HIV infection from established infection, increases turnaround time for test results and incurs additional costs.

How these recommendations differ from previous recommendations

1. Supersedes 1989 WB, 1992 HIV-2, and 2004 rapid test confirmation recommendations
2. Tests for both virologic (p24 antigen) and serologic (antibody) markers of HIV infection
3. Incorporates NAT to resolve discordant IA results, reduce indeterminate test results, and identify acute HIV infection
4. All antibody-positive specimens tested for HIV-2; previously, only those with negative or indeterminate HIV-1 Western blot received specific HIV-2 testing.
5. Emphasizes sensitivity during initial testing. Rare false-positive antibody test results might occur; will be resolved during subsequent laboratory testing (e.g., HIV viral load) recommended as part of initial clinical evaluation.