GEMS
GLOBAL EVALUATION OF MICROBICIDE SENSITIVITY

# HIV Testing Strategies in PrEP Clients

Eligibility for PrEP initiation or continuation requires confirmation that the person is HIV uninfected, to minimize the risk of HIV drug resistance.[1] The HIV detection period following transmission differs based on the point of care test (see HIV Infection Timeline and Table 1), leaving the possibility that a person may use PrEP with an unknown acute HIV infection. The World Health Organization (WHO) recommends HIV testing strategies to identify HIV infection and therefore, minimize the risk of HIV drug resistance for those using PrEP.[2] GEMS modeling results support WHO recommendations for frequency of HIV testing for PrEP users.[3] Using the WHO recommendations, and this factsheet, policy makers and PrEP project implementers should consider HIV testing strategies specific to their PrEP program; including the use of more sensitive HIV testing methods to identify acute HIV infection.

There are three types of HIV tests used that provide same day results. These tests, along with the GEMS Acute Seroconversion Assessment, available at gems.pitt.edu/toolkit, are recommended for PrEP programs to identify acute or established HIV infection prior to PrEP provision.

## Definitions

**Acute Infection:** Occurs immediately after a person contracts HIV; characterized by initial burst of viremia; often includes symptoms such as fever or lymphadenopathy. NAAT and p24 Antigen HIV tests are able to detect acute infection.

**EIA:** Enzyme Immunoassay, also known as the enzyme-linked immunosorbent assay (ELISA), are tests that detect HIV antibodies in your blood.

**Established Infection:** Levels of p24 antigen begin to decline, HIV RNA begins to stabilize at a level that is normally still detectable and HIV antibody levels begin and will continue to rise.

**HIV Antibody:** Antibodies are proteins generated by the immune system as a defense against infections. Antibodies to HIV present distinctive targets for screening tests.

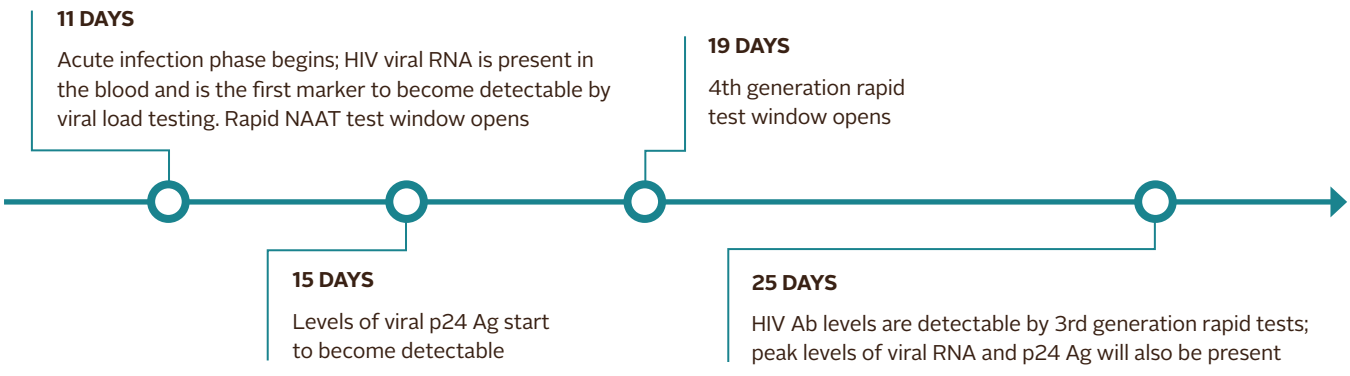
**HIV Diagnostic Testing Window Period:** The time between when a person becomes infected with HIV until the time a test can detect infection.

**HIV Viral Load Testing:** HIV viral load test measures the amount of HIV genetic material (RNA) in the blood.

**HIV Viral p24 Antigen:** A viral protein in blood that antigen assays measure. HIV viral p24 antigen is detectable earlier than HIV antibodies during acute infection.

**Recent Infection:** Typically occurs up to 6 months after infection.

## HIV Infection Timeline: For Testing and Diagnosis[5,9,11]

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## Table 1: Characteristics of Available Point of Care and Rapid HIV Tests

| HIV Assay Group | 3rd generation point of care rapid diagnostic test (RDT) | 4th generation point of care RDT | Rapid NAAT (HIV RNA Viral Load) |
|---|---|---|---|
| **Description** | • Detect antibodies only<br>• Currently part of national HIV testing algorithms and WHO recommendations for HIV diagnosis | • Detect both antibodies and the p24 antigen | • Nucleic Acid Amplification Tests (NAAT) measure viral HIV RNA; the first marker to become detectable after a person is infected<br>• Recommended in suspected cases of acute infection |
| **Common Assays[4]** | • Determine HIV-1/2<br>• STAT-PAK HIV-1/2<br>• Uni-gold Recombigen HIV-1/2<br>• Oraquick Advance HIV-1/2 | • Alere HIV Combo | • Gene Xpert HIV-1 Viral Load<br>• Aptima HIV-1 Quant DX |
| **Reactive Infection Phase** | Established | Acute through established | Acute through established |
| **Test Window Period*[5, 6]** | 26 – 50 days after infection | 19 – 31 days after infection | 11 days after infection |
| **Allowable specimen types*** | Fingerstick and venous whole blood, plasma | Fingerstick and venous whole blood, plasma | Plasma |
| **Time to test completion**** | 20 mins | 20 mins | 1.5 – 2.5 hrs |
| **Advantages** | • Quick and easy to use<br>• Minimal supplies/training required<br>• No blood processing required<br>• Inexpensive | • Quick and easy to use<br>• Minimal supplies/ training required<br>• No blood processing required<br>• Inexpensive compared to Viral Load tests; however, generally more costly than 3rd generation tests | • Able to detect infection the earliest |
| **Disadvantages** | Least sensitive of all assays; however, some 3rd generation tests are able to detect infection at about four weeks, such as the Determine HIV-1/2. | • Data is still limited on the reliability for detecting infection earlier[7,8] | • Not a screening/diagnostic assay; an HIV infected person can have an undetectable HIV RNA result<br>• Most expensive to perform/ maintain<br>• Requires blood processing and skilled technicians |

*These numbers may vary based on the patient's immune response, the test used and sample type.
**Assay specific package inserts must be referenced for specific information about this topic.

## HIV Testing Recommendations for PrEP Implementation Programs

### Rapid Tests

- HIV point of care or rapid tests are important for immediate HIV diagnosis, are convenient, and easy to use.
- Consider use of a 4th generation test in individuals using PrEP to detect HIV infection as early as possible, if feasible, affordable, and performed according to quality assurance standards.
- Rapid NAAT (viral load) tests are useful for confirming infections detected by rapid tests and helping to identify acute infection.
- False negative test results can occur, especially with oral based tests used for HIV self-testing. Oral fluid-based rapid tests are not recommended for PrEP users.[10]

### Symptomatic PrEP Clients

- If a PrEP user reports recent HIV risk behavior, (e.g, unprotected sexual intercourse, needle sharing), and exhibits symptoms reflective of acute infection, conduct HIV testing per the HIV testing algorithm. If the test is negative, consider a confirmatory HIV test to identify an acute infection.
- For confirmation testing, conduct an EIA or supplemental test and an HIV viral load test:
  - A person who has a negative or indeterminate antibody test result, but a detectable viral load, should not use PrEP until additional HIV confirmatory testing is done.
  - If the confirmatory test is not done at the time of the visit, provide condoms and appropriate counseling, and ask the client to return in 30 days for another HIV test.


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3. Effectiveness and cost-effectiveness of condomless sex-targeted PrEP in KwaZulu Natal, South Africa: Influence of HIV testing frequency and 1st line ART regimen. A. Phillips, V. Cambiano, R. Homan, T. Rehle, G. Meyer-Rath, L.F. Johnson, F. Tanser, S. Moyo, D. Castor, E.S. Russell, R.V. Barnabas, U. Parikh, J. Mellors, P. Revill. AIDS 2018. Poster.
4. For a list of WHO Pre-qualified tests, visit: http://www.who.int/diagnostics_laboratory/evaluations/pq-list/hiv-rdts/public_report/en/
5. Cohen, et. al. The Detection of Acute HIV Infection. JID; 2010:202(S2).
6. Delaney, et. al. Time Until Emergence of HIV Test Reactivity Following Infection With HIV-1: Implications for Interpreting Test Results and Retesting After Exposure. CID; 2017:64.
7. Fitzgerald, et. al. Diagnosing acute HIV infection at point of care: a retrospective analysis of the sensitivity and specificity of a fourth-generation point-of-care test for detection of HIV core protein p24. Sex Transm Infect; 2016: 0 (1-2).
8. Klausner and Stafylis. Evaluation of two 4th generation point-of-care assays for the detection of Human Immunodeficiency Virus infection. Plos One; 2017:12(8).
9. Branson, et. al, Centers for Disease Control and Prevention (US), Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations, June 27, 2014.
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