Determining HIV Drug Resistance

**Goal of ART:**
- Achieving and maintaining an undetectable viral load is the primary goal of ART.

**Resistance testing:**
- Resistance testing is recommended when immunocompromise is suspected (A1)

Resources: Drug Resistance Mutations

New resistance mutations and the emerging clinical significance of these mutations frequently change. See the following for more information on drug resistance mutations and resistance testing:

- Stanford University HIV Drug Resistance Database: https://hivdb.stanford.edu/
- HIV Resistance Response Database Initiative: https://www.hivrdi.org/
- Los Alamos National Laboratory HIV Databases: https://www.hiv.lanl.gov/content/index
- HIV French Resistance Database: https://hivfrenchresistance.org/

**Note:** Viral load is defined as an HIV RNA level (viral load) >200 copies/mL.

**Determining HIV Drug Resistance continued:**

HIV clinical resource

Visit HIVGuidelines.ORG to learn more or view complete guide

Virologic and Immunologic Monitoring in HIV Care and HIV Resistance Assays

NYSDOH AIDS Institute HIV Clinical Guideline

JUNE 2023

All recommendations

P.1

Virologic and Immunologic Monitoring Intervals

- To assess a patient’s response to ART and immunologic status and to identify when a change in ART regimen is needed, clinicians should perform plasma HIV-1 RNA level (viral load) and CD4 count testing as detailed in Table 1: Recommended Viral Load and CD4 Count Monitoring in Nonpregnant Patients With HIV. (A1)
- Clinicians should address modifiable barriers to adherence and engagement in care to help ensure optimal virologic suppression. Modifiable barriers may include, but are not limited to, substance use, mental illness, other chronic medical conditions, ART-associated adverse medication effects, unstable housing, or low health literacy. (A2)
- Quarterly CD4 count monitoring is no longer recommended for nonpregnant patients receiving ART who have consistently undetectable viral load levels and CD4 counts >200 cells/mm³ (see Table 1 for recommended intervals). (A2)

Determining HIV Drug Resistance

- Clinicians should consult with an expert HIV care provider to interpret the results of resistance assays because such results can be complex. (A3)
- The NYSDOH AI Clinical Education Initiative line is available for phone consultation: 866-637-2342.
### Table 1: Recommended Viral Load and CD4 Count Monitoring in Nonpregnant Patients With HIV [a]

<table>
<thead>
<tr>
<th>Event</th>
<th>HIV RNA Viral Load</th>
<th>CD4 Count</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Entry into care                            | Baseline viral load (A1) | Baseline CD4 count (A1) | • If a patient is not taking ART, recommend initiation [b] (A1)  
  • Monitor as below                                                                     |

#### Patients Taking ART

<table>
<thead>
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<th>HIV RNA Viral Load</th>
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</table>
| ART initiation or change to address virologic failure |                   |           | • Within 4 weeks after ART start or change (A3)  
  • At least every 8 weeks until complete virologic suppression is documented (A3)  
  • Virologic failure occurs when a viral load <200 copies/mL is either not achieved or not maintained  
  • Virologic suppression is defined as a viral load <20 to <50 copies/mL obtained with a highly sensitive assay |
| ART change for simplification or due to adverse effects | Within 4 weeks after ART change, then as below (A3) | Monitor as below for documented virologic suppression | -- -- |
| Documented viral suppression                        |                   |           | • At least every 6 months if CD4 count is ≤350 cells/mm³ (B2)  
  • Optional if CD4 count is >350 cells/mm³ (B2)  
  • Assess for adherence and drug–drug interactions (A3)  
  • Obtain resistance testing (A1) |
| New HIV RNA ≥500 copies/mL after previous viral suppression | Repeat viral load test 2 weeks after first result (A2) | Obtain CD4 count if previous result is >6 months old (B3) | • Assess for adherence and drug–drug interactions (A3)  
  • Obtain resistance testing (A1) |
| New HIV RNA level over the limit of detection of sensitive assays, 20 to 50 copies/mL, but <500 copies/mL after previous viral suppression | Repeat viral load test within 4 weeks to differentiate low–level transient viremia (“blip”) from virologic failure [c] (A2) | If repeat viral load is detectable, obtain CD4 cell count if previous result is >6 months old (B3) | • Assess for adherence and drug–drug interactions (A3)  
  • If repeat viral load is detectable, consider resistance testing [d] (B3)  
  • Patients with low-level viremia ≤200 copies/mL over a period of 12 months without demonstrated failure may continue routine testing intervals of at least every 4 months [e] |

#### Patients Not Taking ART

| CD4 count ≤500 cells/mm³ (A2) | At least every 4 months | At least every 4 months | At every visit, recommend ART initiation [b] |
| CD4 count >500 cells/mm³ (A2) | At least every 6 months | At least every 6 months | At every visit, recommend ART initiation [b] |

**Abbreviation:** ART, antiretroviral therapy.

**Notes:**

- a. For recommendations on virologic monitoring in pregnancy, see DHHS: Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.
- b. See NYSDOH AI guideline Rapid ART Initiation.
- c. An ART regimen should not be changed based on a single viral load elevation. The risk of virologic rebound (breakthrough) increases when values are ≥500 copies/mL.
- d. Standard genotypic tests may not provide resistance results when viral load is low. For repeated low–level viremia, an assay that detects resistance mutations in archived proviral DNA is available; however, clinical data are insufficient to recommend for or against its use in the patient care setting.
- e. In patients with low–level viremia, clinicians should consult with an experienced HIV care provider; low–level viremia can be due to multiple causes, and its clinical effect is not clear.

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### Table 3: FDA-Approved Quantitative HIV-1 RNA Assays for Viral Load Monitoring

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Method</th>
<th>Lower and Upper LOQ</th>
</tr>
</thead>
</table>
| Abbott RealTime HIV-1 (Abbott Laboratories)  | Real-time PCR | • 40 copies/mL [a]  
  • 1,000,000 copies/mL |
| Cobas Amplicent/Cobas TaqMan HIV-1 Test, version 2.0 (Roche Diagnostics) | Real-time PCR | • 20 copies/mL  
  • 1,000,000 copies/mL |
| Cobas HIV-1 quantitative NAT for use on Cobas 6800/8800 systems (Roche Diagnostics) | Real-time PCR | • 20 copies/mL  
  • 1,000,000 copies/mL |
| Cobas TaqMan HIV-1 Test, v2.0 for use with the high pure system (Roche Diagnostics) | Real-time PCR | • 34 copies/mL  
  • 1,000,000 copies/mL |

**Abbreviations:** FDA, U.S. Food and Drug Administration; LOQ, limit of quantification; NAT, nucleic acid test; PCR, polymerase chain reaction.

**Note:**

- a. This lower LOQ applies when 1.0 mL of plasma is used. When 0.5 and 0.2 mL of plasma are used, the lower LOQ is 75 copies/mL and 150 copies/mL, respectively.