HIV-1 Infection

Laboratory Testing for Diagnosis and Management

Laboratory testing plays a central role in the spectrum of clinical care for patients with human immunodeficiency virus (HIV) infection. This Test Guide provides an overview of the use of laboratory tests in the screening, diagnosis, and management of HIV infection. It also provides an Appendix that lists antiretroviral drugs used to treat HIV infection.

The material provided herein is for informational purposes. Treating physicians should base treatment or diagnostic decisions on their education, learning, and experience and the clinical assessment of the patient.

SCREENING AND DIAGNOSIS

The Centers for Disease Control and Prevention (CDC) recommends HIV screening for all adolescents and adults between the ages of 13 and 64 years.[1] Annual screening is recommended for those with risk factors.[1] Screening is also recommended for all pregnant women.[1] Tests offered by Quest Diagnostics for screening and diagnosis can be found in **Table 1**.

Fourth-Generation Testing Algorithm

Newer screening tests that can detect HIV infection substantially earlier than Western blots have created a need for an algorithm with supplemental testing that is more sensitive for acute infection.[2] The CDC has proposed an HIV testing algorithm designed to 1) detect acute infections more often; 2) reduce the frequency of indeterminate results on supplemental testing; and 3) differentiate HIV-1 and HIV-2 antibodies.[3,4] This algorithm has been reported to have high sensitivity (>99.7%) and specificity (100%)[2,3] and has been adopted by the Clinical Laboratory Standards Institute (CLSI).[5]

HIV Antibodies and p24 Antigen

The fourth-generation testing algorithm begins with a screening test for HIV-1/HIV-2. The screening test of choice is a fourth-generation combination assay that detects not only HIV IgM and IgG antibodies, but also HIV p24 antigen. HIV p24 antigen becomes detectable before seroconversion but rapidly disappears thereafter. Thus, the antigen component allows detection of infection during the pre-seroconversion window period, while the antibody component allows detection after seroconversion. Reports suggest that fourth-generation assays can detect acute infection a median of 5 to 7 days before third-generation antibody assays,[5-7] although this interval can range from roughly 0 to 20 days. This type of antigen/antibody combination assay has >99.7% sensitivity and >99.3% specificity for HIV infection and identifies most (>80%) acute infections that would otherwise require nucleic acid testing for detection.[8,9] As with third-generation assays, reactive screening results require confirmation with a supplemental test.

HIV-1/HIV-2 antibody differentiation assays tend to detect antibodies earlier than Western blots[2,10] and are the recommended supplemental test in the fourth-generation algorithm.[5] These immunoassays not only detect HIV-1 and HIV-2 antibodies but can also differentiate between them. This can have important treatment implications, as HIV-2 does not respond to some antiretroviral agents. Results are interpreted as reactive for HIV-1, reactive for HIV-2, reactive for HIV (nondifferentiated), or nonreactive. A reactive result confirms the presence of HIV-1

Table 1. Laboratory Tests Used for Screening and Diagnosis of HIV Infection

Test Code	Test Name	Primary Clinical Use and/or Differentiating Factors
91431	HIV-1/2 Antigen and Antibodies, Fourth-Generation, with Reflexes[a]	Screen for and confirm HIV-1 and HIV-2 infection, including acute infection; uses "fourth-generation" screening immunoassay; reflexes are consistent with CDC proposed algorithm
16185	HIV-1 RNA, Qualitative TMA	Detect HIV-1 infection, including acute infection; confirm HIV-1 infection in individuals with repeatedly reactive initial results, including those with nonreactive HIV-supplemental test results; detect HIV-1 infection in infants up to 24 months of age
34977	HIV-2 DNA/RNA Qualitative Real-Time PCR[b,c]	Follow-up evaluation of negative results on confirmatory HIV-1 RNA testing, when clinically indicated[5]

[a] Reflex tests are performed at an additional charge and are associated with an additional CPT code(s).
[b] This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by FDA. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.
[c] Polymerase chain reaction (PCR) is performed pursuant to a license agreement with Roche Molecular Systems, Inc.

and/or HIV-2 antibodies, whereas nonreactive (or indeterminate) results prompt confirmation by HIV-1 RNA testing.[5]

HIV-1 RNA

HIV-1 RNA can be detected earlier than HIV antibodies and p24 antigen: as soon as 6 to 12 days after exposure and approximately 12 days before an HIV antibody test and 7 days before a p24 antigen test becomes positive.[6] Ultrasensitive nucleic acid amplification-based tests such as the HIV-1 qualitative transcription-mediated amplification (TMA) assay (sensitive to 30 copies/mL) are thus useful for detecting suspected infection soon after exposure. Positive HIV-1 RNA results in the absence of detectable antibodies indicate acute infection; negative results are consistent with absence of HIV-1 infection. A negative HIV-1 RNA test may be followed with an HIV-2 DNA/RNA test if clinically warranted. When nucleic acid testing is used to diagnose acute infection, subsequent seroconversion should be documented.[5]

Infection in Newborns

HIV-1 RNA testing is also useful for detecting HIV-1 infection in high-risk infants (eg, those born to mothers with HIV infection).[11] Guidelines recommend virologic (RNA or DNA) testing of perinatally-exposed, nonbreastfed infants at 1 to 2 months of age unless they are receiving antiretroviral prophylaxis. If receiving prophylaxis, infants should be tested 2 to 4 weeks after discontinuation.[11] HIV-infected women who are breastfeeding should be counseled to stop. The infant should be tested immediately and at 4 to 6 weeks, 3 months, and 6 months after breastfeeding is discontinued.[11]

Antibody-based testing is not appropriate in high-risk infants younger than 18-24 months, as maternal antibodies can cross the placenta and be detected in the infant for extended periods after birth. At present, p24 antigen testing is also not recommended because of low sensitivity and specificity relative to other virologic assays in the early months after birth.[11] The qualitative HIV-1 RNA TMA assay can be used as the initial test. Positive results need to be followed up with a repeat virologic test on a second sample.[11]

MANAGEMENT

This section provides a brief overview of tests used in the management of HIV infection (**Figure**) along with lists of commonly ordered assays (**Tables 2 and 3**).

Monitoring Immune Status and Viral Load

CD4 (Lymphocyte Subset Testing)

The CD4+ T-cell (CD4) count is the most valuable indicator of immune status in HIV-infected patients and is an important factor in determining when to initiate prophylaxis for opportunistic infections.[13] Although antiretroviral therapy is recommended for all patients with HIV-1 infection, CD4 count still provides an indication of the urgency of beginning treatment. For patients who do not immediately begin therapy, CD4 counts should be monitored every 3-6 months.[13] CD4 measurement also serves as the strongest predictor of disease progression and survival.[13] In general, the risk of opportunistic infections and HIV-1-associated malignancies increases as the CD4 count decreases. The trend in counts is more important than any single value; a 30% or greater change in the absolute CD4 count between tests, or a 3-percentage point change in the CD4 percentage, is considered clinically significant.[13]

The CD4 count should be measured 3 months after antiretroviral treatment is initiated and then every 3 to 6 months to help assess immunologic response and the need to initiate or discontinue treatment for opportunistic infections.[13] After 2 years of antiretroviral treatment, CD4 counts can be measured less frequently (every 12 months) for stable patients with suppressed viremia unless new treatment with interferon, corticosteroids, or antineoplastic agents is initiated.[13]

CD4 counts exhibit substantial diurnal variation (counts are generally lower in the morning) and may be affected by medications or transiently depressed by an intercurrent illness. Because of the potentially wide biologic variation, obtaining 2 measurements may be advisable if the CD4 count will affect treatment decisions; a third measurement would be required if the results are discordant.

HIV-1 RNA, Quantitative

HIV-1 viral load is the primary marker of antiretroviral treatment effectiveness. Before treatment initiation, the viral load provides information on the risk of disease progression and establishes a baseline for assessing the effect of antiviral treatment. After treatment is initiated, a primary goal is to decrease the viral load below the limits of detection (LODs) of the available assays within 12 to 24 weeks.[13] Thereafter, viral load measurement is useful in assessing the continuing effectiveness of therapy. A confirmed viral load >200 copies/mL indicates virologic failure.[13]

The recommended frequency of viral load testing depends on the stage of disease management[13]:

- Entry into care/prior to treatment initiation: at the time of diagnosis; repeat testing in patients not initiating treatment is optional
- Start of treatment: immediately prior to initiation of therapy and every 4 to 8 weeks after treatment initiation until viral load decreases below the level of detection (<20 to 75 copies/mL)
- Change in regimen because of suboptimal viral suppression: 2 to 8 weeks after change
- Change in regimen because of treatment toxicity or regimen simplification: 4 to 8 weeks to assess the effectiveness of the new regimen
- Continuing therapy/stable antiretroviral regimen: every 3 to 4 months or when there is a clinical event or significant decline in CD4 count; consider longer intervals (every 6 months) for patients who are adherent to therapy and exhibit long-term suppression of viral load (>2 years) and stable immunologic status

Figure. Laboratory Tests Used in the Management of Confirmed HIV-1 Infection

Pre-ART		Post-ART Initiation					
Baseline	Pre-ART Follow-Up	ART Initiation or Modification	Soon after ART Initiation or Change	Every 3-6 Months	Every 6 Months	Every 12 Months	ART Failure
• CD4 count/ percentage • HIV viral load • Genotypic resistance testing (consider INSTI genotype test if transmitted resistance is a concern) • Complete blood count with differential • Chemistry profile including Na, K, Cl, HCO_3/ CO_2, BUN, creatinine, eGFR • Fasting lipid profile • Liver function tests including ALT, AST, ALP, total and direct bilirubin • Fasting glucose or hemoglobin A1c • Urinalysis • HAV, HBV, and HCV serology (if HCV positive, confirm with HCV RNA test) • Pregnancy test in women of childbearing age	• CD4 count (q3-6 mo) • HIV viral load optional • Complete blood count with differential (q3-6 mo) • Chemistry profile (q6-12 mo) • Liver function (q6-12 mo) • Fasting glucose or hemoglobin A1c (annually unless abnormal) • Fasting lipid profile (annually unless abnormal)	• CD4 count • HIV viral load • Genotypic resistance testing (optional if done at baseline); consider INSTI genotype test if transmitted resistance is a concern • *HLA-B*5701* testing if considering abacavir • Tropism testing if considering a CCR5 antagonist • Complete blood count with differential • Chemistry profile • Liver function • Fasting glucose or hemoglobin A1c • Fasting lipid profile • Urinalysis • HBV serology if HBsAg neg at baseline and not immune • Pregnancy test in women of childbearing age	• HIV viral load (q2-4 weeks; repeat q4-8 weeks until undetectable) • Complete blood count with differential for patients on zidovudine • Chemistry profile • Liver function • Fasting lipid profile (within 1-3 mo) • Fasting blood glucose or HbA1c (within 1-3 mo)	• CD4 count 3 mo after ART initiation, then q3-6 mo for first 2 years; extend to q12 mo if viral load undetectable and CD4 300-500 cells/ mm^3 • HIV viral load q3-4 mo; consider longer interval (q6 mo) if well controlled (see text) • Complete blood count with differential for patients on zidovudine or if CD4 testing is done • Chemistry profile • Liver function • Fasting glucose or hemoglobin A1c if borderline or abnormal at previous evaluation; otherwise q12 mo	• Complete blood count with differential • Fasting lipid profile if borderline or abnormal at last evaluation • Urinalysis for patients with HIV-associated nephropathy or patients receiving tenofovir	• CD4 count q12 mo if viral load undetectable and CD4 300-500 cells/ mm^3 • Fasting lipid profile if normal at previous evaluation • Fasting glucose or hemoglobin A1c if normal at previous evaluation • Urinalysis • HBV serology if patient nonimmune and not chronically infected • HCV serology for at-risk patients if negative at baseline	• CD4 count • HIV viral load • Resistance testing; consider including INSTIs if part of the failed regimen or being considered for treatment • Tropism testing if considering treatment with CCR5 antagonist or on failure of such treatment • *HLA-B*5701* testing if considering abacavir

Renal function determinations should include an estimation of creatinine clearance or glomerular filtration rate (eGFR). Resistance testing is not useful when changing therapy while a patient has an undetectable viral load. After initiating ART, the CD4 count can be monitored every 12 months (as opposed to 3-6 months) in clinically stable patients with suppressed HIV viral load. Prolonged intervals (every 6 months, rather than 3-4 months) for HIV viral load testing may be considered in patients who are adherent to therapy and exhibit long-term (>2 years) suppression of viral load and stable clinical and immunologic status. Patients receiving tenofovir may benefit from phosphorus measurement, since hypophosphatemia is a reported side-effect. References 12 and 13 provide additional guidance on laboratory evaluations that are not directly related to antiretroviral treatment or that apply to specific patient populations. These include cardiovascular and metabolic markers, testosterone testing (men), Pap testing, and tests for comorbid infectious diseases such as tuberculosis, *Toxoplasma gondii*, cytomegalovirus (CMV), varicella zoster virus, syphilis, trichomoniasis, chlamydia, gonorrhea, and human papillomavirus. ART indicates antiretroviral therapy; INSTI, integrase strand transfer inhibitor; Na, sodium; K, potassium; Cl, chloride; HCO_3/CO_2, bicarbonate/carbon dioxide; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; HAV, HBV, HCV, hepatitis A, B, C virus, respectively; HBsAg, hepatitis B surface antigen; q, every.

This figure was adapted by Quest Diagnostics from IDSA[12] and DHHS[13] guidelines. It is provided for informational purposes only and is not intended as medical advice. A physician's test selection and interpretation, diagnosis, and patient management decisions should be based on his/her education, clinical expertise, and assessment of the patient. See IDSA[12] and DHHS[13] guidelines for detailed recommendations on the use of laboratory testing in the management of HIV infection.

Table 2. Laboratory Tests Used for Monitoring HIV-1 Infection[a]

Test Code	Test Name	Primary Clinical Use and/or Differentiating Factors
Lymphocyte Subset Testing		
8360	Lymphocyte Subset Panel 5 Includes absolute lymphocyte count, absolute CD4, and percentage CD4.	Monitor urgency of therapy initiation; monitor cellular immunocompetence
HIV-1 Viral Load Testing		
40085	HIV-1 RNA, Quantitative, Real-Time PCR[b]	Evaluate prognosis; assess effectiveness of ART and need to switch treatment regimen Reportable range: 20–10,000,000 HIV-1 RNA copies/mL
91691	HIV-1 RNA, Quantitative Real-Time PCR with Reflex to Genotype (RTI, PI, Integrase)[b,c]	Evaluate prognosis; assess effectiveness of ART and need to switch treatment regimen. See **Table 3** for clinical use of genotypic assays

ART, antiretroviral therapy.
[a] This test listing is not intended to be comprehensive. For additional testing options, consult the Quest Diagnostics online Test Center (QuestDiagnostics.com/testcenter). Components of panels and reflex tests may be ordered individually.
[b] Polymerase chain reaction (PCR) is performed pursuant to a license agreement with Roche Molecular Systems, Inc.
[c] Reflex tests are performed at an additional charge and are associated with an additional CPT code(s).

Quest Diagnostics offers an FDA-cleared HIV-1 real-time polymerase chain reaction (PCR) assay for quantitation of HIV-1 RNA in plasma. A change in viral load of 3-fold (0.5 $\log_{10}$ copies/mL) or greater is considered statistically significant.[13]

Antiretroviral Drug Selection

HIV-1 Drug Resistance Testing

The development of drug-resistant HIV-1 variants is an important cause of virologic failure (ie, persistent viremia in the presence of drug treatment). Resistance assays are useful for selecting active drugs when changing regimens because of virologic failure or suboptimal reduction in viral load. Genotypic testing is recommended for patients on their first or second regimen, with the addition of phenotypic testing for patients with complex drug resistance patterns.[13] Ideally, testing should be performed on samples obtained while the patient is still receiving the failing regimen. If samples are taken beyond 4 weeks after a drug is withdrawn, resistant variants may not be detected but may re-emerge if the drug is reinstated. Because drug-resistant HIV-1 variants can be transmitted and may affect response to the initial drug regimen, resistance testing (preferably genotypic) is recommended upon entry into care; if therapy is not begun soon after entry into care, resistance testing may be repeated before treatment initiation to guide selection of the starting regimen.[13]

Quest Diagnostics offers genotypic resistance testing with a rules-based resistance prediction.

HIV-1 Genotype

HIV-1 genotyping identifies mutations that may confer drug resistance. Quest Diagnostics employs a rules-based algorithm developed by experts to interpret the results of this mutation analysis. Thus, predicted drug resistance patterns are reported in addition to the actual mutations. Tests for resistance to currently available protease, reverse transcriptase, and integrase strand transfer inhibitors are available (see **Table 3**).

The absence of resistance-associated mutations does not necessarily imply drug susceptibility; mutations in minor viral populations may not be detected but may become predominant in the future.

HIV-1 Coreceptor Tropism Testing

HIV-1 coreceptor tropism testing helps determine eligibility for treatment with CCR5 antagonists, a class of entry inhibitor. HIV-1 utilizes the CD4 cell surface receptor and 1 of 2 chemokine receptors, CCR5 or CXCR4, to infect cells. CCR5 antagonists such as maraviroc inhibit HIV-1 by binding to CCR5 and are only effective against R5-tropic viruses, which exclusively utilize the CCR5 coreceptor. They do not effectively inhibit either X4-tropic viruses, which exclusively utilize the CXCR4 coreceptor, or dual/mixed (D/M)-tropic viruses, which can utilize both X4 and R5. About 15% to 20% of treatment-naïve and 50% of treatment-experienced patients harbor X4 and D/M viruses.[14] Thus, tropism testing is required before initiating an R5 antagonist to exclude patients with X4 or D/M tropic virus.

Phenotypic tropism testing is generally preferred because of a greater weight of supporting evidence, but genotypic tropism testing is considered an alternative because of its lower cost and faster analytical times.[13] The Quest Diagnostics' genotypic tropism test is comparable to a high-sensitivity phenotypic test in distinguishing between virologic responders and nonresponders.[15] It utilizes next-generation DNA sequencing (ultradeep sequencing) to detect HIV-1 envelope V3 variants associated with X4 and R5 utilization.

Standard coreceptor tropism testing requires a viral load of at least 1,000 HIV-1 RNA copies/mL. For patients with lower viral

loads, the sequencing assay can be performed on proviral HIV-1 DNA rather than HIV-1 RNA.

*HLA-B*5701* Typing

The nucleoside reverse transcriptase inhibitor abacavir is associated with a 2% to 9% risk of a hypersensitivity reaction.[16] Susceptibility to this serious and sometimes fatal reaction has been associated with a specific human genetic variation known as *HLA-B*5701*. Pharmacogenetic screening for *HLA-B*5701* is recommended for abacavir-naïve patients and before reinitiation of abacavir in previously treated patients.[16] A negative result indicates that the patient is unlikely to have a hypersensitivity reaction to abacavir but does not rule out this possibility. A positive result indicates that alternatives to abacavir should be used for treatment. This test uses PCR amplification followed by hybridization with sequence-specific oligonucleotide probes to detect the *HLA-B*5701* allele.

Monitoring Patient Health

Blood Count, Basic Chemistry, Glucose, and Lipid Testing

Both HIV infection and the drugs used to treat it can have adverse effects on various organ systems. Moreover, because patients with HIV infection now tend to live normal lifespans, more emphasis is being given to routine screening. Periodic monitoring of patient health after entry into care typically includes complete blood count, basic chemistry tests, markers of liver and kidney function and bone health, and evaluation of fasting glucose and lipid profile (**Figure**). Please see current guidelines for comprehensive monitoring recommendations[12,13] and refer to the Quest Diagnostics' online Test Center for testing options.

Testing for Comorbid Conditions

Table 4 describes tests used to evaluate conditions that are often associated with HIV infection. Current guidelines address testing for several comorbid infectious diseases, including tuberculosis, viral hepatitis (A, B, and C), trichomoniasis, cytomegalovirus, varicella zoster virus, chlamydia, gonorrhea, syphilis, and *Toxoplasma gondii* infection.[12] HPV screening and Pap testing for cervical and anal neoplasia should also be considered in the context of a patient's clinical history.[12]

References

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Table 3. Laboratory Tests Used for Selection of Antiretroviral Drugs[a]

Test Code	Test Name	Primary Clinical Use and/or Differentiating Factors
34949	HIV-1 Genotype[b]	Detect mutations associated with resistance to RTI and PI
91692	HIV-1 Genotype (RTI, PI, Integrase Inhibitors)[b]	Detect mutations associated with resistance to RTIs, PIs, and integrase inhibitors
94015	HIV-1 Genotype and Coreceptor Tropism, Ultradeep Sequencing[b,c]	Detect mutations associated with resistance to RTI and PI; evaluate eligibility for therapy with CCR5 antagonist
16868	HIV-1 Integrase Genotype[b]	Assess mutations associated with resistance to integrase inhibitors (raltegravir, elvitegravir, and dolutegravir)
94014	HIV-1 Coreceptor Tropism, Ultradeep Sequencing[b,c]	Evaluate eligibility for therapy with CCR5 antagonist (genotypic assay)
91299	HIV-1 Coreceptor Tropism, Proviral DNA[b]	Evaluate eligibility for therapy with CCR5 antagonist (genotypic assay) in patients with low viral load (<1,000 HIV-1 RNA copies/mL)
19774	*HLA-B*5701* Typing[d]	Assess risk of abacavir hypersensitivity reaction

PI, protease inhibitors; RTI, reverse transcriptase inhibitors.

[a] This test listing is not intended to be comprehensive. For additional testing options, consult the Quest Diagnostics online Test Center (QuestDiagnostics.com/testcenter). Components of panels and reflex tests may be ordered individually.

[b] This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by FDA. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

[c] Reflex tests are performed at an additional charge and are associated with an additional CPT code(s).

[d] Typing performed by using AS-PCR with reflex to the FDA-cleared LABType® SSO Kit. The AS-PCR portion of the test was developed and its performance characteristics have been determined by Quest Diagnostics.

Table 4. Laboratory Tests for Comorbid Conditions in Individuals with HIV-1 Infection Entering Care[a]

Test Code	Test Name	Primary Clinical Use
Chlamydia and Gonorrhea Testing		
11361	*Chlamydia trachomatis* RNA, TMA (urine or swab)	Detect infection with *C trachomatis*
16505	*Chlamydia trachomatis* RNA, TMA, Rectal[b]	
70048	*Chlamydia trachomatis* RNA, TMA, Throat[b]	
11362	*Neisseria gonorrhoeae* RNA, TMA (urine or swab)	Detect infection with *N gonorrhoeae*
16504	*Neisseria gonorrhoeae* RNA, TMA, Rectal[b]	
70049	*Neisseria gonorrhoeae* RNA, TMA, Throat[b]	
16506	*Chlamydia/Neisseria gonorrhoeae* RNA, TMA, Rectal[b]	Detect infection with *C trachomatis* or *N gonorrhoeae*
70051	*Chlamydia/Neisseria gonorrhoeae* RNA, TMA, Throat[b]	
11363	*Chlamydia/Neisseria gonorrhoeae* RNA, TMA	
91448	*Chlamydia/N gonorrhoeae* and *T vaginalis* RNA, Qualitative TMA, Pap Vial[c]	Detect infection with *C trachomatis*, *N gonorrhoeae*, or *Trichomonas vaginalis*
16492	SureSwab®, CT/NG, *T vaginalis*	
Hepatitis (Viral) Testing		
508	Hepatitis A Antibody, Total	Indicates prior or acute infection with, or immunization to, hepatitis A virus
498	Hepatitis B Surface Antigen with Reflex to Confirmation[d]	First-line diagnostic test for acute hepatitis B; indicates chronic hepatitis when still positive 6 months after diagnosis of acute HBV infection
556	Hepatitis Be Antibody	Indicator of resolution or carrier state when interpreted along with the other hepatitis B markers
555	Hepatitis Be Antigen	Indicator of active viral replication and high infectivity
34181	Hepatitis B Virus DNA, Qualitative, Real-Time PCR[b,e]	Indicator of chronic hepatitis when still positive 6 months after diagnosis of acute HBV infection; indicator of viral replication in patients with mutant HBV (eg, HBeAg- and HBeAb+ individuals)
8472	Hepatitis C Antibody with Reflex to HCV RNA, Quantitative Real-Time PCR[d]	Screen for and confirm presence of HCV infection; establish viral load at baseline
35645	Hepatitis C Viral RNA, Quantitative Real-Time PCR [e]	Confirm HCV infection; establish viral load at baseline; determine duration of treatment
Syphilis Testing		
36126	RPR Diagnosis with Reflex to Titer and Confirmatory Testing[d] Includes RPR screen with reflex to titer and fluorescent treponemal antibody.	Detect non-treponemal (reagin) antibodies associated with syphilis
90349	Syphilis Antibody Cascading Reflex[d] Includes *Treponema pallidum* antibody immunoassay and reflex to RPR screen, which reflexes to either RPR titer or *T pallidum* antibody particle agglutination assay.	Detect and confirm presence of antibody to *T pallidum*
653	*Treponema pallidum* Ab, Particle Agglutination	Confirm presence of antibody to *T pallidum*
Toxoplasma Testing		
3679	*Toxoplasma* Antibody (IgG)	Screen for *T gondii* infection
Trichomoniasis Testing		
19550	SureSwab® *Trichomonas vaginalis* RNA, Qualitative TMA	Detect infection with *T vaginalis*
90521	*Trichomonas vaginalis* RNA, Qualitative TMA, Pap Vial	
91448	*Chlamydia/N gonorrhoeae* and *T vaginalis* RNA, Qualitative TMA, Pap Vial[c]	Detect infection with *C trachomatis, N gonorrhoeae*, or *Trichomonas vaginalis*
16492	SureSwab®, CT/NG, *T vaginalis*	

(Continued)

Table 4. Laboratory Tests for Comorbid Conditions in Individuals with HIV-1 Infection Entering Care[a] *(Continued)*

Test Code	Test Name	Primary Clinical Use
Tuberculosis Testing		
16603	QuantiFERON® TB Gold (Draw Site Incubated)	Detect infection with *Mycobacterium tuberculosis*
Cancer Screening (Cervical and Anal-rectal)		
18810	SurePath™ Imaging Pap[f]	Detect abnormal cervical cytology including cervical cancer
14471	SurePath™ [Non Imaging] Pap[f]	
58315	ThinPrep® Imaging System Pap[f]	
35455	ThinPrep® [Non Imaging] Pap[f]	
18811	SurePath™ Imaging Pap reflex HPV mRNA E6/E7[d,f] Reflexes to HPV if ASCUS	Detect abnormal cervical cytology including cervical cancer; assess presence or absence of high risk HPV types
90934	ThinPrep® Imaging Pap reflex HPV mRNA E6/E7[d,f] Reflexes to HPV if ASCUS	
15095	SurePath™ Pap and HPV mRNA E6/E7[b,f]	
90931	ThinPrep® Pap and HPV mRNA E6/E7[f]	
15949	HPV DNA, High Risk, Anal-Rectal[b]	Detect anorectal infection with HPV types associated with high risk of cancer
90887	HPV mRNA E6/E7	Detect infection with HPV types associated with high risk of cervical cancer
91826	HPV Genotypes 16, 18/45	
90942	HPV mRNA E6/E7 with Reflex to Genotypes 16,18/45[d]	

ASCUS, atypical squamous cells of undetermined significance; CT, *Chlamydia trachomatis*; NG, *Neisseria gonorrhoeae*; RPR, rapid plasma regain; TB, tuberculosis; TMA, transcription-mediated amplification.

[a] This test listing is not intended to be comprehensive. For additional testing options, including cervical cytology and sexually transmitted infection (STI) testing using liquid-based cytology samples, consult the Quest Diagnostics online Test Center (QuestDiagnostics.com/TestCenter). Components of panels and reflex tests may be ordered individually.

[b] This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by FDA. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

[c] The analytical performance characteristics of this assay when used to test SurePath™ specimens have been determined by Quest Diagnostics. Performance characteristics refer to the analytical performance of the test.

[d] Reflex tests are performed at an additional charge and are associated with an additional CPT code(s).

[e] Polymerase chain reaction (PCR) is performed pursuant to a license agreement with Roche Molecular Systems, Inc.

[f] Pap results requiring physician interpretation will be performed at an additional charge and associated with an additional CPT code(s).

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Appendix. Antiretroviral Drugs Commonly Used in the Treatment of HIV Infection

Drug or Drug Combination	Abbreviation	Brand Name
Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs)		
Abacavir	ABC	Ziagen®
Abacavir/lamivudine	ABC/3TC	Epzicom®
Abacavir/zidovudine/lamivudine	ABC/ZDV/3TC	Trizivir®
Emtricitabine	FTC	Emtriva®
Lamivudine	3TC	Epivir®
Lamivudine/zidovudine	ZDV/3TC	Combivir®
Tenofovir alafenamide/emtricitabine	TAF/FTC	Descovy®
Tenofovir disoproxil fumarate	TDF	Viread®
Tenofovir disoproxil fumarate/emtricitabine	TDF/FTC	Truvada®
Zidovudine	ZDV (AZT)	Retrovir®
Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)		
Efavirenz	EFV	Sustiva®
Etravirine	ETR	Intelence®
Nevirapine	NVP	Viramune®
Rilpivirine	RPV	Edurant®
Protease Inhibitors (PIs)		
Atazanavir/cobicistat	ATV/c	Evotaz®
Atazanavir/ritonavir	ATV/r	Reyataz®/Norvir®
Darunavir/cobicistat	DRV/c	Prezcobix®
Darunavir/ritonavir	DRV/r	Prezista®/Norvir®
Fosamprenavir/ritonavir	FPV/r	Lexiva®/Norvir®
Indinavir/ritonavir	IDV/r	Crixivan®/Norvir®
Lopinavir/ritonavir	LPV/r	Kaletra®
Saquinavir/ritonavir	SQV/r	Fortovase® or Invirase®/Norvir®
Tipranavir/ritonavir	TPV/r	Aptivus®/Norvir®
Entry Inhibitor (CCR5 Coreceptor Antagonist)		
Maraviroc	MVC	Selzentry®
Integrase Strand Transfer Inhibitor		
Dolutegravir	DTG	Tivicay®
Elvitegravir	EVG	Vitekta®
Raltegravir	RAL	Isentress®
Multiclass Combination Therapy		
Dolutegravir, abacavir, lamivudine	DTG/ABC/3TC	Triumeq®
Efavirenz, emtricitabine, tenofovir	EFV/FTC/TDF	Atripla®
Emtricitabine, rilpivirine, tenofovir disoproxil fumarate	FTC/RPV/TDF	Complera®
Emtricitabine, rilpivirine, tenofovir alafenamide	FTC/RPV/TAF	Odefsey®
Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide	EVG/COBI/FTC/TAF	Genvoya®
Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate	EVG/COBI/FTC/TDF	Stribild®