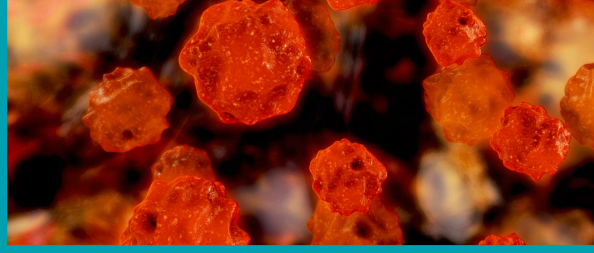
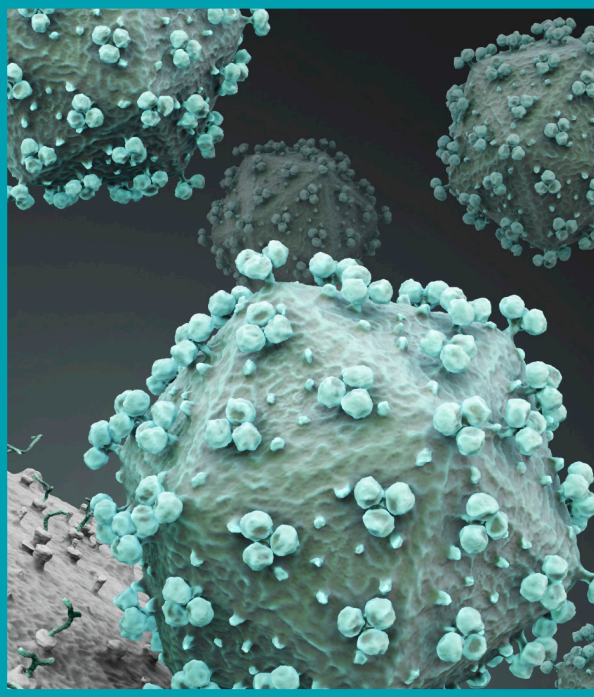
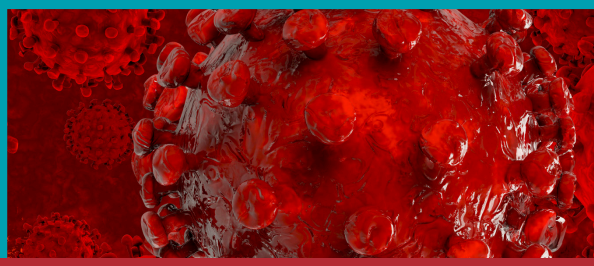
Suggested Reporting Language for the HIV Laboratory Diagnostic Testing Algorithm







JANUARY 2019

APHL ASSOCIATION OF PUBLIC HEALTH LABORATORIES®

Introduction

To maximize public health impact, accurate and timely diagnostic HIV testing should be combined with clear result reporting and expedited linkage to medical care and services for infected persons. Laboratory reports should state each test that was performed, the result of each test, and the laboratory algorithm interpretation for the specimen.

The "Suggested Reporting Language for the HIV Laboratory Diagnostic Testing Algorithm" was originally developed by the Association of Public Health Laboratory's (APHL's) HIV/Hepatitis Subcommittee to provide guidance to laboratories performing the 2014 HIV Laboratory Testing Algorithm.[1] This document and accompanying appendices are intended to clarify complex testing outcomes and guide laboratory reporting of test results to providers and health department surveillance programs. Information about the algorithm and definitions used throughout this document are addressed in Appendix A. The suggested reporting language presented may require adjustments to meet individual facility or jurisdiction requirements; however, major deviations should be considered carefully because misinterpretation of HIV test results may have serious implications.

Rationale for Document Update

This document is updated periodically as new information becomes available and/or changes related to the availability of U.S. Food and Drug Administration (FDA)-approved HIV diagnostic tests occur. This 2019 update to the APHL Suggested Reporting Language for the HIV Laboratory Diagnostic Testing Algorithm supersedes the previous versions[2,3] and has been prepared in response to the following developments:

- The package insert of the Bio-Rad Geenius™ HIV1/2 Supplemental Assay has been revised.
- A new version (V1.3) of the Geenius reader software was approved by the FDA in 2017.[4]
- The CDC released a technical update on the use of the Alere Determine HIV 1/2 Ag/Ab Combo test with serum and plasma in the laboratory algorithm in October 2017.[5]
- Information regarding these changes were incorporated into an updated version of the CDC's Quick Reference Guide[6] for the recommended laboratory HIV testing algorithm for use with serum and/or plasma specimens.

Importance of Standardized Reporting Language

The use of standardized language when reporting laboratory results is particularly important for testing that involves multi-test algorithms. The HIV Laboratory Testing Algorithm[1,6] (Appendix A) involves a series of tests, often performed by more than one laboratory, to determine the presence or absence of HIV infection. Several available HIV diagnostic tests are designed to detect multiple analytes. The addition of multi-analyte tests to a multi-test algorithm complicates the interpretation of results and increases the potential for misinterpretation by both laboratorians and healthcare providers. Lack of clarity in results reporting can lead to incomplete testing, the misinterpretation of results by health care providers, unnecessary additional testing, delays in care for infected persons, and inaccurate estimates of disease burden. In most cases, assay-specific software determines the result and interpretation of each individual assay.

In this document, we have adopted the term "laboratory algorithm interpretation" to represent the interpretation that should be provided for the HIV diagnostic multi-test algorithm. If the algorithm has not been completed for a specimen and the laboratory algorithm interpretation cannot yet be determined, the laboratory report for that specimen should state that test results are pending and recommend that additional tests should be performed to establish the laboratory algorithm interpretation. We strongly suggest that all laboratories that perform testing following the HIV Laboratory Diagnostic Testing Algorithm[1,6] adopt the reporting language suggested in this document.

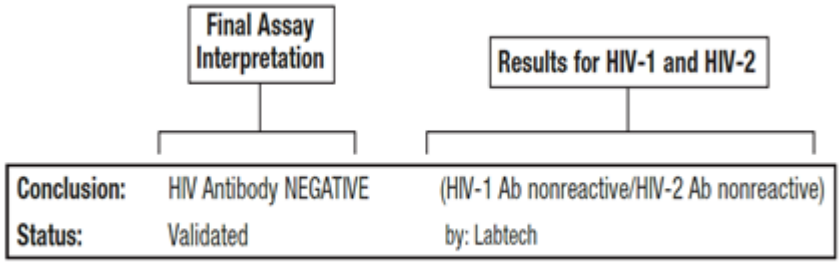
Considerations for Persons Taking Antiretrovirals

In recent years, there has been an increase in the number of patients who initiate antiretroviral therapy (ART) earlier in the course of their infection. Starting antiretroviral therapy earlier can also impact the development of HIV specific antibodies, which in turn can impact the ability of some diagnostic assays to detect HIV infection as expected.[7,8] Therefore, the individual assay results and the laboratory algorithm interpretation need to be considered in the context of the individual's clinical circumstances, including early ART. Likewise, if someone becomes infected while taking antiretrovirals administered for pre-exposure prophylaxis (PrEP), the ability of diagnostic tests to detect the infection may be affected.[9] More data regarding the performance of the algorithm on specimens collected from individuals on PrEP are needed to assess the likelihood of false negative results. If test results fluctuate between detectable and undetectable upon repeated testing of the same individual, the laboratory should consider contacting the submitter for more information. Laboratories may also consider including a note on all negative test reports stating "Antiretroviral drugs taken for treatment or prophylaxis may limit the ability of diagnostic tests to detect HIV infection."

Updates Related to Supplemental Assay

In September 2017, the FDA approved a new version of the Geenius Assay Protocol File (APF) V1.3, as well as revisions to the Geenius™ HIV 1/2 Supplemental Assay Package Insert.[4] A summary of the changes to the Geenius package insert and instructions for installing the mandatory software upgrade were distributed. In APF V1.3, the cutoff of the HIV-2 gp140 band was adjusted. Bio-Rad did not specify the reason for adjusting the HIV-2 gp140 cutoff in these documents. However, the expectation is that this change will reduce the number of false HIV-2 Indeterminate and HIV Indeterminate results and the additional testing that is needed to resolve these indeterminate results. In addition, the reporting language used in the package insert including the individual analyte results and **Final Assay Interpretations** were modified to provide more clarity. *Note: The Geenius package insert uses the term **Final Assay Interpretation** for the overall Geenius result.* On the Geenius report the **Final Assay Interpretation** is displayed as the "Conclusion" (See Figure 1). Throughout this document, we will use the term **Final Assay Interpretation** to reflect the terminology used in the Geenius package insert. With respect to the individual results for HIV-1 and HIV-2, the terms "antibody reactive," "antibody nonreactive" and "antibody indeterminate" have replaced the previous terms "positive," "negative" and "indeterminate." Notably, the **Final Assay Interpretation** for a Geenius assay in which no bands are detected was changed from "HIV Negative" to "HIV Antibody Negative."

Figure 1: Image from Geenius Package Insert of Report from Reader.[5]



Reporting Geenius Results

Overall Comments

The Geenius™ HIV 1/2 Supplemental Assay cassette contains six test bands (four HIV-1 and two HIV-2 bands) to detect HIV-1 and/or HIV-2 antibodies and a control band. The Geenius reader equipped with assay-specific software analyzes the signals for each band to produce the individual results for HIV-1 and HIV-2, which are combined to provide the conclusion or **Final Assay Interpretation**. The Geenius reader

automatically produces a printable report at the completion of every test (Figure 1) which includes the conclusion and the individual results for HIV-1 and HIV-2 in parenthetical notation. While this file can be printed for recordkeeping purposes, most laboratories extract the relevant information from it to create their own laboratory report.

In the updated package insert, Bio-Rad provided clarification on which components from the Geenius test report should be communicated to the ordering provider. The revised package insert states in bold font that "The **Final Assay Interpretation** should always be reported to the ordering provider." Therefore all laboratories reporting Geenius results to healthcare providers and public health surveillance programs should always report the **Final Assay Interpretation** (also referred to as the "Conclusion" on the Geenius report) as determined by the Geenius software.

Reporting of the individual results for HIV-1 and HIV-2 by the laboratory is not specifically prohibited by the manufacturer,[5] but it is our recommendation that laboratories do not report this information. The individual results for HIV-1 and HIV-2 are combined with the relative strength of the signals to produce the **Final Assay Interpretation**. The performance characteristics of the Geenius assay that appear in the package insert are based on the **Final Assay Interpretation** and not the individual results for HIV-1 and HIV-2. This point is clarified in the "Limitations" section of the revised package insert. Therefore the individual results should not be used for diagnostic purposes because they may provide misleading information.

In addition, while band patterns are present on the Geenius instrument printable test report, we strongly recommend that laboratories do not report the band patterns. Information is not available regarding any correlation of banding pattern to stage of disease and, therefore, should not be used for diagnostic purposes or disease staging.

We recommend that all laboratories include the Geenius Final Assay Interpretation on the laboratory report. We also recommend that laboratories exclude the individual results for HIV-1 and HIV-2 from the Geenius Assay on the laboratory report.

Geenius Final Assay Interpretations

In the updated Geenius package insert,[4] explanatory notes for each combination of individual HIV-1 and HIV-2 results and corresponding **Final Assay Interpretation** have been added. The package insert together with the updated Quick Reference Guide[2] and this document provide clarification on how to proceed in each situation. However, three of the Geenius assay results (**Final Assay Interpretations**) may cause confusion, so we have provided further information for consideration.

HIV-2 Positive with HIV-1 cross-reactivity

The **Final Assay Interpretation**, "HIV-2 with HIV-1 cross-reactivity," should be considered equivalent to the **Final Assay Interpretation** of "HIV-2 Positive." In both cases the Geenius software has detected reactivity to HIV-2 antibodies. In the former case it has also detected reactivity to HIV-1, but the HIV-1 reactivity does not meet the criteria to be considered positive. This pattern is indicative of cross-reactivity of the HIV-2 antibodies with the HIV-1 antigens and is not sufficient to be considered HIV-1 Positive. This **Final Assay Interpretation** is distinct from "HIV Positive Untypable" in which the criteria for both HIV-1 Positive and HIV-2 Positive were met, where the HIV-1 and HIV-2 antibodies are strong enough for the individual results for HIV-1 and HIV-2 to be considered positive and which would indicate the possibility of a dual infection with HIV-1 and HIV-2.

Specimens with the **Final Assay Interpretation** "HIV-2 with HIV-1 cross-reactivity" do not require any additional testing. Persons with this **Final Assay Interpretation** should be provided appropriate counseling and linked to medical care.

HIV-2 Indeterminate

Specimens with the **Final Assay Interpretation** "HIV-2 Indeterminate" require additional testing. The first step is to repeat Geenius testing with the same specimen on a new cartridge.

- If upon repeat testing the **Final Assay Interpretation** is "HIV-1 Positive" or "HIV-2 Positive," this result should be reported as the **Final Assay Interpretation** for Geenius and no further testing is needed.
- If upon repeat testing the **Final Assay Interpretation** is "HIV antibody negative" this result should be reported as the **Final Assay Interpretation** for Geenius and testing with an HIV-1 nucleic acid test (NAT) is indicated.
- If upon repeat testing the **Final Assay Interpretation** is "HIV-2 Indeterminate," this result should be reported as the **Final Assay Interpretation** for Geenius and an HIV-1 NAT should be conducted.
    - The following recommendations should be considered based on the HIV-1 NAT results:
        - If HIV-1 RNA is detected, the laboratory algorithm interpretation would be "Positive for HIV-1, laboratory evidence of HIV-1 infection consistent with an acute HIV-1 infection" and the person should be provided with appropriate counseling and linked to medical care.
        - If HIV-1 RNA is not detected, the sample should be referred for testing with a validated supplemental HIV-2 test (antibody test or NAT), if available. Alternatively, the laboratory report may recommend repeating the algorithm with a new specimen in 2-4 weeks to assess HIV-2 infection. Supplemental HIV-2 testing may be available through commercial laboratories, public health laboratories, or CDC.

HIV Indeterminate

Specimens with the **Final Assay Interpretation** "HIV Indeterminate" should prompt the same testing sequence and recommendations as described above for a repeat "HIV-2 Indeterminate" **Final Assay Interpretation**, i.e. an HIV-1 NAT should be conducted.

- If HIV-1 RNA is detected the laboratory algorithm interpretation would be "Positive for HIV-1, laboratory evidence of HIV-1 infection consistent with an acute HIV-1 infection" and the person should be provided with appropriate counseling and linked to medical care.
- If HIV-1 RNA is not detected the sample should be referred for testing with a validated supplemental HIV-2 test (antibody test or NAT), if available. Alternatively, the laboratory report may recommend repeating the algorithm with a new specimen in 2-4 weeks to assess HIV-2 infection. Supplemental HIV-2 testing may be available through commercial laboratories, public health laboratories or CDC.

Table 1: Guidance for Reporting Results from the HIV Laboratory Diagnostic Testing Algorithm for Serum and Plasma

Guidance for Reporting Results from the HIV Laboratory Diagnostic Testing Algorithm for Serum and Plasma Specimens[a]

Test Outcomes

Test Sequence			Laboratory Algorithm Interpretation[d]	Interpretation for Provider Use[e]	Further Actions[f]
Step 1	Step 2	Step 3			
HIV-1/HIV-2 Ag/Ab IA[b]	HIV-1/HIV-2 Antibody Differentiation IA[c]	HIV-1 NAT			
Nonreactive	n/a	n/a	HIV-1 antigen and HIV-1/HIV-2 antibodies were not detected. No laboratory evidence of HIV infection.	HIV negative	If recent HIV exposure is suspected or reported, conduct HIV-1 NAT or request a new specimen and repeat the algorithm according to CDC Guidelines.[g]
Reactive	HIV-1 Positive	n/a	Positive for HIV-1 antibodies. Laboratory evidence of HIV-1 infection is present.	HIV-1 Positive	Link patient to HIV medical care and provide appropriate prevention counseling.[h]
Reactive	HIV-2 Positive	n/a	Positive for HIV-2 antibodies. Laboratory evidence of HIV-2 infection is present.	HIV-2 Positive	Link patient to HIV medical care and provide appropriate prevention counseling.[h]
Reactive	HIV-2 Positive with HIV-1 Cross reactivity	n/a	Positive for HIV-2 antibodies. Laboratory evidence of HIV-2 infection is present.	HIV-2 Positive. This result is distinct from HIV positive untypable (undifferentiated).	Link patient to HIV medical care and provide appropriate prevention counseling.[h]
Reactive	HIV Positive untypable (undifferentiated)	n/a	Positive for HIV-1 and HIV-2 antibodies. Laboratory evidence of HIV-1 and/or HIV-2 infection is present.	HIV Positive	Link patient to HIV medical care and provide appropriate prevention counseling.[h] Provider may consider additional testing for HIV-1 RNA or DNA and HIV-2 RNA or DNA to verify or rule out HIV-1/HIV-2 dual infection. Request additional specimen if original specimen volume is insufficient.
Reactive	HIV-1 indeterminate or, HIV-2 indeterminate[i] or, HIV indeterminate	Detected	Positive for HIV-1. Laboratory evidence of HIV-1 infection consistent with an **acute** HIV-1 infection.	**Acute** HIV-1 Positive	Link patient to HIV medical care and provide appropriate prevention counseling immediately[h] to expedite prevention practices.
Reactive	HIV-1 indeterminate	Not detected	HIV-1 antibodies were not confirmed and HIV-1 RNA was not detected.	HIV Negative	If recent HIV exposure is suspected or reported, request a new specimen and repeat the algorithm according to CDC guidance.[g]
Reactive	HIV-2 indeterminate[i]	Not detected	HIV antibodies were not confirmed and HIV-1 RNA was not detected. HIV-2 inconclusive.	HIV-1 Negative, HIV-2 inconclusive	Refer sample for testing with a different validated supplemental HIV-2 test (antibody test or NAT) if available. Alternatively, redraw and repeat algorithm in 2-4 weeks to assess HIV-2 infection.
Reactive	HIV Indeterminate	Not detected	HIV-1 antibodies were not confirmed and HIV-1 RNA was not detected. HIV-2 inconclusive.	HIV-1 Negative, HIV-2 inconclusive	Refer sample for testing with a different validated supplemental HIV-2 test (antibody test or NAT) if available. Alternatively, redraw and repeat algorithm in 2-4 weeks to assess HIV-2 infection.
Reactive	**HIV Antibody** Negative	Detected	Positive for HIV-1. Laboratory evidence of HIV-1 infection consistent with an **acute** HIV-1 infection.	**Acute** HIV-1 Positive	Link patient to HIV medical care and provide appropriate prevention counseling immediatelyh to expedite prevention practices.
Reactive	**HIV Antibody** Negative	Not detected	HIV antibodies were not confirmed and HIV-1 RNA was not detected.	HIV Negative	If recent HIV exposure is suspected or reported, request a new specimen and repeat the algorithm according to CDC guidance.[g]
Reactive	**HIV Antibody** Negative or Indeterminate	Invalid or not performed	Inconclusive	Inconclusive	Request an additional specimen and repeat the algorithm. Ensure HIV-1 NAT is performed, if indicated by results of HIV-1/HIV-2 Ag/Ab IA and HIV-1/HIV-2 Ab differentiation IA.

a. The tests outlined in this table are not FDA approved for oral fluid or dried blood spots. b. The need for repeating screening immunoassay (IA) on an initial reactive test is assay dependent, refer to product package insert. c. This column contains the Final Assay Interpretation per the Geenius package insert, the only FDA approved test for this step. We recommend excluding the individual HIV-1 and HIV-2 results on the laboratory report. If they are used the Geenius Final Assay Interpretation should also be included. d. This column contains suggested language to be used for the laboratory report and it can be directly used for reporting from LIMS systems. e. This column contains simplified language of the previous column, "Laboratory Algorithm Interpretation," and is included here for healthcare providers or other non-laboratorians that may also use this table as a reference document. This does not need to be included on the laboratory report. f. Comments under "Further Action" can be included as language in the laboratory report or can be used as guidance for laboratorians to discuss test results with healthcare providers or health department staff. g. Please refer to the Centers for Disease Control and Prevention Laboratory Guidance. Available at: https://www.cdc.gov/hiv/testing/laboratorytests.html, https://stacks.cdc.gov/view/cdc/38856 and https://www.cdc.gov/hiv/testing/clinical/index.html h. Please refer to the Centers for Disease Control and Prevention HIV Guidelines and Recommendations to find the most appropriate information by age and risk group for the patient in question. Available at: http://www.cdc.gov/hiv/guidelines/ i. Follow Geenius package insert and refer to the CDC Technical Update. Available at: https://stacks.cdc.gov/view/cdc/40790

Guidance on Reporting Test Results to Health Care Providers

All laboratory reports should include the results for all tests performed, as well as a laboratory algorithm interpretation of the HIV Laboratory Testing Algorithm. Health care providers may be receiving results from one or more laboratories. If the laboratory that reports the results to the provider did not conduct all of the tests, this laboratory may not have access to other results and may not be able to provide a laboratory algorithm interpretation. This reporting language documentcan be used as a resource to help identify the laboratory algorithm interpretation when results are received from multiple laboratories.

The HIV Laboratory Testing Algorithm is intended to maximize the identification of new, previously undiagnosed HIV infections. However, laboratories may receive specimens from previously diagnosed individuals, including individuals on ART or PrEP, for the purpose of verifying positive infection status for the medical record. Over time, effective ART may cause antibody titers to decline. Furthermore, ART initiated during acute infection may preclude seroconversion altogether.[8] In such cases, serological tests may be nonreactive or indeterminate and HIV RNA may be undetectable due to ART or PrEP, leading to a false negative result. Laboratories may not be informed of these circumstances when a specimen is submitted for testing. Therefore, including a statement on all laboratory reports indicating that the test results should be interpreted in the context of all clinically relevant information such as current or recent use of antiretrovirals is recommended.

The table includes a column, "Interpretation for Provider Use," which is a shortened and simplified version of the laboratory algorithm interpretation. The information does not need to be included on the laboratory report, but it may be useful to the provider ordering the testing. Additionally, the "Further Actions" column in the table also can provide help to guide submitters on appropriate next steps following testing.

The following are some general guidelines to follow when reporting HIV test results to health care providers:

1. Laboratories should specify the assays that were used in HIV testing (see Appendix A for links to lists of FDA-approved tests) and the results for each assay.

2. If laboratories use a testing sequence other than the recommended laboratory algorithm or assays other than those currently recommended, reports should describe the limitations associated with the testing sequence used. Refer to Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations for more information on the limitations associated with alternatives to the recommended algorithm.[1,6]

3. Laboratories may issue preliminary reports containing the result from each test in the algorithm as it becomes available. If the recommended testing algorithm is not completed at that time, laboratories should specify which test results are pending, which additional tests are needed to complete the laboratory algorithm interpretation, and recommend any additional testing that may be required. The final report should contain the laboratory algorithm interpretation.

4. Laboratories that refer patient specimens to one or more referral laboratories to perform the algorithm are encouraged to compile the results received from those referral laboratories and transmit all results as a single report to the provider. This action would facilitate clear messaging to the provider. In situations where this is not feasible, these results may be transmitted directly to the provider from multiple testing laboratories. In either case the health care provider should receive a result for each test performed. Where possible and applicable, the laboratory report should include a laboratory algorithm interpretation and recommendations for appropriate next steps; however, in some reporting scenarios, this may not be practical.

5. The diagnosis of acute HIV infection indicates a potential need for public health interventions due to the increased risk of transmission to uninfected partners during acute infection. Laboratories should have arrangements in place to expedite reporting of test results consistent with acute HIV infection to

the health care provider and to the health department to help ensure quick access to treatment.

Guidance on Laboratory Reporting for Surveillance

All states, the District of Columbia, and United States territories and dependent areas require that laboratories report test results indicative of HIV infection to the surveillance program in the department of health in the patient's jurisdiction of residence.[10] Specific requirements of each state or local health department might differ; therefore, ensure the specific requirements of your jurisdiction are followed.

All laboratory reports should include the result for all tests performed as well as a laboratory algorithm interpretation of the HIV Laboratory Testing Algorithm that is generated from the combination of assay results. Health department surveillance programs may receive results from a single specimen from one or multiple laboratories. If the laboratory reporting the results did not conduct all of the tests, the laboratory may not have access to other results and may not be able to provide a laboratory algorithm interpretation. Therefore, the burden of combining these results and determining the laboratory algorithm interpretation for case classification purposes may fall to the surveillance program. The reporting language document can be used as a resource to help identify the laboratory algorithm interpretation when results are received from multiple laboratories.

The table includes a column, "Interpretation for Provider Use," which is a shortened and simplified version of the laboratory algorithm interpretation. The information does not need to be included on the laboratory report, but it may be useful to the provider ordering the testing. Additionally, the "Further Actions" column in the table also can provide help to guide submitters on appropriate next steps following testing.

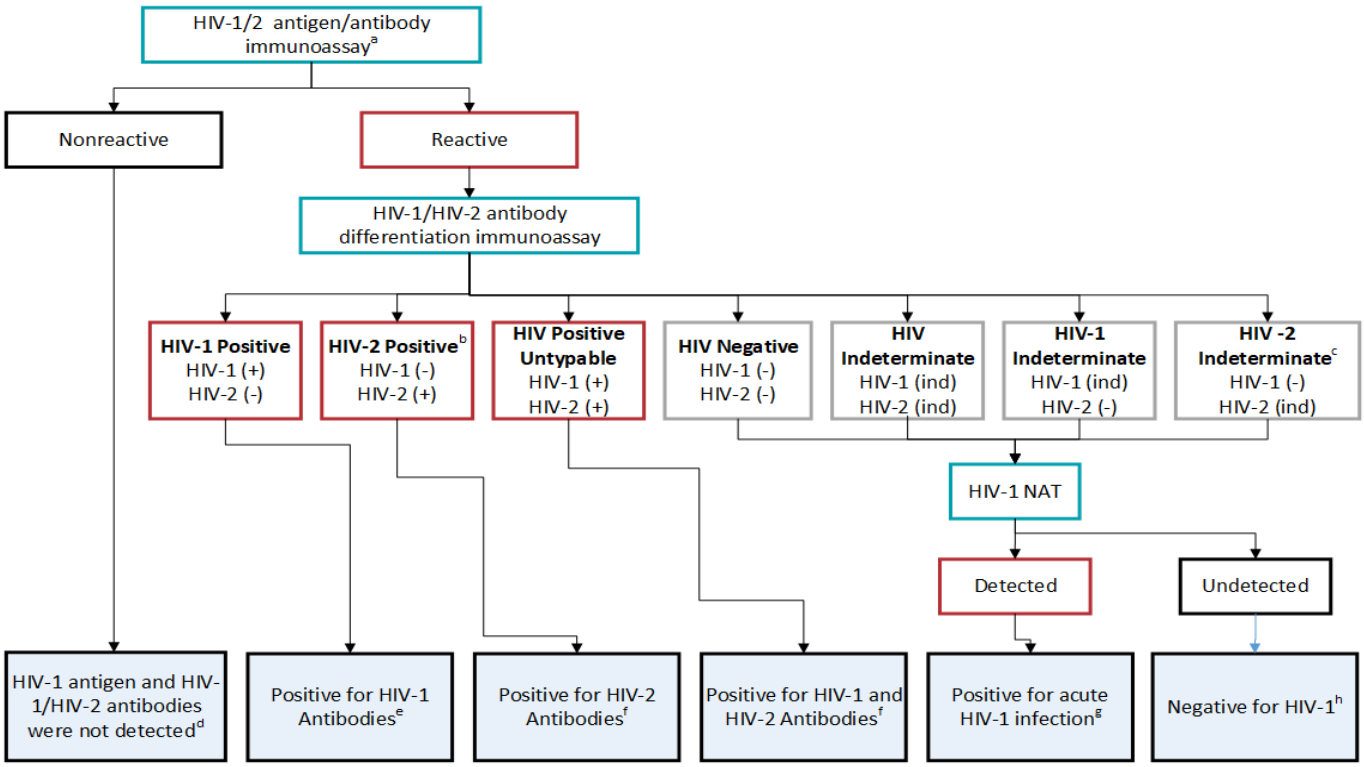
Contact the HIV surveillance coordinator in your jurisdiction for additional information regarding reporting requirements. The National Alliance of State and Territorial AIDS Directors (NASTAD) maintains a contact list for state HIV surveillance coordinators that is available.

CDC has recently developed and published a LOINC (Logical Observation Identifiers Names and Codes) map for all FDA-approved HIV diagnostic tests. The standardized mapping was developed in coordination with APHL, the Regenstrief Institute, Inc. and CDC.

Appendix A

The HIV Laboratory Diagnostic Testing Algorithm[1] should be used for testing serum or plasma to diagnose persons with HIV and for the confirmation of rapid HIV test results, starting from Step 1 of the algorithm, also commonly referred to as the screening test. CDC maintains lists of FDA-approved assays that can be used for Step 1 (the HIV-1/2 Antigen/Antibody [Ag/Ab] Immunoassay).[11] The algorithm recommends initial testing with an HIV-1/2 antigen/antibody immunoassay (IA) which, if reactive, is followed by supplemental testing. Recent updates from CDC allow for the Alere Determine HIV-1/2 Ag/Ab Rapid Test to be used in this first step for serum/plasma, though instrumented antigen/antibody immunoassays are preferred.[5] Specimens that are reactive in Step 1 will undergo supplemental testing in Step 2 with an HIV-1/HIV-2 antibody differentiation assay. The only such assay currently FDA-approved and manufactured is the Geenius HIV-1/2 Supplemental Assay. Specimens with a **Final Assay Interpretation** of HIV antibody negative or indeterminate by the HIV-1/HIV-2 antibody differentiation assay require further testing in Step 3. Specimens with HIV-2 antibodies detected, including those with a **Final Assay Interpretation** of HIV-2 Positive and HIV-2 Positive with HIV-1 cross reactivity, do not require further testing. Step 3 is the HIV-1 NAT, of which there is currently only one FDA-approved test in this category. CDC maintains lists of FDA approved assays for supplemental testing including HIV-1/HIV-2 antibody differentiation immunoassays and HIV-1 NATs.[12] Figure 2 provides an alternative visual representation of the HIV Laboratory Diagnostic Algorithm. It delineates the possible combinations of results from the algorithm and can be used in combination with Table 1 to provide laboratory algorithm interpretations.

Figure 2: Laboratory Testing Algorithm in Serum/Plasma (modified from 2014 algorithm figure and CDC Quick Reference Guide



a. APHL and CDC continue to recommend that laboratories use an FDA-approved instrumented HIV-1/HIV-2 antigen/antibody immunoassays as the initial assay the initial assay in the laboratory HIV testing algorithm for serum or plasma due to their superior sensitivity for detecting acute HIV infection. However, the FDA-approved single-use rapid HIV-1/HIV-2 antigen/antibody immunoassay may be used as the initial assay the initial assay in the laboratory HIV testing algorithm for serum or plasma if an instrumented assay is not available. **b.** This includes specimens reported as HIV-2 positive with HIV-1 cross reactivity. **c.** Per the Geenius Package Insert, specimens with this final assay interpretation should be retested with a new cartridge. If the final assay interpretation is again HIV-2 indeterminate, it should be reported as such and followed with an HIV-1 NAT. **d.** If recent HIV exposure is suspected or reported, conduct HIV-1 NAT or request a new specimen and repeat the algorithm according to CDC Guidance. **e.** Link patient to HIV medical care and provide appropriate prevention counseling. **f.** Link patient to HIV medical care and provide appropriate prevention counseling. Provider may consider additional testing. **g.** Link patient to HIV medical care and provide appropriate prevention counseling immediately to expedite prevention practices. **h.** 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) if available. Alternatively, redraw and repeat algorithm in 2-4 weeks to assess HIV-2 infection.

Definitions

HIV-1/2 antigen/antibody immunoassay: These assays detect both HIV-1 and HIV-2 antibody and HIV-1 antigen. It is the recommended initial test in the HIV algorithm. The result from these tests are either a simple reactive or nonreactive (Examples: Abbott Architect® HIV Ag/Ab Assay or Bio-Rad GS HIV Combo Ag/Ab) or may have more complex results (Example: Bio-Rad BioPlex® 2200 HIV Ag-Ab).

HIV-1/HIV-2 antibody differentiation immunoassay: This assay is able to distinguish between HIV-1 and HIV-2 antibodies and is intended for use as a supplemental assay. This assay is the recommended second step in the HIV testing algorithm following a reactive screening result. The results from this assay are called Final Assay Interpretations and are included in the table in this document.

Assay Result: This is the term given to describe the result for a single assay or test in the HIV diagnostic algorithm. Some assays are capable of detecting or measuring multiple analytes. Laboratories should adhere to the format presented in the package insert for reporting the assay result.

Laboratory algorithm interpretation: This is the term used to describe whether a given specimen has laboratory evidence of an HIV infection. This is based on the combination of the assay results of each test in the HIV multi-test algorithm.

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Association of Public Health Laboratories

The Association of Public Health Laboratories (APHL) works to strengthen laboratory systems serving the public's health in the US and globally. APHL's member laboratories protect the public's health by monitoring and detecting infectious and foodborne diseases, environmental contaminants, terrorist agents, genetic disorders in newborns and other diverse health threats.

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