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EDMUND G. BROWN JR.
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January 20, 2015

TO: LABORATORY DIRECTORS
LOCAL AIDS DIRECTORS
HEALTH CARE PROVIDERS
ALL INTERESTED PARTIES

SUBJECT: HIV TESTING AND REPORTING: CENTERS FOR DISEASE CONTROL AND PREVENTION RECOMMENDATIONS FOR NEW DIAGNOSTIC ALGORITHM

On June 27, 2014 the Centers for Disease Control and Prevention (CDC) issued updated recommendations for laboratory testing for the diagnosis of HIV infection (<http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf>). The California Department of Public Health, Center for Infectious Diseases, Office of AIDS (CDPH/OA) is providing recommendations to assist with HIV testing in health care settings and HIV reporting to local health departments (LHD).

Ordering HIV Testing in Health Care Settings

The California Code of Regulations (CCR), Title 17, Section 1230 allows clinical laboratories to use any HIV diagnostic algorithm that is “recommended by the Clinical and Laboratory Standards Institute (CLSI), CDC, the Association of Public Health Laboratories (APHL), or the U.S. Department of Health and Human Services (HHS).”

CDPH/OA recommends that health care providers order the CDC-recommended 4th generation HIV testing algorithm from their laboratory provider for diagnosing HIV in health care settings (see attached Figure for CDC-recommended algorithm).

The CDC-recommended algorithm begins testing with a combination immunoassay that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen. Specimens reactive on this initial assay undergo supplemental testing with an immunoassay that differentiates HIV-1 and HIV-2 antibodies. Specimens that are reactive on the initial immunoassay and nonreactive or indeterminate on the antibody differentiation assay proceed to HIV-1 nucleic acid testing for resolution.

The 4th generation HIV testing algorithm has been found to be cost effective at all levels of HIV prevalence in a population and it is the only HIV diagnostic algorithm that identifies acute HIV infection. Patients with acute HIV infection who are unaware of their infection may be more likely to engage in high risk sex and/or needle-sharing activities that cause HIV transmission. In addition they are more likely to transmit HIV than those with established HIV infection because

their viral load is higher and the virus itself is more virulent.¹ The recommended HIV testing algorithm is available from commercial and public health laboratories that provide services in California.

Although other laboratory algorithms are approved for use in California (i.e., CLSI algorithms II-VI), these algorithms all have limitations and are therefore not recommended by the CDC for use in health care settings for laboratory diagnosis of HIV based on testing of serum or plasma specimens.

Reporting of HIV Test Results to Local Health Departments

Both health care providers and laboratories registered or licensed in California are required to report all cases of HIV infection to the local health officer per California Health and Safety Code (HSC) 121022 (a). CCR Title 17, Section 2643.10 requires laboratory directors to report within 7 days an HIV diagnosis to the health officer for the local health department where the ordering health care provider facility is located.

CDPH/OA recommends:

- Laboratories report test results of the CDC-recommended 4th generation HIV Diagnostic Testing Algorithm as shown in the attached Figure and Table.
- Laboratories report test results as they become available, particularly when they provide evidence of acute HIV infection. Reporting acute HIV infection to both the ordering health care provider and the local health department is critical to facilitate prompt notification and provision of HIV care and partner services for acutely infected persons.
- Laboratories also report final results when all testing is complete. This ensures that a complete record of the testing algorithm is available for case management and surveillance data collection.

CDPH/OA recommends that laboratories specify the following HIV test information on laboratory results sent to health care providers and the local health department:

- All HIV test assays that were used to determine the diagnosis of HIV infection.
- The results of each HIV test assay. This includes results from all tests (including negative/nonreactive or indeterminate results) performed as part of the testing algorithm (see attached Figure for CDC-recommended algorithm).
- The interpretation of the results of each test (see attached Table for recommended procedure and language for reporting results).
- Any additional testing that is recommended or pending using existing specimens or new specimens that should be submitted.
- If the entire recommended testing algorithm was not completed, which additional tests are necessary to establish the laboratory diagnosis.

¹ http://www.denverptc.org/Handouts/4Gen_Branson.pdf, Slides 21 & 24

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- If alternatives to the recommended algorithm sequence were used, the assays that were used and the limitations of these tests or sequence compared with the recommended algorithm.

CDPH/OA is working with local public health departments and the CDC to collect laboratory data resulting from the new testing algorithm for HIV surveillance. We will continue to work with laboratories and local public health departments to ensure complete, timely, and accurate reporting of all HIV-related test results. Our staff are available to answer questions or assist with implementation and reporting of test results from the new testing algorithm. If you have any questions or would like assistance regarding HIV reporting requirements or reporting recommendations for the new HIV testing algorithm, please contact Jessica Brown, HIV surveillance laboratory coordinator: Jessica.Brown@cdph.ca.gov, (916) 445-9231.

Sincerely,



Karen Mark, M.D., Ph.D.

Chief, Office of AIDS

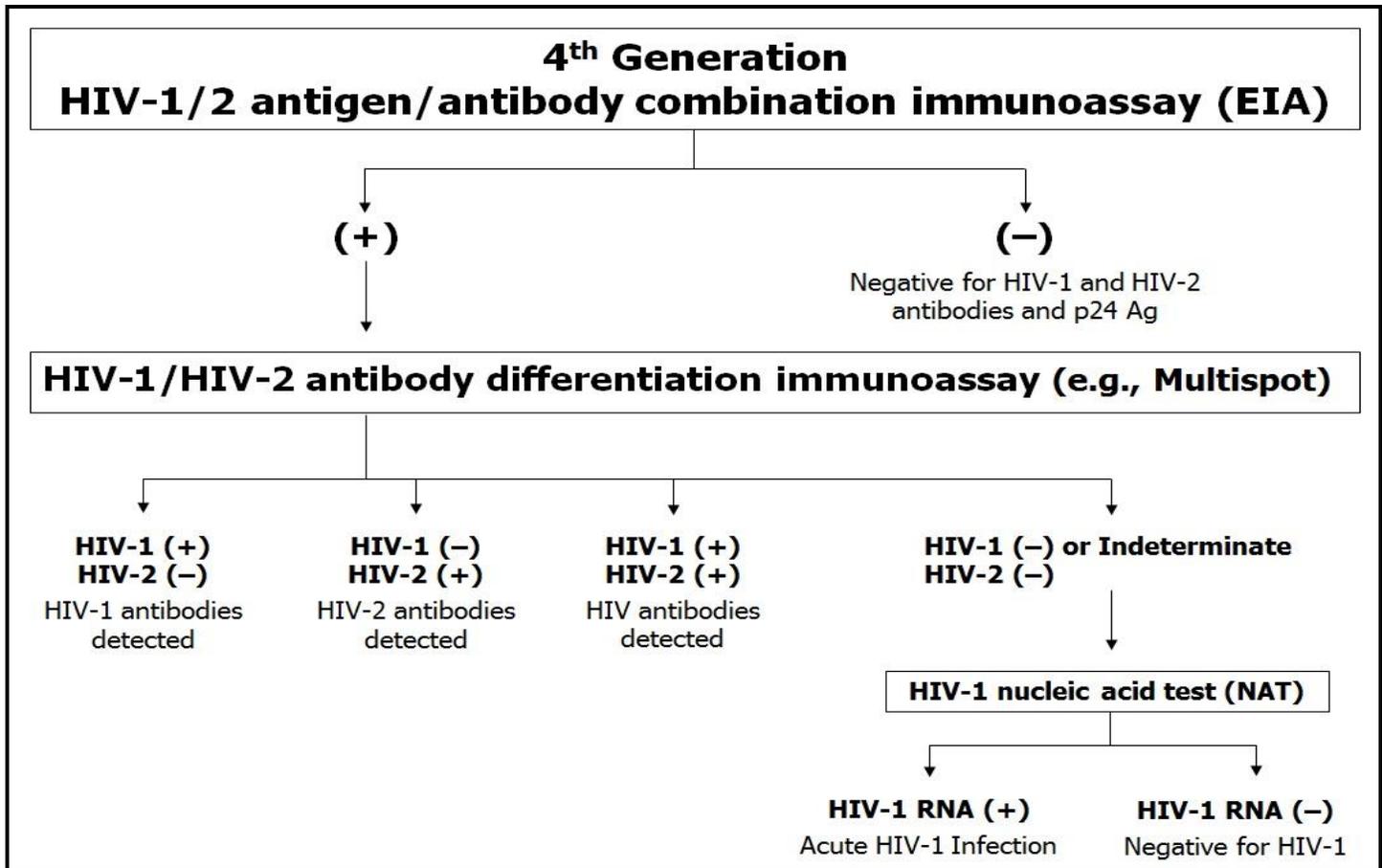
California Department of Public Health

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Attachments:

1. Figure: CDC-recommended laboratory HIV testing algorithm for serum or plasma specimens
2. Table: Recommended procedure for reporting results from CDC-recommended HIV Diagnostic Testing Algorithm to ordering health care providers and local public health departments

Figure. CDC-recommended laboratory HIV testing algorithm for serum or plasma specimens



Source: Centers for Disease Control and Prevention & Association of Public Health Laboratories. *Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations*, June 27, 2014. Available at: <http://stacks.cdc.gov/view/cdc/23447>. Accessed August 5, 2014.

CDPH recommends that:

1. Laboratories conduct initial testing for HIV with an FDA-approved 4th generation antigen/antibody combination immunoassay[†] that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen to screen for established infection with HIV-1 or HIV-2 and for acute HIV-1 infection. No further testing is needed for specimens that are nonreactive on the initial immunoassay.
2. Specimens with a reactive antigen/antibody combination immunoassay result (or repeatedly reactive, if repeat testing is recommended by the manufacturer or required by regulatory authorities) be tested with an FDA-approved antibody immunoassay that differentiates HIV-1 antibodies from HIV-2 antibodies. Specimens with reactive results on the initial antigen/antibody combination immunoassay and the HIV-1/HIV-2 antibody differentiation immunoassay, be interpreted as positive for HIV-1 antibodies, HIV-2 antibodies, or HIV antibodies, undifferentiated.
3. Specimens that are reactive on the initial antigen/antibody combination immunoassay and nonreactive or indeterminate on the HIV-1/HIV-2 antibody differentiation immunoassay be tested with an FDA-approved HIV-1 nucleic acid test (NAT).
 - A reactive HIV-1 NAT result and nonreactive HIV-1/HIV-2 antibody differentiation immunoassay result indicates laboratory evidence of acute HIV-1 infection.
 - A reactive HIV-1 NAT result and indeterminate HIV-1/HIV-2 antibody differentiation immunoassay result indicates the presence of HIV-1 infection confirmed by HIV-1 NAT. This may represent acute HIV-1 infection.
 - A negative HIV-1 NAT result and nonreactive or indeterminate HIV-1/HIV-2 antibody differentiation immunoassay result indicates a false-positive result on the initial immunoassay.
4. Laboratories use this same testing algorithm, beginning with a 4th generation antigen/antibody combination immunoassay, for serum or plasma specimens submitted for testing after a reactive (preliminary positive) result from any rapid HIV test.

[†] Exception: As of August 2014, data are insufficient to recommend use of the FDA-approved single-use rapid HIV-1/HIV-2 antigen/antibody combination immunoassay as the initial assay in the algorithm.

Table. Recommended procedure for reporting results from CDC-recommended HIV Diagnostic Testing Algorithm to ordering health care providers and local public health departments

Tests administered	Result interpretation reported to ordering health care provider	Basis for interpretation and recommendations	Results reported to local public health department
1. HIV-1/2 Ag/Ab combination immunoassay	1. Nonreactive	Negative for HIV-1 antigen and HIV-1/HIV-2 antibodies. No laboratory evidence of HIV infection. If acute HIV infection is suspected, consider testing for HIV-1 RNA.	Reporting this test result is not required.
1. HIV-1/2 Ag/Ab combination immunoassay	1. Reactive	Positive for HIV-1 antibodies. Laboratory evidence consistent with established HIV-1 infection is present.	Report test results 1 and 2.
2. HIV-1/HIV-2 antibody differentiation immunoassay	2. HIV-1 reactive and HIV-2 nonreactive		
1. HIV-1/2 Ag/Ab combination immunoassay	1. Reactive	Positive for HIV-2 antibodies. Laboratory evidence consistent with established HIV-2 infection is present.	Report test results 1 and 2.
2. HIV-1/HIV-2 antibody differentiation immunoassay	2. HIV-1 nonreactive and HIV-2 reactive		
1. HIV-1/2 Ag/Ab combination immunoassay	1. Reactive	HIV antibodies were not confirmed and HIV-1 RNA was not detected. No laboratory evidence of HIV-1 infection. Follow-up testing for HIV-2 should be performed if clinically indicated.	Reporting this test result is not required.
2. HIV-1/HIV-2 antibody differentiation immunoassay	2. Nonreactive or indeterminate		
3. HIV-1 RNA assay	3. RNA not detected		
1. HIV-1/2 Ag/Ab combination immunoassay	1. Reactive	Positive for HIV-1. Laboratory evidence consistent with acute HIV-1 infection is present.	Report test results 1, 2, and 3.
2. HIV-1/HIV-2 antibody differentiation immunoassay	2. Nonreactive		
3. HIV-1 RNA assay	3. RNA detected		
1. HIV-1/2 Ag/Ab combination immunoassay	1. Reactive	Positive for HIV-1 antibodies. Laboratory evidence of HIV-1 infection confirmed by HIV-1 RNA.	Report test results 1, 2, and 3.
2. HIV-1/HIV-2 antibody differentiation immunoassay	2. Indeterminate		
3. HIV-1 RNA assay	3. RNA detected		
1. HIV-1/2 Ag/Ab combination immunoassay	1. Reactive	Positive for HIV antibodies. Laboratory evidence of HIV infection is present. HIV antibodies could not be differentiated as HIV-1 or HIV-2. Additional testing for HIV-1 RNA or HIV-2 RNA should be performed if clinically indicated.	Report test results 1 and 2.
2. HIV-1/HIV-2 antibody differentiation immunoassay	2. HIV-1 and HIV-2 reactive		
1. HIV-1/2 Ag/Ab combination immunoassay	1. Reactive	HIV-1 antibodies were not confirmed and HIV-1 RNA testing was not performed. Result could indicate acute HIV infection. Testing of this specimen is incomplete. Follow-up testing for HIV-1 RNA is recommended as soon as possible.	Report test results 1 and 2.
2. HIV-1/HIV-2 antibody differentiation immunoassay	2. Nonreactive or indeterminate		

Note. Ag/Ab = antigen/antibody. RNA = ribonucleic acid.

Adapted from: Centers for Disease Control and Prevention & Association of Public Health Laboratories. *Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations*, June 27, 2014. Available at: <http://stacks.cdc.gov/view/cdc/23447>. Accessed August 5, 2014.