12-ID-05

Committee: Infectious Diseases

Title: Revisions Recommended for the Surveillance Case Definition for HIV infection

I. Statement of the Problem
Several aspects of the surveillance case definition for HIV infection [1], particularly the criteria for reporting a potential case, criteria for a confirmed case, and the case classification (staging system), as stated in sections VI and VII of the previous Position Statement 09-ID-01 [2], need to be revised because they are out of date, incomplete, unnecessary, unclear, contradictory, or impractical.

II. Background and Justification
The reasons why the following components of the surveillance case definition for HIV infection need revision are as follows:

A. New HIV Testing Algorithms
In June 2011, the Clinical and Laboratory Standards Institute (CLSI) published *Criteria for Laboratory Testing and Diagnosis of Human Immunodeficiency Virus Infection: Approved Guideline* [CLSI document M53-A, ISBN 1-56238-758-8], which outlines recommended laboratory testing procedures for diagnosis of HIV infection by laboratories and clinicians. It describes multi-test algorithms in which HIV antibody tests playing a "supplemental" (confirmatory/verifying) role may now include immunoassays formerly used only for initial screening (e.g., conventional enzyme immunoassay [EIA], rapid test, chemiluminescent immunoassay). The new algorithms are based on faster and more sensitive tests, enabling earlier diagnosis of acute HIV infection. The current surveillance case definition for HIV infection [1] is not clearly consistent with the new algorithms, because it states that an antibody test used for confirmation must be a "supplemental HIV antibody test (e.g., Western blot or indirect immunofluorescence assay test)."

The surveillance case definition for HIV infection should include these new testing algorithms because laboratories and clinicians have begun to use them without the Western blot or immunofluorescence assay as the basis for diagnosis as well as for reporting to HIV surveillance programs. According to the CLSI guideline, some of the multi-test algorithms lead to a conclusion of "presumptive positive," after which additional testing is said to be "optional". Cases based on such "presumptive" positive test results, which would have a predictive value of >90% in most settings, should be included by a revised surveillance case definition because not doing so could lead to delayed reporting or non-reporting of a substantial number of cases due to loss to follow-up. For simplicity, surveillance programs need not distinguish between presumptive and definitive cases in tabulations.

B. HIV tests that should be added to the list of tests used to report or define a case
The surveillance case definition should explicitly state that a combination HIV antigen/antibody test is an acceptable initial test in an HIV testing algorithm. In addition, a nucleotide sequence from an HIV genotype test should be considered indicative of a case of HIV infection, equivalent to a positive/detectable HIV nucleic acid (RNA or DNA) test (NAT) result.

C. HIV-2 Infection
HIV surveillance includes "all HIV variants (e.g., HIV-1 or HIV-2)," but the current case definition lacks criteria for differentiating between HIV-1 and HIV-2. A revised surveillance case definition for HIV infection should incorporate criteria specific for HIV-2.

D. Stage 0 HIV Infection

HIV infection surveillance should include monitoring the number of cases diagnosed within several months after infection. This period includes acute HIV infection, the most highly infectious stage, when viral loads are extremely high and intervention to prevent further transmission should be given priority. However, the current classification (staging) system for HIV infection does not include acute HIV infection. A new category (Stage 0) that includes acute HIV infection should be added to the staging system to enhance its usefulness for prevention (including partner notification services). It would also reduce confusion between acute HIV infection and stage 3 that can arise due to low CD4+ T-lymphocyte counts and opportunistic infections—usually interpreted as evidence of advanced disease—sometimes occurring during acute HIV infection.

E. Opportunistic Illnesses as Staging Criteria

The current case definition's requirement that some opportunistic illnesses indicative of Stage 3 must be diagnosed only by "definitive" methods is impractical because the criteria for "definitive" methods are not interpreted in a standard, uniform way. In addition, it is unnecessary because CD4+ T-lymphocyte counts associated with "presumptively" diagnosed opportunistic illnesses are similar to those associated with "definitively" diagnosed opportunistic illnesses, which implies that the method of diagnosis of opportunistic illnesses does not affect their usefulness as indicators of immunodeficiency. This requirement should, therefore, be removed. In addition, lymphoid interstitial pneumonia (also known as pulmonary lymphoid hyperplasia) should be deleted from the list of opportunistic illnesses indicative of stage 3 (AIDS) in children because it is associated with moderate rather than severe immunodeficiency [3].

F. CD4+ T-lymphocyte Test Results as Staging Criteria for Adults and Adolescents

In the current staging system, if the CD4+ T-lymphocyte percentage indicates a different stage than the CD4+ T-lymphocyte count, the stage is determined by whichever test result indicates the more severe stage. Giving the same weight to the CD4+ T-lymphocyte percentage as to the CD4+ T-lymphocyte count in this staging algorithm exaggerates the proportion of cases in the more severe stages. In clinical practice, greater importance is given to the CD4+ T-lymphocyte count than to the CD4+ T-lymphocyte percentage. The CD4+ T-lymphocyte percentage has been found to have little effect on prognosis after adjusting for the CD4+ T-lymphocyte count [4]. Therefore, the staging criteria should be changed to base the stage on only the CD4+ T-lymphocyte count, with the CD4+ T-lymphocyte percentage to be used only when the corresponding CD4+ T-lymphocyte count is unknown. In addition, an unpublished CDC analysis of national HIV surveillance data from areas where all values of CD4+ T-lymphocyte test results have been reported for the past few years found that the mean CD4+ T-lymphocyte percentage corresponding to a CD4+ T-lymphocyte count of 500 cells/μL (the threshold value between stages 1 and 2) is 26% rather than the 29% used in the current staging system. Therefore, this threshold value should be changed to 26% if further review of available data supports this change.

G. Incompatibility between Staging Systems for Children and Adults/Adolescents

Although there is a classification system for HIV infection among children [3], it is incompatible with the staging system for HIV infection among adults/adolescents. Stages 1 and 2 have not yet been defined for children. This position statement recommends that a pediatric workgroup be convened to address this issue.

H. HIV Infection Surveillance Case Definition for Children Less than 18 Months of Age

The 2008 case definition's requirement that a case in a child less than 18 months of age may be accepted only if the child's biologic mother was HIV-infected seems to apply to all children less than 18 months of age, but should apply only to those with insufficient laboratory evidence of HIV infection. Therefore, this requirement should be removed from the criteria for definitive and presumptive HIV infection.

I. Clinical Criteria (Physician-Documented Diagnosis)

The current case definition's clinical criteria for a case to be accepted on the basis of a "physician-documented diagnosis", i.e., without meeting the laboratory criteria, are contradictory because they do not clearly allow cases to be accepted with insufficient laboratory data. They actually require cases to meet the laboratory criteria, which is sometimes impractical, as laboratory test information for the initial diagnosis may not be retrievable for some cases. Therefore, the clinical criteria should be revised so as not to require knowledge of the result, type, and date of the diagnostic laboratory test.

In addition, the current guidance to define the date of the physician-documented diagnosis as the date on which physician's note was written tends to make the diagnosis date more recent than it actually was and thus misrepresents trends in the annual number of new diagnoses. Therefore, the date of diagnosis accepted for surveillance should be re-defined to the diagnosis date reported in the body of the physician's note; if it is missing from the note, the date on which the note was written should be used as a proxy.

III. Statement of the desired action(s) to be taken

1. Establish standard reporting and notification methods for HIV infection and recommend that any State or Territory conducting surveillance for this condition use these standard methods.

2. CSTE recommends that States and Territories conducting surveillance according to these methods report case information to CDC.

3. CSTE recommends that CDC publish data on HIV infection as appropriate in *MMWR* and other venues.

4. CSTE recommends that CDC revise the surveillance case definition for HIV infection as described below in Sections VI and VII and make modifications to eHARS or provide other software that will allow these changes to be reported electronically to CDC.

5. CSTE recommends that CDC convene a workgroup of consultant experts in pediatric HIV infection to review available data on the correlation of CD4 test results with clinical status in children. If possible, they should design an HIV infection staging system for children that would be more aligned with that for adults/adolescents.

IV. Goals of Surveillance

To provide information on the temporal, geographic, and demographic occurrence of HIV infection along the spectrum of its stages to facilitate its prevention and control.

V. Methods for Surveillance: Surveillance for HIV infection should use the following recommended sources of data and the extent of coverage listed in Table V.

Surveillance for HIV infection should use the sources of data and the extent of coverage listed in Table V. In addition, the CDC's *Technical Guidance for HIV Surveillance Programs* outlines other potential sources for ascertaining cases (see the "Access to Source Data, Case Finding, and Completeness of Reporting" chapter of Volume I).

Table V. Recommended sources of data for case identification and extent of coverage for ascertaining cases of HIV infection.

Source of data for case identification	Coverage	
	Population-wide	Sentinel sites
Clinician reporting	X	
Laboratory reporting	X	
Reporting by other entities (e.g., hospitals, veterinarians, pharmacies)	X	
Birth certificates	X	
Death certificates	X	
Hospital discharge or outpatient records	X	
Extracts from electronic medical records	X	
Telephone survey		
School-based survey		
Other: public health disease registries (tuberculosis STD, hepatitis, cancer); HIV-related programs (Ryan White programs, HIV Partner Services, etc.); insurance companies (health, life, disability); blood/plasma centers	X	

VI. Criteria for case identification The criteria for reporting a potential case by laboratories or healthcare providers (e.g., hospitals, clinics) to state/local public health agencies, and for those agencies to identify a potential case from administrative or clinical data files (e.g., death certificates, hospital discharge abstracts, HIV-specific clinical files) are described in the following narrative in Section VI-A and in Table VI-B in Section VI-B.

A. Narrative: A description of suggested criteria that may be for case ascertainment of a specific condition.

Laboratory Evidence

Reporting of a potential case of HIV infection should be triggered by a positive/reactive result on any test for HIV, including an initial test used as part of a multi-test algorithm. Reporting of positive/reactive results on tests previously used primarily as initial tests (e.g., for screening) has become necessary to make it possible to distinguish them from the supplemental tests in new diagnostic algorithms. Reporters of test results to HIV surveillance programs may not be able to know the role (initial or supplemental) of a test in a testing algorithm simply by knowing the test type (e.g., EIA, Western blot), because the types of tests formerly used only as initial tests (e.g., EIA) may now be used for verification in new testing algorithms. If known, the brand name, manufacturer, and the role the test is playing in the algorithm should also be reported to facilitate interpretation of the test results, particularly if the initial test and the supplemental test are of the same type (e.g., both are EIAs or both are rapid tests) to help surveillance programs avoid confusing them with two unrelated initial tests. Initial positive test results for which supplemental test results are missing should also be reported to enable health departments with the necessary resources to help the patient obtain further testing to resolve the uncertain infection status. The test results that should be reported include the following:

- A positive (reactive) result on an HIV antibody test (e.g., conventional EIA, "rapid" EIA, chemiluminescent immunoassay, Western blot, other immunoblot, line immunoassay, immunofluorescence assay)
- A positive result on an HIV antigen (e.g., p24) test
- A positive result on a combination HIV antigen/antibody test (in which it may not be possible to know whether the positive component was the antibody or the antigen without performing separate antibody and antigen tests)

- A positive or detectable result on a qualitative nucleic acid (RNA or DNA) test (NAT) (e.g., polymerase chain reaction [PCR] test)
- A quantitative HIV NAT (viral load), regardless of the result (including undetectable results)
- A positive result on an HIV isolation test (viral culture)
- A nucleotide sequence from an HIV genotype test

In addition, negative (nonreactive) results on HIV antibody tests should be reported if they were on the same date, within 30 days after, or 180 days before a positive result on one of the above tests, because this combination of positive and negative results may indicate a case of acute or Stage-0 HIV infection, which should receive priority for further investigation and preventive intervention. The patient should be referred for follow-up testing and, in the interim, counseled to prevent transmission. However, if a testing algorithm has reached a conclusion that a person is uninfected, then none of the tests for that person need to be reported.

Clinical Evidence

In addition to HIV test results, the following should be reported to surveillance programs or searched by surveillance staff as indicators of potential cases:

- HIV infection documented in a medical record as diagnosed by a physician or other qualified medical care provider, even if laboratory test results on which the diagnosis was based are not documented
- Death certificates that mention HIV infection
- Medical records that mention HIV infection or that are limited to HIV-infected persons such as those in an AIDS Drug Assistance Program (ADAP) or Ryan White Care program.

Epidemiological Evidence

- Birth certificates that mention HIV infection in the mother

B. Table of criteria to determine whether a case should be reported to public health authorities

Table VI-B. Criteria to determine whether a case should be reported to public health authorities.

Criterion	Potential HIV infection
Laboratory Evidence	
Positive HIV antibody test	S
Positive HIV antigen test	S
Positive HIV combination antigen/antibody test	S
Positive qualitative HIV nucleic acid test	S
Quantitative HIV nucleic acid test (viral load), any result*	S
Viral isolation (culture)	S
HIV genotype test result	S
Clinical Evidence	
HIV diagnosis documented in medical record or death certificate	S
Epidemiological Evidence	
Child born to HIV-infected mother, documented in medical record or birth certificate	S

Legend: S = This criterion alone is **S**ufficient to report a potential case.

***Even undetectable viral loads should be reported unless the patient is known not to have HIV infection, because they could represent potential cases or may help to monitor whether known cases are in care.

C. Disease-specific data elements
When a potential HIV case has been identified, a complete case report should be made to surveillance. Reporters should include the data elements on CDC's Adult HIV Confidential Case Report form CDC 50.42C and Pediatric HIV Confidential Case Report form CDC 50.42B.

VII. Case Definition for Case Classification

A. Narrative: Description of criteria to determine how a case should be classified

The case definition below builds on CDC's MMWR article entitled "Revised Case Definitions for HIV Infection Among Adults, Adolescents, and Children <18 months and for HIV Infection and AIDS Among Children Aged 18 Months to <13 Years ---United States, 2008" (MMWR 2008;57 (No. RR10). It incorporates revisions recommended to address the issues described in Section II-A through ll-I above, and combines the confirmation and staging criteria for different age groups into a single definition. The definition is intended for public health surveillance and prevention, not as a guide for clinical diagnosis or patient management. The definition applies to all HIV variants (e.g. HIV-1 or HIV-2). Criteria for a confirmed case of HIV infection may not be met solely by the diagnosis of a Stage-3-defining opportunistic illness (see Appendix).

A.1: CRITERIA FOR A CONFIRMED CASE

Persons Aged 18 Months Through Adult

Laboratory Evidence
Laboratory criteria require three things:

1) A test result specified as positive (or reactive or detectable)
2) Specification of the date of the test (at least the year); this should be the date of specimen collection, if known
3) The type of test and, if applicable and known, the role it plays in a testing algorithm.

The test types, results, and algorithms may be any of the following:

- A multi-test algorithm consisting of
  - a positive result on an initial serologic test, which may be
    - an HIV antibody test or
    - a combination HIV antigen/antibody test
  - accompanied or followed by a positive result on a supplemental HIV test different from the initial test,

  as recommended by the Clinical and Laboratory Standards Institute (CLSI) in the *Criteria for Laboratory Testing and Diagnosis of Human Immunodeficiency Virus Infection: Approved Guideline* [CLSI document M53-A, ISBN 1-56238-758-8], published in June 2011. The initial HIV serologic test and the supplemental HIV antibody test that is used to verify the result of the initial test may be of any type approved by the federal Food and Drug Administration for screening or diagnosis of HIV infection, but they must not be identical (FDA website: http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/BloodDonorScreening/InfectiousDisease/UCM080466). For surveillance purposes, supplemental tests for diagnosing HIV-2 infection (Section VII-A.2 below) may include some not approved by the FDA (e.g., HIV-2 Western blot/immunoblot, HIV-2 NAT) if validated by the laboratory performing them. The type of HIV antibody test that verifies the initial test may be one formerly used only as an initial or preliminary test (e.g., conventional EIA, rapid immunoassay, chemiluminescent assay, HIV-1/2 type-differentiating immunoassay), or it may be one traditionally used as a supplemental test for confirmation (e.g., Western blot, immunofluorescence assay). For the purpose of HIV infection

surveillance, the CLSI algorithms that conclude with a "presumptive positive" are to be considered equivalent to those that conclude with a definitive positive.

Or

- Positive conclusion of a multi-test HIV antibody algorithm from which only the final result was reported (including a single positive result on a test that is used only as a supplemental test (e.g., HIV Western blot, immunofluorescence assay)

Or

- Positive result or report of a detectable quantity (i.e., within the established limits of the laboratory test) from any of the following HIV virologic (i.e., non-antibody) tests:
    - Qualitative HIV nucleic acid (DNA or RNA) test (NAT) (e.g., polymerase chain reaction [PCR])
    - Quantitative HIV NAT (viral load assay)
    - HIV p24 antigen test
    - HIV isolation (viral culture)
    - HIV genotype nucleotide sequence

Clinical (Non-Laboratory) Evidence

Clinical criteria for a confirmed case (i.e., a "physician-documented" diagnosis rather than a laboratory-test-documented diagnosis) are met by the combination of

- A note written by a physician or other qualified medical-care provider that does not meet the laboratory criteria described above but states that the patient has HIV infection,

and

- One or both of the following:
    - The laboratory criteria for a confirmed case were met based on tests done after the physician's note was written (validating the note retrospectively)

    or

    - Circumstantial evidence of HIV infection (e.g., receipt of HIV-related care [antiretroviral therapy, prophylaxis for an opportunistic infection], an otherwise unexplained low CD4+ T-lymphocyte count or diagnosis of an opportunistic illness indicative of Stage 3 [see Appendix])

Children Aged <18 Months

For a child <18 months, the following criteria classify a child as definitively or presumptively HIV-infected, or definitively or presumptively not HIV-infected. These criteria largely reflect CDC's 2008 case definition [1], with the exception of eliminating the requirement that the child be born to an HIV-infected mother as a criterion for definitive and presumptive HIV infection.

Laboratory Evidence

Definitive HIV Infection

A child aged <18 months is categorized for surveillance purposes as definitively HIV infected if there are:

- Positive results on two separate specimens (not including cord blood) from one or more of the following HIV virologic (non-antibody) tests:
    - HIV nucleic acid (DNA or RNA) detection
    - HIV p24 antigen test, including neutralization assay, for a child aged >1 month
    - HIV isolation (viral culture)
    - HIV genotype nucleotide sequence
- Specification of the date(s) of the test(s) (at least the year); this should be the date of specimen collection, if known

Presumptive HIV Infection
A child aged <18 months is categorized for surveillance purposes as presumptively HIV infected if the following four criteria are met:

- The criteria for definitive HIV infection are not met
- Positive results on only one specimen (not including cord blood) from any of following HIV virologic tests
    - HIV nucleic acid (DNA or RNA) detection
    - HIV p24 antigen test, including neutralization assay, for a child aged >1 month
    - HIV isolation (viral culture)
    - HIV genotype nucleotide sequence
- Specification of the date of the test (at least the year); this should be the date of specimen collection, if known

and

- No subsequent negative results on HIV virologic or HIV antibody tests

Clinical Evidence
Same as for persons aged 18 months through adult (see above)

Definition of Date of Diagnosis of a Confirmed Case for all Ages
Laboratory Criteria
If the diagnosis is based on laboratory evidence, the diagnosis date is defined as the date on which the specimen was obtained for the initial positive HIV test result.
Clinical Criteria
If the diagnosis was based on clinical evidence ("physician-documented") rather than on HIV test results, the diagnosis date is defined as the date (at least the year) of diagnosis reported in the content of the physician's note. If the diagnosis date was not reported in the note, the date on which the note was written may be used as a proxy. However, both of these dates should be reported, as well as the date of diagnosis stated by the patient, if it differs from the other two.

A.2: CRITERIA FOR CLASSIFYING THE HIV TYPE AS HIV-2
Only laboratory evidence is used to classify the HIV type as HIV-2. Clinical or epidemiologic evidence may lead to laboratory testing for HIV-2, but are not among criteria for classifying the HIV type as HIV-2

Persons Aged 18 Months Through Adult
For HIV-2 infection, the following laboratory criteria are required:

- Positive result on initial/screening test that can detect HIV-2 antibody (e.g., HIV-1/2 immunoassay) and
- One or more of the following to distinguish HIV-2 from HIV-1:
    - FDA-approved HIV1/2 type-differentiating antibody test result positive for HIV-2 and negative for HIV-1

    or
    - Positive HIV-2 nucleic acid test (NAT) result

    or
    - Positive HIV-2 Western blot (WB) (or immunoblot or line assay) result and negative HIV-1 WB result

    or
    - Diagnosis of HIV-2 infection by a CDC-recognized expert in interpretation of Western blots and/or differential diagnosis of HIV-2 if HIV-2 WB is positive and HIV-1 WB is positive or indeterminate

Children Aged <18 Months

In children aged <18 months, antibody tests are not used to diagnose HIV infection, but after the diagnosis is made by use of virologic tests (e.g., NAT) as described above, the HIV type may be classified as HIV-2 by the same criteria used for older persons.

A.3: CRITERIA FOR OTHER CLASSIFICATIONS OF THE HIV INFECTION STATUS OF PERINATALLY EXPOSED CHILDREN AGED <18 MONTHS

UNINFECTED

A child aged <18 months who was born to an HIV-infected mother or had a positive HIV antibody test result is classified for surveillance purposes as not infected with HIV if the following criteria are met:

- Laboratory criteria for definitive or presumptive HIV infection not met and
- No diagnosis of a Stage-3-defining opportunistic illness (see Appendix) that could not be attributed to a cause of immunosuppression other than HIV.

and

Laboratory Evidence

Definitively Uninfected

- At least one of the following two criteria are met:
  - At least two negative HIV DNA or RNA nucleic acid tests from separate specimens, both of which were obtained at age >1 month and one of which was obtained at age >4 months

  or
  - At least two negative HIV antibody tests from separate specimens obtained at age >6 months

or

Presumptively Uninfected

- Criteria for definitively uninfected with HIV not met and
- At least one of the following four criteria are met:
  - At least two negative RNA or DNA virologic tests, from separate specimens, both of which were obtained at age >2 weeks and one of which was obtained at age >4 weeks

  or
  - One negative nucleic acid (RNA or DNA) test (NAT) from a specimen obtained at age >8 weeks

  or
  - One negative HIV antibody test from a specimen obtained at age >6 months

  or
  - If criteria for presumptive HIV infection had initially been met by one positive HIV NAT test then it must have been followed by at least two negative tests from separate specimens, one of which is
    - a NAT from a specimen obtained at age >8 weeks or
    - an HIV antibody test from a specimen obtained at age >6 months;

Clinical Evidence

- Laboratory criteria are not met for definitive or presumptive absence of HIV infection, and
- Note written by physician or other qualified medical-care provider states that the patient is not infected with HIV

INDETERMINATE

A child aged <18 months born to an HIV-infected mother is categorized as having perinatal exposure with an indeterminate HIV infection status if neither the criteria for being HIV-infected nor the criteria for not being HIV-infected are met.

A.4: CRITERIA FOR CLASSIFYING THE STAGE OF HIV INFECTION

This definition is intended for public health surveillance and prevention of transmission and not as a guide for clinical diagnosis or patient management. To distinguish the stages of HIV infection defined in this document for surveillance from stages defined for clinical management or other purposes, they should be called "Surveillance Stages".

Persons Aged 13 Years through Adult

A confirmed case that meets the above criteria for diagnosis of HIV infection may be classified in one of five HIV infection stages (stage 0, stage 1, stage 2, stage 3, or stage unknown). The stage characterizes the status of HIV infection at a particular date. The stage may be defined in alternative ways with reference to the date of interest. For example:

- the stage on the date of initial diagnosis,
- the most advanced stage last known through a particular date.

Stages 1, 2, and 3 are based primarily on the CD4+ T-lymphocyte count. If the CD4 count is missing or unknown, the CD4+ T-lymphocyte percentage of total lymphocytes may substitute for the CD4 count. Although cases with no information on CD4+ T-lymphocyte count or percentage can be classified as stage unknown, every effort should be made to report CD4+ T-lymphocyte counts or percentages at the time of diagnosis. All subsequent CD4+ T-lymphocyte counts or percentages should also be reported to help monitor disease progression and whether the person is receiving on-going care. The stages are defined as follows:

Stage 0

Stage 0 is defined either by the relationship between positive and prior negative HIV test dates or by a testing algorithm that detects early HIV infection prospectively. It is independent of CD4+ T-lymphocyte test results. A "test date" means the date on which the specimen for the test was obtained, if known, not necessarily the date on which the test was conducted. The stage is 0 if the following criteria are met:

Retrospective Criteria:

The date of a negative or indeterminate HIV test was 1 to 180 days before the date of the first confirmed positive HIV test, or

Prospective Criteria:

- The a negative or indeterminate HIV antibody test was 0 to 30 days after the initial confirmed positive HIV test, and
- The negative or indeterminate HIV antibody test was 0 to 30 days before the positive supplemental test that confirmed the initial positive HIV test, and
- The negative or indeterminate antibody test was less sensitive than the initial confirmed positive HIV test (based on the test sensitivity ranking listed below), and
- The negative or indeterminate antibody test was less sensitive than the positive supplemental HIV test (based on the test sensitivity ranking listed below) if those tests were on the same date.

HIV Test Sensitivity Ranking, in descending order of sensitivity

1. Nucleic acid test (NAT), qualitative or quantitative (assumed most sensitive)
2. Combination antigen/antibody test
3. Immunoassays (IA) (not rapid, not type-differentiating, assumed able to detect IgM)
4. Rapid immunoassay (assumed unable to detect IgM), including HIV-1/HIV-2 viral type-differentiating rapid tests
5. HIV-1 Western blot, immunoblot, line immunoassay, or immunofluorescence assay (assumed least sensitive)

Exceptions: A confirmed case of HIV infection is not in Stage 0 if any of the following are true:

- The negative or indeterminate HIV test used as the criterion for the earliness of infection was preceded by >60 days by evidence of an earlier onset of HIV infection: an HIV infection diagnosis based on a clinical ("physician-documented") diagnosis, a CD4 T-lymphocyte count <200 cells/µL in an adult/adolescent, or a Stage-3-defining opportunistic illness [see Appendix])
- The case definition for HIV-2 infection is met. (An HIV-1 antibody test may be nonreactive or indeterminate due to its inability to detect HIV-2 antibodies, and an HIV-1 NAT may be negative due to its inability to detect HIV-2 nucleic acid, rather than due to absence or earliness of HIV-2 infection.)

If the criteria for Stage 0 are not met at diagnosis, the stage is classified as 1, 2, 3, or Unknown, depending on the CD4+ T-lymphocyte test results at diagnosis (or within 3 months of diagnosis), as described below.

Progression of stage after initial diagnosis:
Although the stage at diagnosis does not change, if >180 days have elapsed after diagnosis in Stage 0, the stage at the later date is classified as 1, 2, 3, or Unknown, depending on CD4+ T-lymphocyte test results on that later date (or within 3 months of it), as described below.

Stage 1

- Criteria for Stage 0 not met
- No Stage-3-defining opportunistic illness (see Appendix)
- CD4+ T-lymphocyte test results:
    - CD4 count of >500 cells/µL or
    - If CD4 count is unknown, a CD4+ T-lymphocyte percentage of total lymphocytes of >26%.[1]

Stage 2

- Criteria for Stage 0 not met
- No Stage-3-defining opportunistic illness (see Appendix)
- CD4+ T-lymphocyte test results:
    - CD4 count of 200--499 cells/µL or
    - If CD4 count is unknown, a CD4 percentage of 14%--26.[1]

Stage 3

- Criteria for Stage 0 not met
- One or both of the following:
    - Stage-3-defining opportunistic illness(see Appendix), or
    - CD4+ T-lymphocyte test results:
        - CD4 count of <200 cells/µL or
        - If CD4 count is unknown, a CD4 percentage of <14%

Whatever method was used to make the diagnosis of any of the opportunistic illnesses will be accepted as sufficient (eliminating the previous requirement for some of them to be "definitively" diagnosed). These changes will be applied only to cases reported after implementation of this revision, not retroactively to previously reported cases.

[1] The change in the CD4 percentage threshold from 29% (as in the current case definition) to 26% (as in the revision proposed above) should be contingent on data being published that support it.

Stage Unknown

- Criteria for Stage 0 not met
- No information available on CD4+ T-lymphocyte count or percentage
- No information available on Stage-3-defining opportunistic illness (see Appendix).

Children Aged <13 years

The opportunistic illnesses listed in the previous case definition are used as indicators of clinical category C in the 1994 revised classification system for HIV infection among children aged <13 years [1,3]. They will continue to be used as indicators of acquired immunodeficiency syndrome (AIDS) in children, corresponding to what in adults/adolescents is called “Stage 3”. However, lymphoid interstitial pneumonia will no longer be one of them, because it is associated with moderate rather than severe immunodeficiency. Whatever method was used to make the diagnosis of any of the opportunistic illnesses will be accepted as sufficient (eliminating the previous requirement for some of them to be “definitively” diagnosed). These changes will be applied only to cases reported after implementation of this revision, not retroactively to previously reported cases.

In addition, the criteria for Stage 0 in adults/adolescents may also be applied to children if they are known not to have acquired HIV infection perinatally from their mother. For those aged <18 months, this requires previously meeting the criteria for definitive absence of HIV infection. If the criteria for Stage 0 are not met or >180 days have elapsed after diagnosis in Stage 0, the stage at the later date is classified as either 3 or “U” (undefined), depending on whether an opportunistic illness has been diagnosed (see Appendix).

The criteria for staging in children differ from those in adults/adolescents. Stage 3 in children is based on the diagnosis of opportunistic infections, and not on CD4+ T-lymphocyte test results [1]. Stages 1 and 2 in children are undefined because a consensus has not yet been reached on which CD4 test results should define the boundaries between stages 1, 2, and 3 in children.

B. Classification Tables

Table VII-B.1. Criteria for defining a confirmed case of HIV infection
Note: The criteria in the following table are intended to reflect the criteria for a confirmed case in the narrative description in Section VII-A.1 above.

Criteria for a confirmed case	Age at Diagnosis						
	≥18 months				<18 months		
Laboratory Evidence	Definitive			Clinical	Definitive*	Presumptive*	Clinical
HIV test date (at least the year)	N	N	N		N	N	
Positive result on initial HIV antibody test in algorithm	N						
Positive result on initial HIV combination antigen/antibody test wherein which of the two components (antibody or antigen) was positive cannot be differentiated		N					
Positive result on supplemental HIV antibody test that verifies result of initial test in algorithm	N	N					
Positive result on HIV antibody test used only as supplemental test (e.g., Western blot, immunofluorescence assay) or on conclusion of antibody test algorithm			O				
Positive result on HIV p24 antigen test			O		O (if age ≥1 month)	O (if age ≥1 month)	
Positive result on HIV nucleic acid test (DNA or RNA)			O		O	O	
Positive result on HIV isolation (viral culture)			O		O	O	
HIV genotype nucleotide sequence			O		O	O	
At least 2 such results from separate specimens					O		
Results from only one specimen						O	
No subsequent negative results on HIV virologic or HIV antibody tests						N	
Clinical evidence							
Physician's note stating patient has HIV infection				N			N
Retrospective validation of note by subsequent laboratory evidence as described above				O			O
Circumstantial evidence of HIV infection (e.g., antiretroviral therapy, low CD4 count, diagnosis of opportunistic illness)				O			O

Legend:
N = All "N" criteria in the same column are **N**ecessary to classify a case as confirmed.
O = At least one of the "O" (**O**ptional) criteria in each category in the same column—in conjunction with the "N" criterion in the same column—is required to classify a case as confirmed.
*"Definitive" diagnosis requires positive results from two separate specimens (excluding cord blood) for one or more of the tests marked by an "N". "Presumptive" diagnosis requires a positive result from only one specimen for the test.

Table VII-B.2. Criteria for classifying the HIV type as HIV-2

Note: The laboratory criteria in the following table are intended to reflect the criteria in the narrative description in Section VII-A.2 above. In children aged <18 months, a confirmed diagnosis of HIV infection must be established (Table VII-B.1) before the following criteria are applied to determine the HIV type.

Criteria	Classification	
HIV test date (at least the year)	N	N
Positive result on initial/screening HIV antibody test that can detect HIV-2 antibody (e.g., HIV-1/2 immunoassay)	N	
Positive result on initial HIV combination antigen/antibody test that can detect HIV-2 antibody		N
Positive result for HIV-2 AND negative result for HIV-1 on FDA-approved HIV-1/2 type-differentiating antibody test	O	O
Positive result on HIV-2 Western blot (or immunoblot or line assay) antibody test AND negative result on HIV-1 Western blot antibody test	O	O
Positive result on HIV-2 nucleic acid (DNA or RNA) test	O	O
Diagnosis of HIV-2 infection by CDC-recognized expert in interpretation of Western blots if HIV-2 WB is positive and HIV-1 WB is positive or indeterminate	O	O

Legend:
N = All "N" criteria in the same column are **N**ecessary to classify the HIV type as HIV-2.
O = At least one of these "O" (**O**ptional) criteria in each category in the same column—in conjunction with the "N" criteria in the same column—is required to classify the HIV type as HIV-2.

Table VII-B.3. Criteria for classifications of HIV infection status other than definitively or presumptively infected in perinatally exposed children aged <18 months

Note: The criteria in the following table are intended to reflect the criteria in the narrative description in Section VII-A.3 above.

Criteria	**Classification**			
	Definitively uninfected based on lab evidence	Presumptively uninfected based on lab evidence	Uninfected based on clinical evidence	Indeterminate infection status
Laboratory Evidence				
Laboratory criteria for definitive or presumptive HIV infection not met	N	N	N	N
No diagnosis of Stage-3-defining opportunistic illness that could not be attributed to a cause of immunosuppression other than HIV	N	N		
At least two negative HIV DNA or RNA tests from separate specimens, both of which were obtained at age >1 month and one of which was obtained at age >4 months	O			
At least two negative HIV antibody tests from separate specimens obtained at age >6 months	O			
Criteria for definitively uninfected with HIV not met		N		
At least two negative nucleic acid (RNA or DNA) tests (NATs), from separate specimens, both obtained at age >2 weeks and one obtained at age >4 weeks		O		
One negative NAT from a specimen obtained at age >8 weeks		O		
If criteria for presumptive HIV infection were initially met by one positive HIV NAT: At least two negative tests from separate specimens, one of which is a NAT from a specimen obtained at age >8 weeks		O		
If criteria for presumptive HIV infection were initially met by one positive HIV NAT: At least two negative tests from separate specimens, one of which is an HIV antibody test obtained at age >6 months		O		

Table VII-B.3. Criteria for classifications of HIV infection status other than definitively or presumptively infected in perinatally exposed children aged <18 months (continued)

Criteria	Classification			
	Definitively uninfected based on lab evidence	Presumptively uninfected based on lab evidence	Uninfected based on clinical evidence	Indeterminate infection status
Laboratory Evidence				
Laboratory criteria for definitive or presumptive HIV infection not met	N	N	N	N
Clinical Evidence				
Note written by qualified medical-care provider states patient is not HIV-infected			N	
Combined laboratory and clinical evidence				
Above criteria in this table for being uninfected not met				N

Legend:
N = All "N" criteria in the same column are **N**ecessary to classify a case as confirmed.
O = At least one of these "O" (**O**ptional) criteria in each category in the same column—in conjunction with the "N" criteria in the same column—is required to classify a case as confirmed.

Table VII-B.4a. Criteria for classifying the stage of HIV infection as Stage 0

Note: The criteria in the following table are intended to reflect the first part of the criteria for staging in the narrative description in Section VII-A.4 above.

Laboratory Evidence	**Retrospective Detection**	**Prospective Detection**
First positive HIV test was 1 to 180 days after negative, undetectable, or indeterminate HIV test.	N	
First positive HIV test was 0 to 30 days before negative or indeterminate HIV antibody test.		N
First positive test was confirmed by a second positive HIV test 0 to 30 days after negative/indeterminate antibody test.		N
The negative/indeterminate antibody test was less sensitive than first positive test (based on the test sensitivity ranking listed below).		N
The negative/indeterminate antibody test was less sensitive than the second positive test (based on the test sensitivity ranking listed below) if those tests were on the same date.		N
Type of HIV is not HIV-2 (See criteria for HIV-2 in Table VII.B.2)	N	N
The negative, indeterminate, or undetectable HIV test result used as the criterion for earliness of infection was not >60 days after an HIV infection diagnosis based on clinical (non-laboratory) evidence, a CD4+ T-lymphocyte count <200 cells/μL, or diagnosis of an opportunistic illness indicative of Stage 3 HIV infection (see Appendix).	N	N
Combined laboratory and clinical evidence		
Criteria for confirmed case of HIV infection (Table VII.B.1) were met	N	N
≤180 days have elapsed after diagnosis	N	N
Epidemiologic Evidence		
HIV infection was not acquired perinatally from biological mother	N	N

Legend:
N = All "N" criteria in the same column are **N**ecessary to classify the stage as Stage 0.

HIV Test Sensitivity Tiers, ranked in descending order of sensitivity:
1. Nucleic acid test (NAT), qualitative or quantitative (assumed most sensitive)
2. Combination antigen/antibody test
3. EIA (not rapid, not type-differentiating, assumed able to detect IgM)
4. rapid immunoassay, including HIV-1/HIV-2 viral type-differentiating rapid tests
5. HIV-1 Western blot, immunoblot, line immunoassay, or immunofluorescence assay (assumed least sensitive)

Table VII-B.4b. Criteria for classifying the stage of HIV infection as Stage 1, 2, 3, or U

Note: The criteria in the following table are intended to reflect the remaining part of the criteria for staging in the narrative description in Section VII-A.5 above.

Criteria for stage	Age					
	≥13 years				<13 years	
Stage	1	2	3	U	3	U
Laboratory Evidence						
Criteria for Stage 0 not met	N	N	N	N	N	N
CD4+ T-lymphocyte count >500 cells/μL, or, if unknown, CD4+ T-lymphocyte percentage of total lymphocytes >26%	N					
CD4+ T-lymphocyte count 200--499 cells/μL, or, if unknown, CD4+ T-lymphocyte percentage 14%--26%		N				
CD4+ T-lymphocyte count <200 cells/μL, or, if unknown, CD4+ T-lymphocyte percentage <14%			O			
CD4+ T-lymphocyte count and percentage unknown				N		
Clinical evidence						
Diagnosis of opportunistic illness			O		N	
No diagnosis of opportunistic illness						N

Legend:
N = All "N" criteria in the same column are **N**ecessary to classify the stage as 1, 2, 3, or U (Unknown/undefined).
O = At least one of these "O" (**O**ptional) criteria in each category in the same column—in conjunction with the "N" criteria in the same column—is required to classify the stage.

Note: The stage characterizes the status of HIV infection at a particular date. The stage may be defined in alternative ways with reference to the date of interest. For example, the stage on the date of initial diagnosis (which does not change over time, and may be based on CD4+ T-lymphocyte values within a short time [e.g., 3 months] of diagnosis), the stage based on the lowest CD4+ T-lymphocyte values through a particular date (for which changes in stage are in only one direction--from less to more severe), or the stage based on the most recent CD4+ T-lymphocyte test results (for which changes can be in either direction-- from more to less severe, or from less to more severe). "U" means "unknown stage" for persons aged ≥13 years or "stage undefined" for persons aged <13 years.

VIII. Period of Surveillance
Surveillance should be ongoing.

IX. Data sharing/release and print criteria
It is recommended that HIV surveillance programs notify CDC of all confirmed HIV infection cases as well as all perinatally exposed infants.

CDC does not release case-level data. CDC routinely releases aggregate data to their partners for use in describing the HIV burden (e.g., Kaiser Foundation and WHO) and for funding allocations and care program planning (e.g., HRSA and the United States Congress). Additionally, CDC has a mechanism for outside parties to submit data requests for aggregate level data. If these requests are for appropriate public health purposes and meet CDC's data release policies, CDC may approve them and provide the requested data

X. References

1. CDC. Revised Surveillance Case Definitions for HIV Infection Among Adults, Adolescents, and Children Aged <18 Months and for HIV Infection and AIDS Among Children Aged 18 Months to <13 Years. MMWR 2008;57:1-8.
2. CSTE Position Statement 09-ID-01 (available at http://www.cste.org/ps2009/09-ID-01.pdf, accessed March 23, 2012).
3. CDC. 1994 Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR 1994;43(No. RR-12).
4. Gebo KA, et al. Absolute CD4 vs.CD4 percentage for predicting the risk of opportunistic illness in HIV infection. J Acquir Immun Defic Syndr 2004; 36:1028–1033

XI. Coordination

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Appendix: Stage-3-Defining Opportunistic Illnesses

- Bacterial infections, multiple or recurrent*
- Candidiasis of bronchi, trachea, or lungs
- Candidiasis of esophagus
- Cervical cancer, invasive†
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1 month's duration)
- Cytomegalovirus disease (other than liver, spleen, or nodes), onset at age >1 month
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy, HIV-related
- Herpes simplex: chronic ulcers (>1 month's duration) or bronchitis, pneumonitis, or esophagitis (onset at age >1 month)
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (>1 month's duration)
- Kaposi sarcoma
- Lymphoma, Burkitt (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary, of brain
- Mycobacterium avium complex or Mycobacterium kansasii, disseminated or extrapulmonary
- Mycobacterium tuberculosis of any site, pulmonary†, disseminated, or extrapulmonary
- Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
- Pneumocystis jirovecii pneumonia
- Pneumonia, recurrent†
- Progressive multifocal leukoencephalopathy
- Salmonella septicemia, recurrent
- Toxoplasmosis of brain, onset at age >1 month
- Wasting syndrome attributed to HIV

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* Only among children aged <13 years. (CDC. 1994 Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR 1994;43[No. RR-12].)
†Only among adults and adolescents aged >13 years. (CDC. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR 1992;41[No. RR-17].)