Attachment F. *Supplemental Surveillance Activity 1*: HIV Incidence Surveillance Data Elements and Procedures

Status: new

Description: These data elements will be an electronic extension of the case report forms **(Attachment C)**; as such, there is no new form for this activity.

Standard HIV Incidence Surveillance Data Elements

Variable Description	Valid Value
Number of HIV tests in 2 years prior to the first positive (For people who previously tested positive)	1 - 99 R=refused D=don't know
Anonymous HIV test at first positive test	0=no 1=yes 7=refused 9=don't know
Antiretroviral medications within the last 6 months	0=no 1=yes 7=refused 9=don't know
ARV meds taken	22=Agenerase 30=Aptivus 24=Combivir 06 =Crixivan 11=Emtriva 03=Epivir 28=Epzicom 25=Fortovase 10=Fuzeon 19=Hepsera 02=Hivid 23=Hydroxyurea 18=Invirase 16=Kaletra 31=Lexiva 07=Norvir 88=Other 09=Rescriptor 26=Retrovir 15=Reyataz 08=Saquinavir
CLIA code for source lab where specimen originated	text
Currently taking antiretroviral medications	0=no 1=yes 7=refused

	9=don't know
Date HAART use began	yyyymmdd
Date HAART use ended	yyyymmdd
Date information is extracted	yyyymmdd
Date of first HIV test ever	yyyymmdd
Date of first positive HIV test	yyyymmdd
Date of STARHS test	yyyymmdd
Date of the HIV test that resulted in a case report	yyyymmdd
Date specimen was obtained	yyyymmdd
Has specimen been approved for STARHS?	0=no 1=yes 2=pending
Laboratory ID	33D0654341=NYST 33D0654341=CDCSTARHS 33D0654341=NY 33D0654341=CDCSTAR 21D0649758=MARY01 50D0661430=WASH
Date of last HIV negative test before first positive	yyyymmdd
Date of last HIV negative test before first positive (or before test that resulted in a case report if never previously tested positive)	yyyymmdd
Name of site where first tested positive for HIV	text
Name of site where last tested negative for HIV	text
Ever tested for HIV	0=no 1=yes 7=refused 9=don't know

Ever tested negative	0=no 1=yes 7=refused 9=don't know
Number of HIV tests in last 2 years before first positive (including first positive test)	1 - 99 R=refused D=don't know
Number of HIV tests in last 2 years before first positive (People who never had previous positive)	1 - 99 R=refused D=don't know
Optical density	text
Ever tested positive	0=no 1=yes 7=refused 9=don't know
Reason for first positive HIV test*	text
Reason for testing at first positive - exposure to HIV within the last 6 months*	0=no 1=yes 7=refused 9=don't know
Reason for testing at first positive - just checking to make sure you are HIV negative*	0=no 1=yes 7=refused 9=don't know
Reason for testing at first positive - other reason*	0=no 1=yes 7=refused 9=don't know
Reason for testing at first positive - regular tester; time for routine HIV test*	0=no 1=yes 7=refused 9=don't know
Reason for testing at first positive - required by either insurance, military, court order, or for some other required reason*	0=no 1=yes 7=refused 9=don't know

Reason for the test that led to the case report - exposure to HIV within the last 6 months*	0=no 1=yes 7=refused 9=don't know
Reason for the test that led to the case report- just checking to make sure you are HIV negative*	0=no 1=yes 7=refused 9=don't know
Reason for the test that led to the case report- other reason*	0=no 1=yes 7=refused 9=don't know
Reason for the test that led to the case report- regular tester; time for routine HIV test*	0=no 1=yes 7=refused 9=don't know
Reason for the test that led to the case report - required by either insurance, military, court order, or for some other required reason*	0=no 1=yes 7=refused 9=don't know
Reason STARHS not performed	1=QNS 2=specimen never received at public lab 3=broken in transit 4=other
Results received	0=no 1=yes
Specify other reason for testing at fist positive*	text
Specify other reason for the test that led to the case report*	text
Specimen ID number from source lab	text
STARHS ID	text
STARHS regional lab specimen ID number (same as STARHS lab imported variable SPECIMEN ID)	text

STARHS test result	01=long term 02=recent 91=QNS 92=not rec'd by STARHS lab 93=broken 94=other
State lab CLIA code	text
State lab specimen ID number	text
State of site where first tested positive for HIV	text
State of site where last tested negative for HIV	text
Test assay	BED=BED BVLS=BVLS (Vironostika LS) OTLS=OTLS (Vironostika LS) OTV=OTV (Vironostika LS) AVID=AVID
Type of site where first tested positive for HIV	F01=inpatient facility F01.01=inpatient facility/hospital F01.04=inpatient facility/long term care F01.50=inpatient facility/drug treatment F01.OTH=inpatient facility/other F01.UNK=inpatient facility unknown F.OTH=facility/other F.UNK=facility/unknown
Type of site where participant last tested negative for HIV	F01=inpatient facility F01.01=inpatient facility/hospital F01.04=inpatient facility/long term care F01.50=inpatient facility/drug treatment F01.OTH=inpatient facility/other F01.UNK=inpatient facility unknown F.OTH=facility/other F.UNK=facility/unknown
Type of test performed on specimen (LOINC)	5220-9=EIA / Elisa 21009-6=Western Blot 5472-6=CD4 25835-0=Viral Load (NASBA) 5017-9=Viral Load (bDAN) 25836-8=Viral Load (RT-PCR)

What type of specimen was obtained	1=blood finger stick 2=blood venipuncture 3=blood spot 4=oral mucosal transudate 5=urine 8=other 9=unknown

* The reason for testing for first positive test or for the test that led to the case report will no longer be part of the standard HIV Incidence Surveillance data elements beginning January 1, 2007.

Technical Guidance for HIV/AIDS Surveillance
Policies and Procedures for HIV Incidence Surveillance
DRAFT 10/31/2006

Although historically AIDS surveillance data have been of great value, current data do not represent the entire population affected by the HIV epidemic, which in the United States consists primarily of HIV type 1 (HIV-1) infections. Unlike AIDS data, HIV data provide a window into the epidemic at an earlier stage of disease, thereby allowing public health officials to monitor the epidemic more effectively and completely, allocate resources, and plan and implement programs, particularly prevention programs. In the past, however, biomedical technology did not discriminate between recent and chronic HIV infection and as a result the incidence of HIV infection in the United States could not be measured directly. The serologic testing algorithm for recent HIV seroconversion (STARHS) distinguishes between recent and long-standing HIV-1 infection on a population level and should allow the estimation of local and national HIV incidence.

HIV Incidence Surveillance (HIS) is the aspect of the national HIV/AIDS surveillance system that uses STARHS results as well as data on the history of testing and use of medications with antiretroviral (ARV) properties for each case reported to HIV/AIDS surveillance programs to generate an HIV incidence estimate. HIS will give a more representative picture of the HIV epidemic, its trends, and its impact on the public's health. CDC's human subjects protection process has determined that the implementation of HIS programs using STARHS, like other public health surveillance activities, is not research < *National Center for HIV, STD, and TB Prevention's Non-research Determination for HIV Incidence Surveillance* >.

The primary functions of HIS are to:

1. Incorporate STARHS into routine HIV surveillance activities by testing HIV seropositive specimens obtained from newly diagnosed individuals using an assay approved for this purpose
2. Collect HIV testing and ARV use history information from individuals with newly reported HIV infections as part of routine HIV surveillance
3. Apply a statistical model(s) to estimate HIV incidence locally and nationally using a combination of STARHS results, information from surveillance case reports, including testing and ARV use history information for all newly diagnosed individuals
4. Assist with local HIV prevention program planning and evaluation using incidence data.

The tasks to achieve the functions of HIS include:

1. Elicit collection and reporting of testing and ARV use history information by all providers reporting HIV cases to the health department
2. Ensure that an aliquot of each confirmed seropositive specimen from a newly diagnosed case is shipped to the CDC STARHS laboratory in New York
3. Determine the disposition of remnant HIV-positive specimens and coordinate communication between the Incidence Surveillance Coordinator (ISC) and the public health laboratory or the CDC STARHS laboratory regarding specimens shipped to and stored at the respective laboratories
4. Enter STARHS and testing and ARV use history information into the designated HIS database
5. Electronically transfer data to CDC
6. Ensure that HIS data handling procedures comply with all security and confidentiality guidelines as described in the <*Technical Guidance for HIV/AIDS Surveillance Programs, Vol.III: Security and Confidentiality Guidelines*>
7. Analyze and disseminate data locally
8. Train staff in the policies and procedures of the HIV/AIDS surveillance system as well as the HIS System

The prerequisites (structural requirements), best practices (process standards), and outcome standards for HIS are described next.

Structural Requirements

All individuals with a new diagnosis of HIV infection tested confidentially should be reported to the HIV surveillance system in accordance with the < *Technical Guidance for HIV/AIDS Surveillance Programs, Vol.I: Policies and Procedures* >. In areas incorporating HIS into their HIV/AIDS surveillance systems, an HIV testing history, information about ARV use, and the STARHS result of a remnant of the diagnostic HIV positive specimen will complete information collection for a case. HIV/AIDS surveillance case report data, in combination with these data elements will be used to make population-based HIV incidence estimates.

Policies and Procedures – HIS is a fully integrated component of HIV/AIDS surveillance, therefore documentation of HIS activities should be incorporated into locally tailored policy and procedures manuals developed for HIV/AIDS surveillance < *Technical Guidance for HIV/AIDS Surveillance Programs, Vol.I: Policies and Procedures*> to establish standardization, maintain continuity of meaning, document changes over time, and develop training programs. All manuals describing policies and procedures of the local surveillance program should address the needs of HIV/AIDS surveillance as well as the specific policies related to HIS. In addition to the information listed in < *Technical Guidance for HIV/AIDS Surveillance Programs, Vol.I: Policies and Procedures*> HIS specific policies and procedures should include information related to:

- Training of testing providers in collection of additional data used for HIV incidence estimation
- Laboratory contacts
- Determining which specimens should be tested using STARHS (and which should be discarded)
- Specimen aliquoting
- Specimen shipping guidance

The BED Assay for STARHS – The assay STARHS currently uses is the BED HIV-1 Capture EIA (2) manufactured by Calypte Biomedical Corporation®. The principle of the BED HIV-1 Capture EIA is based on the observation that the ratio of HIV-specific IgG to total IgG increases with time after HIV infection (2). The BED HIV-1 Capture EIA is applied to the diagnostic HIV-positive specimen and the assay is sensitive to the length of time since the infection (i.e., antibody level present). The time from when a specimen would first be reactive on the standard EIA to the time when the serum or plasma, if tested with the BED HIV-1 Capture EIA, reaches an optical density (OD) level pre-determined to distinguish recent from non-recent infections is defined as the STARHS mean window period. Although the mean STARHS window period may vary slightly by HIV subtype, the mean window period for calculating population-based incidence estimates in the United States is 156 days when using the BED HIV-1 Capture EIA.

The BED HIV-1 Capture EIA for STARHS is performed only on HIV-positive sera (2) and is not approved as a diagnostic test. Because of the variability in antibody development in individuals, the predictive value of an individual's STARHS result is low; the results are only reliable as part of the population-based HIV incidence estimate. The Food and Drug Administration (FDA) has ruled that the BED HIV-1 Capture EIA be labeled "For Surveillance use. Not for diagnostic or clinical use." Under FDA regulations, results of STARHS performed for purposes of HIS cannot be returned to individuals or their health care providers or used for clinical management. As with earlier assays used for STARHS, data show that the BED HIV-1 Capture EIA can produce a substantial number of false positive and false negative classifications on the

individual level (4). At the population level, the number of false positives is approximately equal to the number of false negatives thus effectively "canceling" each other out. However, the number of misclassifications can be large, and each of the misclassified individual results would receive an incorrect interpretation. STARHS results may also be misclassified due to the use of ARV therapies or late stage of the disease. Evaluation of the BED HIV-1 Capture EIA has determined that the specimens of persons with low HIV-1–specific antibodies resulting from ARV therapy or disease progression (i.e., AIDS) could lead to the incorrect conclusion that these persons were recently infected. When a person has AIDS, this is thought to be due to a loss of immune response as immune deficiency progresses. When a person is taking ARV therapy, this result is thought to be due to suppression of the HIV viral load, which in turn reduces antigenic stimulation and the quantity of circulating HIV-1–specific antibodies. The effect of ARVs taken for post exposure prophylaxis or for concurrent hepatitis B infection, for example, is not known. Theoretically, it could take longer to develop a full immune response to HIV infection. CDC data only reliably support using STARHS for estimating incidence at the population level.

Testing and ARV Use History Data – Information on testing behavior is needed, such as recency of testing and testing frequency. Additionally, history of ARV use (for example, pre- or post-exposure prophylaxis or treatment for hepatitis) and immunological status (CD4 cell counts and viral loads) must be included for all cases reported to the surveillance system.

Information needed for HIV incidence estimation is available as part of a standard case report and nearly all testing and ARV use history information is gathered as part of a comprehensive HIV counseling session. However, not all of the required HIS data elements have been collected uniformly, and many have not previously been recorded. Therefore, a standard set of HIV testing and ARV use history data elements needed for the HIV incidence estimate has been developed <*Standard HIV Incidence Surveillance Data Elements*> and providers of HIV testing should be trained in the appropriate collection of those data.

Staffing Needs – Implementation of the HIS system requires personnel with specific skills and dedicated time to integrate HIS into the existing core HIV/AIDS surveillance system effectively. Generally, HIS staff should have:

- An understanding of HIS and the characteristics of the HIV/AIDS surveillance in their area
- Good communication skills
- Strong leadership skills
- Enthusiasm about disease reporting for public health purposes.
- Dedication to the successful implementation of HIS
- Ability to work closely with CDC, other States, local sites, private providers, and laboratories

The recommended staffing plan including roles and responsibilities follows. In terms of personnel time, CDC recommends that one full-time equivalent (FTE) be dedicated to the ISC position. Successful implementation and integration of HIS requires a full time ISC dedicated to implementing and maintaining the system. Other personnel assigned to HIS may vary depending on the implementation phase, prevalence of HIV/AIDS, and available resources.

ISC

- Provide overall management of the HIS system
    - Serve as lead on the area specific implementation of the HIS guidance
- Oversee data collection processes
    - Determination of the disposition of HIV-positive specimens reported to the surveillance system

    - Receipt of STARHS results
    - Oversee collection of HIV testing and treatment history information from public HIV testing sites and private providers
- Collaborate with other HIS staff
    - HIV incidence epidemiologist
        - Development of training materials and courses
        - Data collection procedures
    - HIV incidence data manager
        - Data collection methods
        - Data entry and quality assessment
        - Data editing and file correction
        - Data transport procedures
        - Preparation of monthly reports
        - Security and confidentiality procedures
    - HIV incidence laboratory liaison
        - Specimen transfer
        - Specimen tracking
- Manage any employee or other service contracts related to HIS
- Serve as the primary point of contact for CDC on HIS
- Participate in CDC site visits, trainings, and workshops

Epidemiologist/Trainer

- Serve as lead on training HIV testing providers and laboratories on HIS, including development/modification of surveillance area specific training materials
- Coordinate HIS and epidemiology activities with the ISC
- Participate in the development or modification of testing and ARV use history data elements
- Participate in data dissemination activities
    - Collaborate with stakeholders to determine data needs and frequency of reporting
    - Identify results and surveillance issues for review and dissemination
    - Develop a data dissemination plan in collaboration with the ISC and CDC
- Participate in CDC site visits, trainings, and workshops as appropriate

Laboratory Liaison

- Act as the liaison between the public health, private, and community laboratories and the ISC
- Oversee preparation and shipping of public health laboratory specimens to the CDC STARHS laboratory
- Monitor quality control procedures outlined for preparing specimens for testing using STARHS
- Monitor security and confidentiality of specimens and STARHS results
- Track specimens identified for testing using STARHS (all laboratories)
- Participate in CDC site visits, trainings, and workshops as appropriate

Data Manager

- Assist ISC with daily management of HIS data
- Conduct data collection from areas
    - Serve as subject matter expert on HIV incidence data elements and data management programs

    - Receive data transfer from other health department entities and the CDC STARHS lab and incorporate those data into the HIS database and datasets for transfer to CDC
    - Conduct data quality assessments
- Conduct data management
    - Modify CDC's generic data management programs for use at the area level
    - Develop and implement edit checks and conduct data cleaning
    - Collaborate with the ISC, epidemiologist, and other area surveillance and prevention staff, as needed, on data cleaning, data entry, and data set preparation
    - Prepare datasets for local analysis
    - Collaborate with CDC on dataset preparation for national incidence estimates
    - Prepare HIV incidence data reports for local use in collaboration with the ISC, epidemiologist, and CDC
- Maintain security and confidentiality of HIV incidence data
- Participate in CDC site visits, trainings, and workshops as appropriate

Process Standards

HIS involves the following:

- Obtaining testing and ARV use history data from providers
- Identifying laboratories that perform HIV related tests and obtaining remnant specimens for testing using STARHS
- Determining specimen disposition as it relates to testing using STARHS
- Establishing a schedule for contact between the ISC and the Public Health Laboratory and the CDC STARHS Laboratory to communicate regarding shipping, testing, and discarding remnant specimens that are housed at the laboratory
- Entering data into the HIS database
- Electronically transferring data to CDC
- Ensuring that data handling procedures comply with Security and Confidentiality Guidelines <*Technical Guidance for HIV/AIDS Surveillance Programs, Vol.III: Security and Confidentiality Guidelines*>, <*Model State Public Health Privacy Act*>
- Analyzing and disseminating data locally
- Training of staff in HIV/AIDS surveillance and HIS methods

Obtaining Testing and ARV Use History Data – The primary purpose of gathering HIV testing and ARV use history is to calculate a statistical weight <*Statistical Methodology for Generating Population-Based HIV Incidence Estimates*> that will allow inference to the general population. The weight reflects the probability that an individual will be tested during the STARHS window period and depends on the following:

- HIV testing frequency
- Reason for the first positive test
- Information related to the most recent negative test
    - Date
    - Place
- Information related to the first positive test
    - Date
    - Place

- ARV use history
    - Type
    - Date started
    - Date stopped

Testing and ARV use history data are collected by providers and surveillance staff using the area standard reporting procedures or other procedures meeting the routine HIV/AIDS surveillance security and confidentiality guidelines. These data:

- Should be included for all adult/adolescent (≥ 13 years at diagnosis) HIV/AIDS cases newly reported to the HIV/AIDS surveillance system by all providers of HIV testing
- May be collected through client/patient interview or chart abstraction given that the provider has been trained to obtain the data
- Can be collected when an individual presents for an HIV test or returns for the results
    - Takes advantage of the individual's ability to recall information that is more proximal to the event
- Should be reported and recorded based on the patient's self-report within three months of the HIV diagnosis
    - Longer intervals may increase the risk of recall bias, yet this consideration should not prevent efforts to obtain the information even after three months if necessary

CDC has assisted in the development of materials for use in training providers to collect HIV testing and ARV use history data. These materials are available at all sites, or upon request to CDC.

Obtaining Remnant HIV-Positive Specimens for Testing Using STARHS – To be most useful, testing using STARHS should be performed on the HIV-positive diagnostic serum or plasma specimen. For the purposes of this guidance, the HIV-positive diagnostic specimen is the HIV-positive specimen from the diagnostic test that resulted or should have resulted in the case being reported to the HIV/AIDS surveillance system. Remnant specimens for all confirmed HIV-positive diagnostic specimens should be tested using STARHS.

- Laboratories performing routine diagnostic confirmatory HIV testing by Western Blot, indirect fluorescent antibody (IFA) tests, immunological status tests such as CD4, or viral load counts should report to the state/local health department surveillance program per existing requirements.
- In each surveillance area, all laboratories should be identified from a review of local HIV surveillance data and laboratory licensing records and must be approached to request that remnants of all diagnostic specimens be made available for testing using STARHS.
    - Surveillance areas should maintain a directory of laboratory contacts at all reporting laboratories to facilitate communication in the event that reporting or shipping of specimens is disrupted or that changes in policy or procedures need to be communicated.
    - Originating laboratories are those to which a specimen is first sent for testing
    - Reference laboratories are those to which a specimen is sent for confirmatory testing when the originating laboratory does not do confirmatory testing
- All remnant specimens from HIV-diagnostic Western Blot or IFA tests must be shipped to the CDC STARHS laboratory in New York for testing using STARHS.
    - A minimum of 0.5 ml HIV-positive serum or plasma specimen is necessary for testing using STARHS
    - Private or community laboratories performing HIV diagnostic testing should choose one of two options for shipping the remnant HIV-positive serum or plasma specimen to the CDC STARHS laboratory<*Guidance for the Transportation of Remnant HIV-positive Specimens to the CDC STARHS Laboratory from Private and Public Testing Laboratories*>.

        - Ship the specimen directly to the CDC STARHS laboratory.
        - Ship the specimen to the state public health laboratory affiliated with the health department that receives the new HIV case report for processing or
            - State public health laboratories can then batch and ship all specimens identified for testing using STARHS to the CDC STARHS laboratory.
    - State public health laboratories conducting HIV diagnostic testing should ship their own HIV-positive specimens identified for testing using STARHS directly to the CDC STARHS laboratory.

Specimen availability for testing using STARHS depends on the testing needs for the specimen. Uses of the remnant of specimens should follow the CDC HIS recommended hierarchy (described below) for specimen aliquoting to ensure adequate specimen volume for multiple diagnostic tests. When multiple tests must be performed on a collected serum or plasma specimen, the aliquots must be made available with the following hierarchy in mind:

1. HIV diagnostic testing
2. Testing with STARHS
3. HIV drug resistance genotyping (known as Variant, Atypical, and Resistant HIV Surveillance [VARHS])

Aliquots made following this hierarchy will ensure that adequate specimen volume is available according to the priority for data determined by CDC.

Determining the Disposition of Specimens and Communicating with the Public Health and CDC STARHS Laboratories – A specimen will be held at the state public health laboratory or the CDC STARHS laboratory (i.e., specimens shipped directly from private or commercial laboratories) until the area ISC, using routine HIV/AIDS surveillance reporting procedures (i.e., HARS/eHARS), determines whether the specimen represents the person's first reported positive HIV test result in the HIS area. A specimen should be tested using STARHS if:

1. the specimen represents the diagnostic specimen (the HIV-positive specimen that led, or should have led a case to be reported to HARS/eHARS) **or**
2. the diagnostic specimen is unavailable and the specimen was drawn within 3 months of the diagnostic specimen **and**
3. the specimen was drawn for an HIV-related test (viral load, qualitative PCR, CD4 level).

A specimen should not be tested using STARHS if:

1. the specimen is not the diagnostic specimen that led, or should have led the individual to be reported to HARS/eHARS **and**
2. the individual had a previous specimen that was tested using STARHS **or**
3. the individual did not have a previous specimen tested using STARHS but the specimen was drawn more than three months after the diagnostic specimen.

Because a remnant sample of every Western Blot positive blood specimen will be shipped by originating or reference laboratories to either the state or local Public Health Laboratory or to the CDC STARHS laboratory, the HIS program must inform the appropriate laboratory of the disposition of the specimen.

- Specimens for cases not previously reported to HARS/eHARS (or those drawn within three months of a diagnostic specimen that is unavailable) will constitute the **test list**. A test list should:
    - Be compiled for the state or local Public Health Laboratory and for the CDC STARHS Laboratory

    - Include those specimens located at the individual laboratory and that should be tested using STARHS.
    - Be cumulative
- Specimens that are neither diagnostic specimens nor drawn within three months of a diagnostic specimen that is unavailable will constitute the **toss list** A toss list should:
    - Be compiled for the state or local Public Health Laboratory and for the CDC STARHS Laboratory
    - Include those specimens held at the laboratory that should not be tested using STARHS.
    - Be cumulative

Specimens will be handled, packaged, and shipped according to the CDC STARHS laboratory shipping protocol <*Guidance for the Transportation of Remnant HIV-positive Specimens to the CDC STARHS Laboratory from Private and Public Testing Laboratories*>. Specimens shipped as diagnostic specimens and using dry ice for packing must follow the procedures for packing and shipping specimens using dry ice <*Guidance for Processing, Storage, and Shipping to the CDC STARHS Laboratory*>.

The ISC will regularly, at an interval to be determined locally (e.g., monthly), inform area laboratory designees (e.g., at the public health laboratory) and the CDC STARHS laboratory of all stored specimens, or remnants specimens, with a positive HIV diagnostic test to be tested using STARHS (the test list) and those to be discarded (the toss list).

- For those specimens on the test list:
    - An aliquot of blood to be used for STARHS is drawn from the specimen
        - At the local public health laboratory prior to shipping
        - At the CDC STARHS laboratory if the specimen was shipped directly to the CDC STARHS laboratory
    - The aliquot is relabeled with a unique STARHS identification number (SID)
    - The SID is paired with the corresponding specimen number and is sent to the ISC with no other identifying data
    - After STARHS the results are returned to the ISC with results identified by SID only
- Specimens on the toss list should be discarded according to routine laboratory protocols for HIV-positive serum or plasma specimens.
- The ISC should inform the CDC STARHS lab to discard all specimens that have been tested with STARHS. If the ISC would like to have these specimens returned at the surveillance area's expense he/she should make arrangements with the CDC STARHS lab.

<u>Entering Data into the Surveillance Database</u> – Data elements needed for the calculation of statistical weights used to make population-based HIV incidence estimates fall into one of four categories.

- Demographic data
    - Age
    - Sex
    - Race/ethnicity
    - Risks associated with HIV infection
- HIV testing and ARV use history data
- Clinical data
    - CD4 count
    - Viral load
- Laboratory Data
    - Specimen collection date
    - SID

- STARHS results

All data elements needed for HIS are included in eHARS, but could not be added to HARS. As a result, an HIS Access database was developed to store additional data related to HIS. Until a surveillance area begins using eHARS, the jurisdiction should enter data into both HARS and the HIS Access database as appropriate. Testing and ARV use history information and laboratory data related to the diagnostic HIV test (including specimen collection date and SID) are variables entered into the separate HIS Access database along with the unique state number (HARS/eHARS "stateno") assigned to each case.

Creating the HIS Dataset and Transferring Data to CDC – HIS data entry and management take place at state or local health departments using one of three data management systems:

- HIS Access database (until conversion to eHARS)
- eHARS
- Software that is compatible with CDC software

Information is merged into the data management systems from other sources:

- Excel spreadsheet containing STARHS results identified by SID only from the CDC STARHS laboratory
- PEMS
- Other databases

For states that have not transitioned to eHARS, data are merged using unique identifiers reported with each case for data transfer to CDC:

- the HARS/eHARS stateno links HARS/eHARS records to corresponding HIS Access database records

When eHARS has the ability to import HIS data, merging datasets prior to transferring data to CDC will no longer be necessary.

Prior to the 15th of each month, the complete dataset is transmitted to CDC over the Secure Data Network (SDN). Data transmitted to CDC will include no personal identifiers and will be encrypted and password protected according to the <*Technical Guidance for HIV/AIDS Surveillance Programs, Vol.III: Security and Confidentiality Guidelines*>.

Security and Confidentiality – HIV testing is a medical procedure. Therefore, policies and procedures are in place to protect the confidentiality of tested individuals and their medical records. STARHS will be performed only on specimens that have tested positive for HIV. HIS data are considered part of routine HIV surveillance data and should be held to the standards of security and confidentiality for HIV/AIDS surveillance outlined in <*Technical Guidance for HIV/AIDS Surveillance Programs, Vol.III: Security and Confidentiality Guidelines*>. Policies and procedures, based on these guidelines and local laws, are already in place at state and local health departments and are used to secure hard copy and electronic information to protect the confidentiality of persons reported as having HIV infection. These measures must be extended to protect the STARHS information held locally. Access by HIS staff to information in HARS, HIV testing and ARV use history, and STARHS data is governed by the same security and confidentiality requirements.

Data Analysis and Dissemination – Data from individuals who choose to have an HIV test and who test positive will be used to estimate the incidence of HIV nationally and in participating areas, including the

incidence of undiagnosed HIV infection. HIV incidence estimates will be used to assess current HIV prevention programs locally, regionally, and nationally. HIS data will be stratified by selected factors such as demographic or behavioral factors, thus creating subpopulation data at the national and local levels. If the sampling procedure has sufficient statistical power, this stratification will allow comparisons between different areas and among different risk groups. The methods used to generate the population-based incidence estimate are described in <*Statistical Method for Generating Population-Based HIV Incidence Estimates*> which introduces the methods, statistical formulas, and different groups for which incidence estimates will be made.

It is expected that analysis, interpretation, and dissemination of these data will be the primary responsibility of CDC with appropriate contributions from surveillance areas. Results from the aggregate CDC database will be analyzed regularly and feedback provided to areas. Aggregate results will also be published in CDC's HIV/AIDS Surveillance Reports. Area-specific analyses will be conducted at the discretion of participating areas. As appropriate, results will be presented at conferences and published in peer reviewed journals. The number of representative authors from areas and CDC will be determined for each presentation or paper.

In addition to the variables needed to estimate HIV incidence, the following data elements will be used to evaluate the performance of the BED HIV-1 Capture EIA for the determination of estimates of HIV incidence:

- Whether AIDS has been diagnosed and if so, the date of diagnosis.
- At the time of HIV diagnosis,
    - whether HIV ARV agents have been used for post exposure prophylaxis or for any other medical condition (e.g., lamivudine for treatment of hepatitis B), and if so, the name(s) of the agent, and dates and duration of use,
    - where available, CD4 count, viral load, and HIV-1 subtype along with the type of test used to determine the subtype.

As a result, all HIV-positive diagnostic specimens should be tested using STARHS irrespective of the time to AIDS diagnosis for an individual, or evidence of previous ARV use.

Staff Training – Because HIS is a fully integrated component within the HIV/AIDS surveillance system, all HIS staff should receive training in the local policies and procedures for core surveillance including:

- active and passive surveillance methods
- laboratory reporting mechanisms
- data management processes

In accordance with <*Technical Guidance for HIV/AIDS Surveillance Programs, Vol.III: Security and Confidentiality Guidelines*> HIS staff must also receive training in security and confidentiality procedures, and should sign a confidentiality statement upon being hired and annually thereafter.

Outcome Standards

Outcome standards described within the <*Introduction to Policies and Procedures*> and <*Data Quality*> sections of <*Technical Guidance for HIV/AIDS Surveillance Programs, Vol.I: Policies and Procedures*> can be applied to HIS. These sections address issues of completeness of case ascertainment, timeliness of reporting, passing standard data edits, and elimination of missing/unknown information.

Meeting core surveillance standards for case ascertainment and timeliness are essential for HIS to be successful given the time sensitive nature of HIS data elements including testing and ARV use history data and STARHS. In addition, the quality of the HIV incidence estimate is dependent on the quality of data included in the HIS system. As with core surveillance data elements, the minimum standard for passing standard data edits related to HIS data is 97% with a target of 100%.

At least 85% of newly reported HIV/AIDS cases for a diagnosis year should have testing history and ARV use data within 12 months of the date of the initial HIV/AIDS case report, measured at 12 months after the close of the diagnosis year.

Related to shipment of specimens for testing using STARHS, the minimum standard is that 85% of newly reported HIV/AIDS cases reported to the surveillance system in a jurisdiction should have a remnant of the HIV-positive diagnostic blood sample (or a remnant of a sample drawn for an HIV related blood test drawn within 3 months of an unavailable HIV-positive diagnostic specimen) transported to the CDC STARHS laboratory within 12 months of diagnosis assessed for the most recent diagnosis year at 12 months after that diagnosis year.

References

1. Janssen RS, Satten GA, Stramer SL, et al. New testing strategy to detect early HIV-1 infection for use in incidence estimates and for clinical and prevention purposes. *JAMA* 1998; 280:42–48.
2. Parekh B, Kennedy MS, Dobbs T, et al. Quantitative detection of increasing HIV type 1 antibodies after seroconversion: a simple assay for detecting recent HIV infection and estimating incidence. *AIDS Research & Human Retroviruses* 2002;18(4):295-307.
3. White E, Goldbaum G, Rao V. Application of the serologic testing algorithm to detect recent HIV seroconversion (STARHS) in a clinical population. In: Program and abstract of the 9th Annual Conference on Retroviruses and Opportunistic Infections; February 2002; Seattle. Abstract 766W.
4. Linley L, Reed C. Applicability of Population-Based STARHS HIV Incidence Measure in Determining Recency of Individual Infection among Patients Attending STD Clinics. In Program and abstract of the 11th Annual Conference on Retroviruses and Opportunistic Infections; February 2004; San Francisco. Abstract 854.
5. Coutinho RA, Duermeyer W, Van der Veen J. Epidemiology of hepatitis A in Amsterdam October 1978–December 1979. *J Virol Methods* 1980;2(1-2):47–55.

National Center for HIV, STD, and TB Prevention's Non-research Determination for HIV Incidence Surveillance

NCHSTP Research/Non-research Determination

(Request to Classify Project as Not Involving Human Subjects or Research)

This form should be used to submit to NCHSTP ADS materials for projects involving CDC investigations that are not subject to human subjects regulations. Projects are eligible for this classification either as "non-research" projects (primary intent is not to generate generalizable knowledge) or as research projects that do not involve identifiable human subjects. Such projects do not require submission to the CDC Human Subjects Office for IRB review. Do **NOT** use this form for IRB "EXEMPT" research.

Project Title___ Standard HIV Incidence Surveillance Procedures Guidance _____

_____

Project Locations/Sites: _____33 funded incidence sites, eventually all HIV/AIDS Surveillance areas___

Project Officer(s)____Lisa M. Lee, PhD __ Division:__ DHAP-SE _____ Telephone: __404.639.2052

Proposed Project Dates: Start: 03/__01__/_2005_ End: N/A, routine surveillance _____/_____/_____

Categories of data collection that do not constitute human subjects research include are listed below. Please check appropriate category:

_X__ **I. Activity is not research** . Primary intent is public health practice or a disease control activity.
- ___**A**. Epidemic/endemic **disease control** activity; collected data directly relate to disease control needs.
- _X__**B**. Routine **disease surveillance** activity; data used for disease control program or policy purposes.
- ___**C**. **Program evaluation** activity; data are used primarily for that purpose.
- ___**D**. **Post-marketing surveillance** of efficacy and/or adverse effects of a new regimen, drug or device.
- ___E. **Activity is purely administrative** (e.g., purchase orders or contracts for services or equipment) and not related to research [this category I-E may be determined by Divisional ADS]

-OR-

___ **II. Activity is research but does NOT involve identifiable human subjects.**
- ___**A.** Activity is research involving collection/analysis of data about health facilities or other organizations or units which are not individual persons....**or**...
- ___**B.** Activity is research involving data and/or specimens from deceased persons...**or**...
- ___**C.** Activity is research using unlinked anonymous data or specimens: **All** (1-4) of the following are required:
  - ___ 1. No contact with human subjects is involved for the proposed activity...**and**...
  - ___ 2. Data or specimens are/were collected for another purpose...**and**...
  - ___ 3. No extra data/specimens are/were collected for **this** purpose...**and**...
  - ___ 4. Identifying information either was not obtained **or** has been removed so that data cannot be linked or re-linked with identifiable human subjects. (Note: under certain conditions, research *may* qualify as non-human subjects when identifiers are removed by local staff; contact NCHSTP ADS office for details.)

Attach project description (standard format at end of this form) in enough detail to clarify its non-human subject research nature. Submit through division ADS/Director to: NCHSTP ADS, Attn: Janella Dodson (MS E-07)

☐ Check here if this request is an **amendment** of an existing non-research determination.

Approval initials: _____ 3/2/05 _____ 3/2/05
Branch/Section Chief Date **ADS or Div. Director** Date

res-nonres.det.form.0704

Project Title_____ Standard HIV Incidence Surveillance Procedures Guidance _____

NCHSTP ADS Review **Date rec'd in NCHSTP ADS Office:**_____

X **Concur, project does not constitute human subjects research**

This project is national HIV/AIDS surveillance & not research.

or

___**Project constitutes human subjects research**, submission for Human Subjects review required

Comments/Rationale:

Additional Comments:

1. This form cannot be used to document "IRB Exempt Research," which must instead be submitted to the CDC IRB. (Please contact the NCHSTP ADS Office for details).
2. Although CDC Human Subjects (IRB) review is not required in this instance, investigators/project officers are expected to adhere to ethical principles and standards by respecting and protecting to the maximum extent possible the privacy, confidentiality and autonomy of participants. All applicable State and Federal privacy laws must be followed.
3. Although this project does not constitute human subjects research, informed consent may be appropriate. Information disclosed in the consent process should address the eight standard consent elements.
4. Other:

Signed: _____ 3/9/05

Terence Chorba, MD, MPH, MPA, MA
Acting Associate Director for Science, NCHSTP
National Center for HIV, STD, and TB Prevention

Date

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Standard HIV Incidence Surveillance Data Elements

Variable Description	Valid Value
Number of HIV tests in 2 years prior to the first positive (For people who previously tested positive)	1 - 99 R=refused D=don't know
Anonymous HIV test at first positive test	0=no 1=yes 7=refused 9=don't know
Antiretroviral medications within the last 6 months	0=no 1=yes 7=refused 9=don't know
ARV meds taken	22=Agenerase 30=Aptivus 24=Combivir 06 =Crixivan 11=Emtriva 03=Epivir 28=Epzicom 25=Fortovase 10=Fuzeon 19=Hepsera 02=Hivid 23=Hydroxyurea 18=Invirase 16=Kaletra 31=Lexiva 07=Norvir 88=Other 09=Rescriptor 26=Retrovir 15=Reyataz 08=Saquinavir
CLIA code for source lab where specimen originated	text
Currently taking antiretroviral medications	0=no 1=yes 7=refused

	9=don't know
Date HAART use began	yyyymmdd
Date HAART use ended	yyyymmdd
Date information is extracted	yyyymmdd
Date of first HIV test ever	yyyymmdd
Date of first positive HIV test	yyyymmdd
Date of STARHS test	yyyymmdd
Date of the HIV test that resulted in a case report	yyyymmdd
Date specimen was obtained	yyyymmdd
Has specimen been approved for STARHS?	0=no 1=yes 2=pending
Laboratory ID	33D0654341=NYST 33D0654341=CDCSTARHS 33D0654341=NY 33D0654341=CDCSTAR 21D0649758=MARY01 50D0661430=WASH
Date of last HIV negative test before first positive	yyyymmdd
Date of last HIV negative test before first positive (or before test that resulted in a case report if never previously tested positive)	yyyymmdd
Name of site where first tested positive for HIV	text
Name of site where last tested negative for HIV	text
Ever tested for HIV	0=no 1=yes 7=refused 9=don't know

Ever tested negative	0=no 1=yes 7=refused 9=don't know
Number of HIV tests in last 2 years before first positive (including first positive test)	1 - 99 R=refused D=don't know
Number of HIV tests in last 2 years before first positive (People who never had previous positive)	1 - 99 R=refused D=don't know
Optical density	text
Ever tested positive	0=no 1=yes 7=refused 9=don't know
Reason for first positive HIV test*	text
Reason for testing at first positive - exposure to HIV within the last 6 months*	0=no 1=yes 7=refused 9=don't know
Reason for testing at first positive - just checking to make sure you are HIV negative*	0=no 1=yes 7=refused 9=don't know
Reason for testing at first positive - other reason*	0=no 1=yes 7=refused 9=don't know
Reason for testing at first positive - regular tester; time for routine HIV test*	0=no 1=yes 7=refused 9=don't know
Reason for testing at first positive - required by either insurance, military, court order, or for some other required reason*	0=no 1=yes 7=refused 9=don't know

Reason for the test that led to the case report - exposure to HIV within the last 6 months*	0=no 1=yes 7=refused 9=don't know
Reason for the test that led to the case report- just checking to make sure you are HIV negative*	0=no 1=yes 7=refused 9=don't know
Reason for the test that led to the case report- other reason*	0=no 1=yes 7=refused 9=don't know
Reason for the test that led to the case report- regular tester; time for routine HIV test*	0=no 1=yes 7=refused 9=don't know
Reason for the test that led to the case report - required by either insurance, military, court order, or for some other required reason*	0=no 1=yes 7=refused 9=don't know
Reason STARHS not performed	1=QNS 2=specimen never received at public lab 3=broken in transit 4=other
Results received	0=no 1=yes
Specify other reason for testing at fist positive*	text
Specify other reason for the test that led to the case report*	text
Specimen ID number from source lab	text
STARHS ID	text
STARHS regional lab specimen ID number (same as STARHS lab imported variable SPECIMEN ID)	text

STARHS test result	01=long term 02=recent 91=QNS 92=not rec'd by STARHS lab 93=broken 94=other
State lab CLIA code	text
State lab specimen ID number	text
State of site where first tested positive for HIV	text
State of site where last tested negative for HIV	text
Test assay	BED=BED BVLS=BVLS (Vironostika LS) OTLS=OTLS (Vironostika LS) OTV=OTV (Vironostika LS) AVID=AVID
Type of site where first tested positive for HIV	F01=inpatient facility F01.01=inpatient facility/hospital F01.04=inpatient facility/long term care F01.50=inpatient facility/drug treatment F01.OTH=inpatient facility/other F01.UNK=inpatient facility unknown F.OTH=facility/other F.UNK=facility/unknown
Type of site where participant last tested negative for HIV	F01=inpatient facility F01.01=inpatient facility/hospital F01.04=inpatient facility/long term care F01.50=inpatient facility/drug treatment F01.OTH=inpatient facility/other F01.UNK=inpatient facility unknown F.OTH=facility/other F.UNK=facility/unknown
Type of test performed on specimen (LOINC)	5220-9=EIA / Elisa 21009-6=Western Blot 5472-6=CD4 25835-0=Viral Load (NASBA) 5017-9=Viral Load (bDAN) 25836-8=Viral Load (RT-PCR)

What type of specimen was obtained	1=blood finger stick 2=blood venipuncture 3=blood spot 4=oral mucosal transudate 5=urine 8=other 9=unknown

* The reason for testing for first positive test or for the test that led to the case report will no longer be part of the standard HIV Incidence Surveillance data elements beginning January 1, 2007.

Statistical Method for Generating Population-Based HIV Incidence Estimates

I. Background

This appendix contains a description of the procedures for estimating the total number of people infected with HIV in a specific population of interest during a one-year period. These estimation procedures use data collected from a population-based surveillance system for newly diagnosed HIV infections. The information required to estimate the number of recent HIV infections falls into three general categories:

1) Data collected as part of HIV/AIDS surveillance
2) HIV testing history prior to the first positive HIV test and
3) Test results that indicate whether an infection is recent.

These procedures provide an estimate of the number of incident infections in the population covered by the surveillance system and not merely the number of new infections among the persons tested for HIV.

Since it is not feasible to test everyone at risk for HIV infection in a given year to determine who has seroconverted, the statistical approach that we will use to estimate population-based HIV incidence is analogous to the sample survey approach (Karon et al., 2005). In this approach, all individuals who seroconvert in the year of interest are considered to be the sampling frame, whereas those who have been identified as recent seroconverters are regarded as a sample chosen from that sampling frame.

Based on the sample survey approach, the size of the sampling frame is estimated from the observed sample by assigning a weight to each person in the sample. This weight is the inverse of the probability that a person with similar characteristics is included in the sample. Thus, for estimating HIV incidence, the weight assigned to each person identified as recently infected is the inverse of the probability that a seroconverted person had a positive HIV test and was identified as having a recent infection based on the serologic testing algorithm for recent HIV seroconversion (Janssen et al., 1998).

A person identified as recently infected is defined as a person who tests HIV positive by the standard (sensitive) test, but negative by the BED test. The interval between the time an individual tests positive by the sensitive HIV test and the time he/she tests positive by the BED HIV test is called the window period. It depends both on the assay used and the critical SOD (standard optical density) value chosen to define a positive reaction. The window period differs from person to person and is unknown for each individual. However, the distribution of window period durations among all seroconverters can be estimated.

II. Statistical procedure for estimating population-based incidence

The statistical procedure contains three major steps: stratification, weight calculation, and incidence estimation. In the stratification step, all new HIV cases diagnosed in a specific time interval (e.g., a specific calendar year) are stratified into incidence groups according to HIV transmission category or factors associated with risk intensity and testing pattern. The number of new HIV diagnoses in each incidence group should be sufficient large so that there will be at least 100 BED "recent" persons in each group. Cases in each incidence group are then further divided into subgroups according to testing history, motivation, and BED test information. In the weight calculation step, every newly diagnosed HIV case is assigned an incidence weight. There are different types of weights determined by previous negative HIV test, testing motivation, type of HIV diagnosis (HIV diagnosed with or without AIDS), result of the BED test, and availability of needed information. The final step is to add weights in each incidence group to get the incidence estimate for that group, and then aggregate the group estimates to get the incidence estimate for the population.

A. Stratification

Since the accuracy of incidence estimates depends on homogeneity of risk level and testing pattern in the group considered, we first stratify the population into groups with similar risk for HIV infection and testing pattern in each group. However, the size of each group must be sufficiently large in order to have reliable incidence weights assigned for cases in each group. Variables that could be used for stratification include sex, race, transmission category, age at HIV diagnosis, state of diagnosis, or the type of testing facility. The resulting strata are called incidence groups.

Within each incidence group, cases are divided into mutually exclusive subgroups. They are determined by the availability of testing history information, the eligibility of BED testing, and the result of the BED test. There are three major subgroups determined by previous negative HIV test. They are:

G_x – Cases without information on HIV testing before the first positive test for HIV
G_0 – Cases without previous test before the first positive test for HIV
G_1 – Cases not in groups G_x and G_0, or tested before the first positive test for HIV

Each of the three groups is further divided into ten smaller groups based on (1) whether the first positive test is motivated by a unique recent risk incident (2) whether AIDS is diagnosed at the same month of HIV diagnosis (3) whether the case is eligible for BED test (no medication within six months prior the first positive test) and BED tested with determinate result and (4) BED test result. These incidence subgroups are shown in Tables 1-3. These subgroups are labeled as G_{ABC} with the following convention:

The first subscript is an indicator on previous test with A = 0 for cases with no test before the first positive test, A = 1 for cases ever tested negative before the first positive test, and A = x for cases without information on previous test.

The second subscript refers to test motivation with B = 0 for cases not motivated by a unique recent risk incident, B = m for cases motivated by a unique recent risk incident, and B = x for cases without information on test motivation.

The third subscript implies the status of BED test:

C = a for cases diagnosed with AIDS at HIV diagnosis

C = 0 for cases not AIDS at HIV diagnosis, no HIV related medication within 6 months before HIV diagnosis, BED tested, and BED recent
C = b for cases not AIDS at HIV diagnosis, no HIV related medication within 6 months before HIV diagnosis, BED tested, but not BED recent
C = x cases not in anyone of the above three subgroups.

B. Weight calculation

In this section, each newly diagnosed HIV case is assigned an incidence weight based on the incidence subgroup associated with the case. There are four types of weights. They are (1) zero weight, (2) unit weight, (3) calculated weight based on detection probability or testing frequency, and (4) derived weight based on proportional method for cases with incomplete information.

Zero weight is assigned to AIDS cases (incidence subgroups G_{ABC} with C = a) and cases not BED recent (incidence subgroups G_{ABC} with C = b and B = 0 or x):

$$\begin{aligned} W_{0ma} &= W_{00a} = W_{0xa} = 0, \quad W_{00b} = W_{0xb} = 0 \\ W_{1ma} &= W_{10a} = W_{1xa} = 0, \quad W_{10b} = W_{1xb} = 0 \\ W_{xma} &= W_{x0a} = W_{xxa} = 0, \quad W_{x0b} = W_{xxb} = 0 \end{aligned} \tag{1}$$

Unit weight is assigned to cases that were motivated by unique recent risk incident but not diagnosed with AIDS at HIV diagnosis (incidence subgroups G_{ABC} with B = m but C ≠ a, they are G_{0mx}, G_{1mx}, and G_{xmx}):

$$W_{0mx} = W_{1mx} = W_{xmx} = 1 \tag{2}$$

Weights are calculated for cases that are known on previous test, not motivated by risk incident, eligible for BED test (not AIDS and not on HIV medication within six months prior to the first positive test), and BED recent. There are two types of calculated weights, one for those with no previous negative test (incidence subgroup G_{000}) and the other for those ever tested before the first positive test (incidence subgroup G_{100}).

The weight for cases in G_{000} is given by

$$W_{000} = \frac{1}{1 + \int_0^\infty e^{-t(q^{-1/\alpha_A} - 1)/\beta_A} S_A(t) dS_W(t)} \tag{3}$$

where

$$q = N_{00a} / (N_{00a} + N_{00x} + N_{000} + N_{00b}) \tag{4}$$

is the proportion of individuals diagnosed with AIDS (CDC, 1993 definition) at the time of their HIV diagnosis among those who had no previous HIV negative test and who's first positive test was not motivated by risk incident, $S_A(t)$ and $S_W(t)$ are the survival functions for the AIDS incubation time and the duration of window period, respectively. The AIDS incubation time has a Gamma distribution (Longini et al., 1991) with a shape parameter $\alpha_A = 2$ and a scale parameter $\beta_A = 48$ months. Note that all of these weights are equal. The duration of window period has a generalized log-logistic distribution with a survival function given by (Robert H. Byers, Jr., personal communication)

$$S_W(t) = \left(1 + \lambda e^{[Ln(t)-\theta]/\sigma}\right)^{-1/\lambda} \tag{5}$$

With a SOD cut-off value equal to 1, the mean window period is about 184 days and the corresponding parameters are $\lambda = 1.044$, $\theta = 5.048$, and $\sigma = 0.299$. Using these parameters for the two survival functions, weights for selected values of q from 0.01 to 0.45 are provided in Table 4.

The weights for cases in G_{100} and G_{1x0} are given by

$$W_{100}(T) = W_{1x0}(T) = \frac{T}{\int_0^T S_W(t)dt} \tag{6}$$

where T is the time from the last negative HIV test to the first positive HIV test. When T is greater than 24 months, the denominator is approximately equal to the mean window period $\mu = 184$ days. Weights for selected values of T from 0 to 24 months are provided in Table 5.

For all other cases (incidence subgroups G_{ABC} with A =x or B = x or C = x but B ≠ m), weights are derived from other weights using the proportional method.

For cases in subgroup G_{x00}, the weight is

$$W_{x00} = p_0 W_{000} + (1 - p_0)\overline{W}_{100} \tag{7}$$

where

$$\overline{W}_{100} = \frac{1}{N_{100}} \sum_{i=1}^{N_{100}} W_{100}(T_i) \tag{8}$$

$$p_0 = M_0 / (M_0 + M_1) \tag{9}$$

and for $A = 0,1$,

$$\begin{aligned} M_A &= N_A q_A p_{A00} \\ N_A &= N_{Ama} + N_{Amx} + N_{A0a} + N_{A0x} + N_{A00} + N_{A0b} + N_{Axa} + N_{Axx} + N_{Ax0} + N_{Axb} \\ q_A &= (N_{A0x} + N_{A00} + N_{A0b}) / (N_{Ama} + N_{Amx} + N_{A0a} + N_{A0x} + N_{A00} + N_{A0b}) \\ p_{A00} &= N_{A00} / (N_{A00} + N_{A0b}) \end{aligned} \tag{10}$$

For cases in subgroups G_{00x}, G_{10x} and G_{x0x}, the weights are

$$W_{00x} = p_{000} W_{000}, \quad W_{10x} = p_{100}\overline{W}_{100}, \quad W_{x0x} = p_{x00} W_{x00} \tag{11}$$

where

$$p_{x00} = N_{x00} / (N_{x00} + N_{x0b}) \tag{12}$$

For cases in subgroups G_{0x0}, G_{1x0} and G_{xx0}, the weights are

$$
\begin{aligned}
W_{0x0} &= p_{0mx} + (1 - p_{0mx})W_{000} \\
W_{1x0} &= p_{1mx} + (1 - p_{1mx})W_{1x0}(T) \\
W_{xx0} &= p_{xmx} + (1 - p_{xmx})W_{x00}
\end{aligned}
\tag{13}
$$

where

$$
\begin{aligned}
p_{0mx} &= N_{0mx} / [N_{0mx} + N_{000} + N_{00x} \cdot N_{000} / (N_{000} + N_{00b})] \\
p_{1mx} &= N_{1mx} / [N_{1mx} + N_{100} + N_{10x} \cdot N_{100} / (N_{100} + N_{10b})] \\
p_{xmx} &= N_{xmx} / [N_{xmx} + N_{x00} + N_{x0x} \cdot N_{x00} / (N_{x00} + N_{x0b})]
\end{aligned}
\tag{14}
$$

$W_{1x0}(T)$ is calculated using formula (6) and T is the time from the last negative HIV test to the first positive HIV test.

Finally, for cases in subgroups G_{0xx}, G_{1xx} and G_{xxx}, the weights are

$$
W_{0xx} = p_{0x0}W_{0x0}, \quad W_{1xx} = p_{1x0}[p_{1mx} + (1 - p_{1mx})\overline{W}_{1x0}], \quad W_{xxx} = p_{xx0}W_{xx0} \tag{15}
$$

where

$$
\begin{aligned}
p_{0x0} &= N_{0x0} / (N_{0x0} + N_{0xb}) \\
p_{1x0} &= N_{1x0} / (N_{1x0} + N_{1xb}) \\
p_{xx0} &= N_{xx0} / (N_{xx0} + N_{xxb})
\end{aligned}
\tag{16}
$$

$$
\overline{W}_{1x0} = \frac{1}{N_{1x0}} \sum_{i=1}^{N_{1x0}} W_{1x0}(T_i) \tag{17}
$$

C. Incidence estimation

After each case has been assigned an incidence weight, the incidence for a specific population group can be easily estimated by summing the weights of cases in the population considered:

$$
I = \sum_i W_i \tag{18}
$$

However, calculating the confidence interval for the incidence estimate is not straightforward because the variance associated with the incidence estimate is complex. To estimate the variance, we need to know the number of cases in each incidence group and each incidence subgroup.

Let r be the number of main incidence groups and I_i the incidence estimate for the i-th incidence group. Then the total incidence in the population is the sum of incidences of all incidence groups:

$$
I = \sum_{i=1}^{r} I_i \tag{19}
$$

The variance of this estimate is

$$V(I) = \sum_{i=1}^{r} V(I_i) \tag{20}$$

Within each incidence group, e.g., group *i*, let k_{ABC} be the number of HIV/AIDS diagnoses in incidence subgroups G_{ABC} within the specific population group of interest. Then the incidence estimate for the *i*-th incidence group is

$$I_i = I_{i0} + I_{i1} + I_{ix} \tag{21}$$

where

$$\begin{aligned} I_{i0} &= k_{0mx} + k_{000}W_{000} + k_{00x}W_{00x} + k_{0x0}W_{0x0} + k_{0xx}W_{0xx} \\ &= k_{0mx} + (k_{0x0} + k_{0xx}p_{0x0})p_{0mx} \\ &\quad + [k_{000} + k_{00x}p_{000} + (k_{0x0} + k_{0xx}p_{0x0})(1 - p_{0mx})]W_{000} \end{aligned} \tag{22}$$

$$\begin{aligned} I_{i1} &= k_{1mx} + k_{100}W_{100} + k_{10x}W_{10x} + k_{1x0}W_{1x0} + k_{1xx}W_{1xx} \\ &= k_{1mx} + (k_{1x0} + k_{1xx}p_{1x0})p_{1mx} + (k_{100} + k_{10x}p_{100})\overline{W}_{100} \\ &\quad + (k_{1x0} + k_{1xx}p_{1x0})(1 - p_{1mx})\overline{W}_{1x0} \end{aligned} \tag{23}$$

and

$$\begin{aligned} I_{ix} &= k_{xmx} + k_{x00}W_{x00} + k_{x0x}W_{x0x} + k_{xx0}W_{xx0} + k_{xxx}W_{xxx} \\ &= k_{xmx} + (k_{xx0} + k_{xxx}p_{xx0})p_{xmx} \\ &\quad + [k_{x00} + k_{x0x}p_{x00} + (k_{xx0} + k_{xxx}p_{xx0})(1 - p_{xmx})]W_{x00} \end{aligned} \tag{24}$$

Let

$$\vec{X} = (X_1, ..., X_{28}) = (\vec{K}_0, \vec{K}_1, \vec{K}_x, \vec{P}_0, \vec{P}_1, \vec{P}_x, p_0, W_{000}, \overline{W}_{100}, \overline{W}_{1x0})$$

where

$$\vec{K}_0 = (k_{0mx}, k_{00x}, k_{000}, k_{0xx}, k_{0x0})$$
$$\vec{K}_1 = (k_{1mx}, k_{10x}, k_{100}, k_{1xx}, k_{1x0})$$
$$\vec{K}_x = (k_{xmx}, k_{x0x}, k_{x00}, k_{xxx}, k_{xx0})$$

$$\vec{P}_0 = (p_{0mx}, p_{000}, p_{0x0})$$
$$\vec{P}_1 = (p_{1mx}, p_{100}, p_{1x0})$$
$$\vec{P}_x = (p_{xmx}, p_{x00}, p_{xx0})$$

Then, we have

$$I_i = f(\vec{X})$$

Using the delta method, the variance of the incidence estimate can be approximated by

$$V(I_i) \approx \sum_{j,l} \frac{\partial f}{\partial X_j} \frac{\partial f}{\partial X_l} Cov(X_j, X_l) \tag{25}$$

The partial derivatives are

$$\partial f/\partial k_{0mx} = 1$$
$$\partial f/\partial k_{00x} = p_{000} W_{000}$$
$$\partial f/\partial k_{000} = W_{000}$$
$$\partial f/\partial k_{0xx} = p_{0x0}[p_{0mx} + (1 - p_{0mx}) W_{000}]$$
$$\partial f/\partial k_{0x0} = p_{0mx} + (1 - p_{0mx}) W_{000}$$

$$\partial f/\partial k_{1mx} = 1$$
$$\partial f/\partial k_{10x} = p_{100} \overline{W}_{100}$$
$$\partial f/\partial k_{100} = \overline{W}_{100}$$
$$\partial f/\partial k_{1xx} = p_{1x0}[p_{1mx} + (1 - p_{1mx}) \overline{W}_{1x0}]$$
$$\partial f/\partial k_{1x0} = p_{1mx} + (1 - p_{1mx}) \overline{W}_{1x0}$$

$$\partial f/\partial k_{xmx} = 1$$
$$\partial f/\partial k_{x0x} = p_{x00}[p_0 W_{000} + (1 - p_0) \overline{W}_{100}]$$
$$\partial f/\partial k_{x00} = [p_0 W_{000} + (1 - p_0) \overline{W}_{100}]$$
$$\partial f/\partial k_{xxx} = p_{xx0}\{p_{xmx} + (1 - p_{xmx})[p_0 W_{000} + (1 - p_0) \overline{W}_{100}]\}$$
$$\partial f/\partial k_{xx0} = p_{xmx} + (1 - p_{xmx})[p_0 W_{000} + (1 - p_0) \overline{W}_{100}]$$

$$\partial f/\partial p_{0mx} = (k_{0x0} + k_{0xx} p_{0x0})(1 - W_{000})$$
$$\partial f/\partial p_{000} = k_{00x} W_{000}$$
$$\partial f/\partial p_{0x0} = k_{0xx} p_{0mx} + [k_{0xx}(1 - p_{0mx})] W_{000}$$

$$\partial f/\partial p_{1mx} = (k_{1x0} + k_{1xx} p_{1x0})(1 - \overline{W}_{1x0})$$
$$\partial f/\partial p_{100} = k_{10x} \overline{W}_{100}$$
$$\partial f/\partial p_{1x0} = k_{1xx} p_{1mx} + [k_{1xx}(1 - p_{1mx})] \overline{W}_{1x0}$$

$$\partial f/\partial p_{xmx} = (k_{xx0} + k_{xxx} p_{xx0})\{1 - [p_0 W_{000} + (1 - p_0) \overline{W}_{100}]\}$$
$$\partial f/\partial p_{x00} = k_{x0x}[p_0 W_{000} + (1 - p_0) \overline{W}_{100}]$$
$$\partial f/\partial p_{xx0} = k_{xxx} p_{xmx} + [k_{xxx}(1 - p_{xmx})][p_0 W_{000} + (1 - p_0) \overline{W}_{100}]$$

$$\partial f/\partial p_0 = [k_{x00} + k_{x0x} p_{x00} + (k_{xx0} + k_{xxx} p_{xx0})(1 - p_{xmx})][W_{000} - \overline{W}_{100}]$$

$$\begin{aligned}\partial f/\partial W_{000} &= [k_{000} + k_{00x} p_{000} + (k_{0x0} + k_{0xx} p_{0x0})(1 - p_{0mx})] \\ &\quad + [k_{x00} + k_{x0x} p_{x00} + (k_{xx0} + k_{xxx} p_{xx0})(1 - p_{xmx})] p_0\end{aligned}$$
$$\begin{aligned}\partial f/\partial \overline{W}_{100} &= [k_{100} + k_{10x} p_{100}] \\ &\quad + [k_{x00} + k_{x0x} p_{x00} + (k_{xx0} + k_{xxx} p_{xx0})(1 - p_{xmx})](1 - p_0)\end{aligned}$$
$$\partial f/\partial \overline{W}_{1x0} = (k_{1x0} + k_{1xx} p_{1x0})(1 - p_{1mx})$$

We assume that each k is an independent proportion of the corresponding N and all N's are independent random variables each with a Poisson distribution. Therefore, the covariances between k_z's are zero and the variances of k_z's can be estimated as

$$\hat{V}(k_z) = k_z$$

Note that the p's are functions of N's. Using the delta method, the variances of p's can be estimated as (with $A = 0, 1, x$):

$$\hat{V}(p_{A00}) = p_{A00}(1-p_{A00})/(N_{A00}+N_{A0b})$$
$$\hat{V}(p_{Ax0}) = p_{Ax0}(1-p_{Ax0})/(N_{Ax0}+N_{Axb})$$
$$\hat{V}(p_{Amx}) \approx p_{Amx}(1-p_{Amx})/[N_{Amx}+N_{A00}+N_{A0x}N_{A00}/(N_{A00}+N_{A0b})]$$

Also, we have

$$\hat{V}(p_0) \approx p_0(1-p_0)/(M_0+M_1)$$

$$\hat{V}(W_{000}) = [W'_{00}(q)]^2\, q(1-q)/(N_{00a}+N_{00x}+N_{000}+N_{00b})$$
$$\hat{V}(\overline{W_{100}}) = \frac{1}{N_{100}^2}\sum_{i=1}^{N_{100}} W_{100}^2(T_i)$$
$$\hat{V}(\overline{W_{1x0}}) = \frac{1}{N_{1x0}^2}\sum_{i=1}^{N_{1x0}} W_{1x0}^2(T_i)$$

Covariances between p's and k's that are not independent can be estimated as:

$$\hat{Cov}(p_{A00}, k_{A00}) = (\partial p_{A00}/\partial N_{A00})k_{A00}$$
$$\hat{Cov}(p_{Ax0}, k_{Ax0}) = (\partial p_{Ax0}/\partial N_{Ax0})k_{Ax0}$$
$$\hat{Cov}(p_{Amx}, k_{Amx}) = (\partial p_{Amx}/\partial N_{Amx})k_{Amx}$$
$$\hat{Cov}(p_{Amx}, k_{A0x}) = (\partial p_{Amx}/\partial N_{A0x})k_{A0x}$$
$$\hat{Cov}(p_{Amx}, k_{A00}) = (\partial p_{Amx}/\partial N_{A00})k_{A00}$$
$$\hat{Cov}(p_{Amx}, p_{A00}) = [(\partial p_{Amx}/\partial N_{A00}) - (\partial p_{Amx}/\partial N_{A0b})]p_{A00}(1-p_{A00})$$
for $A = 0, 1, x$

and

$$\hat{Cov}(p_0, k_{Amx}) = (\partial p_0/\partial N_{Amx})k_{Amx}$$
$$\hat{Cov}(p_0, k_{A0x}) = (\partial p_0/\partial N_{A0x})k_{A0x}$$
$$\hat{Cov}(p_0, k_{A00}) = (\partial p_0/\partial N_{A00})k_{A00}$$
$$\hat{Cov}(p_0, k_{Axx}) = (\partial p_0/\partial N_{Axx})k_{Axx}$$
$$\hat{Cov}(p_0, k_{Ax0}) = (\partial p_0/\partial N_{Ax0})k_{Ax0}$$
$$\hat{Cov}(p_0, p_{Amx}) = \frac{\partial p_0}{\partial N_{Amx}}\frac{\partial p_{Amx}}{\partial N_{Amx}}N_{Amx} + \frac{\partial p_0}{\partial N_{A00}}\frac{\partial p_{Amx}}{\partial N_{A00}}N_{A00}$$
$$+ \frac{\partial p_0}{\partial N_{A0x}}\frac{\partial p_{Amx}}{\partial N_{A0x}}N_{A0x} + \frac{\partial p_0}{\partial N_{A0b}}\frac{\partial p_{Amx}}{\partial N_{A0b}}N_{A0b}$$

$$\hat{Cov}(p_0, p_{A00}) = \left(\frac{\partial p_0}{\partial N_{A00}} - \frac{\partial p_0}{\partial N_{A0b}} \right) p_{A00}(1 - p_{A00})$$

for $A = 0, 1,$

where

$$\begin{aligned}
\partial p_{A00} / \partial N_{A00} &= p_{A00}(1 - p_{A00}) / N_{A00} \\
\partial p_{Ax0} / \partial N_{Ax0} &= p_{Ax0}(1 - p_{Ax0}) / N_{Ax0} \\
\partial p_{Amx} / \partial N_{Amx} &= p_{Amx}(1 - p_{Amx}) / N_{Amx} \\
\partial p_{Amx} / \partial N_{A0x} &= -(p_{Amx}^2 / N_{Amx}) p_{A00} \\
\partial p_{Amx} / \partial N_{A00} &= -(p_{Amx}^2 / N_{Amx})[1 + N_{A0x}\ p_{A00}(1 - p_{A00}) / N_{A00})] \\
\partial p_{Amx} / \partial N_{A0b} &= (p_{Amx}^2 / N_{Amx}) N_{A0x}\ p_{A00}(1 - p_{A00}) / N_{A0b}
\end{aligned}$$

for $A = 0, 1, x$

and

$$\frac{\partial p_0}{\partial N_{Amx}} = (-1)^A p_0(1 - p_0) \left(\frac{1}{N_A} + \frac{q_A}{N_{A0x} + N_{A00} + N_{A0b}} \right)$$

$$\frac{\partial p_0}{\partial N_{A0x}} = (-1)^A p_0(1 - p_0) \left(\frac{1}{N_A} + \frac{1}{q_A} \frac{(1 - q_A)^2}{N_{Ama} + N_{Amx} + N_{A0a}} \right)$$

$$\frac{\partial p_0}{\partial N_{A00}} = (-1)^A p_0(1 - p_0) \left(\frac{1}{N_A} + \frac{1}{q_A} \frac{(1 - q_A)^2}{N_{Ama} + N_{Amx} + N_{A0a}} + \frac{1 - p_{A00}}{N_{A00}} \right)$$

$$\frac{\partial p_0}{\partial N_{A0b}} = (-1)^A p_0(1 - p_0) \left(\frac{1}{N_A} + \frac{1}{q_A} \frac{(1 - q_A)^2}{N_{Ama} + N_{Amx} + N_{A0a}} - \frac{1 - p_{A00}}{N_{A0b}} \right)$$

$$\frac{\partial p_0}{\partial N_{Axx}} = (-1)^A \frac{p_0(1 - p_0)}{N_A}$$

$$\frac{\partial p_0}{\partial N_{Ax0}} = (-1)^A \frac{p_0(1 - p_0)}{N_A}$$

$$\frac{\partial p_0}{\partial N_{Axb}} = (-1)^A p_0(1 - p_0) \frac{1}{N_A}$$

for $A = 0, 1.$

We estimate the coveriances between W's and other components that are correlated with W's by

$$\begin{aligned}
\hat{Cov}(W_{000}, k_{000}) &= -W'_{000}(q)(q^2 / N_{00a}) k_{000} \\
\hat{Cov}(W_{000}, k_{00x}) &= -W'_{000}(q)(q^2 / N_{00a}) k_{00x} \\
\hat{Cov}(W_{000}, p_0) &= W'_{000}(q)\{q(1 - q)(\partial p_0 / \partial N_{00a}) - (q^2 / N_{00a})[(\partial p_0 / \partial N_{00x}) N_{00x} \\
&\qquad + (\partial p_0 / \partial N_{000}) N_{000} + (\partial p_0 / \partial N_{00b}) N_{00b}]\}
\end{aligned}$$

where

$$\frac{\partial p_0}{\partial N_{00a}} = p_0(1 - p_0) \left(\frac{1}{N_0} + \frac{-q_0}{N_{00x} + N_{000} + N_{00b}} \right)$$

Finally, a 95% confidence interval for the total incidence is given by:

$$I \pm 1.96\sqrt{\hat{V}(I)} \tag{26}$$

III. Data required for estimating HIV incidence

For each person reported with a newly diagnosed HIV infection:

1. Demographic information: sex, race, transmission category, age, and state of residence at first positive HIV test.
2. Information about the first positive HIV test: testing date, type of testing site, reason for the positive HIV test.
3. Testing history information: whether or not tested before the first positive HIV test. If tested before the first positive HIV test:
   a. Date of the last negative HIV test,
   b. Date of the very first HIV test, and
   c. Testing frequency and pattern in the last two years.
   Note: b and c are needed to evaluate the potential truncation effect on incidence estimation.
4. Information about eligibility for BED test: whether AIDS has been diagnosed, whether HIV antiretroviral agents have been used in 6 months prior to the HIV diagnostic test, and if available, the CD4 count and viral load at time of HIV diagnosis.
5. Information on BED test: date of blood drawn for BED test, (type of assay), BED result.

References

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2. Janssen RS, Satten GA, Stramer SL, et al. New testing strategy to detect early HIV-1 infection for use in incidence estimates and for clinical and prevention purposes. *JAMA* 1998; 280:42–48.
3. Centers for Disease Control and Prevention. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR* 1992; 41(no.RR-17).
4. Longini IM, Clark WS, Gardner LI, et al. The dynamics of $CD4^+$ T-lymphocyte decline in HIV-infected individuals: A Markov modeling approach. *JAIDS* 1991; 4:1141–1147.

Table 1. Incidence subgroups and weights for those who were not HIV tested before their first positive test (group G_0)

Motivate unique r incide	AIDS at HIV	On medication BED or BED ur	BE rec	Su gr	N ca	Incidence weight
Yes	Ye			G	N	$W_{0ma} = 0$
	No			G	N	$W_{0mx} = 1$
No	Ye			G	N	$W_{00a} = 0$
	No	Yes		G	N	$W_{00x} = p_{000}W_{000}$
		No	Y	G	N	W_{000}, see equation (3)
			N	G	N	$W_{00b} = 0$
Unkno	Ye			G	N	$W_{0xa} = 0$
	No	Yes		G	N	$W_{0xx} = p_{0x0}W_{0x0}$
		No	Y	G	N	$W_{0x0} = p_{0mx} + (1 - p_{0mx})W$
			N	G	N	$W_{0xb} = 0$

Table 2. Incidence subgroups and weights for those who were HIV tested before their first positive test (group G_1)

Motivate unique r incide	AIDS at HIV	On medication BED or BED ur	BE rec	Su gr	N ca	Incidence weight
Yes	Ye			G	N	$W_{1ma} = 0$
	No			G	N	$W_{1mx} = 1$
No	Ye			G	N	$W_{10a} = 0$
	No	Yes		G	N	$W_{10x} = p_{100}\overline{W}_{100}$
		No	Y	G	N	$W_{100}(T)$, use equation (
			N	G	N	$W_{10b} = 0$
Unkno	Ye			G	N	$W_{1xa} = 0$
	No	Yes		G	N	$W_{1xx} = p_{1x0}(p_{1mx} + (1 - p_{1mx})\overline{W}_{1x0})$
		No	Y	G	N	$W_{1x0} = p_{1mx} + (1 - p_{1mx})$ $W_{1x0}(T)$ use equation (6)
			N	G	N	$W_{1xb} = 0$

Table 3. Incidence subgroups and weights for those who had no information on previous HIV test (group G_x)

Motivate unique r incide	AIDS at HIV	On medication BED or BED ur	BE rec	Su gro	N cas	Incidence weight
Yes	Ye			G_x	N_x	$W_{xma} = 0$
	No			G_x	N_x	$W_{xmx} = 1$
No	Ye			G_x	N_x	$W_{x0a} = 0$
	No	Yes		G_x	N_x	$W_{x0x} = p_{x00}W_{x00}$
		No	Y	G_x	N_x	$W_{x00} = p_0 W_{000} + (1 - p_0)W$
			N	G_x	N_x	$W_{x0b} = 0$
Unkno	Ye			G_x	N_x	$W_{xxa} = 0$
	No	Yes		G_x	N_x	$W_{xxx} = p_{xx0}W_{xx0}$
		No	Y	G_x	N_x	$W_{xx0} = p_{xmx} + (1 - p_{xmx})W$
			N	G_x	N_x	$W_{xxb} = 0$

Table 4. Weights and their first derivative values for selected values of q.

q	W_0	W'_0	q	W_0	W'_0	q	W_0	W'_0
0.0	1.6	47.4	**0.1**	5.7	25.1	**0.3**	9.8	30.4
0.0	2.0	37.0	**0.1**	6.0	25.3	**0.3**	10.1	30.9
0.0	2.3	32.5	**0.1**	6.2	25.5	**0.3**	10.5	31.5
0.0	2.6	29.9	**0.1**	6.5	25.7	**0.3**	10.8	32.1
0.0	2.9	28.3	**0.2**	6.8	25.9	**0.3**	11.1	32.8
0.0	3.2	27.2	**0.2**	7.0	26.2	**0.3**	11.4	33.5
0.0	3.5	26.4	**0.2**	7.3	26.5	**0.3**	11.8	34.2
0.0	3.7	25.9	**0.2**	7.6	26.8	**0.3**	12.1	34.9
0.0	4.0	25.5	**0.2**	7.8	27.2	**0.3**	12.5	35.7
0.1	4.2	25.2	**0.2**	8.1	27.6	**0.4**	12.8	36.5
0.1	4.5	25.0	**0.2**	8.4	28.0	**0.4**	13.2	37.3
0.1	4.7	24.9	**0.2**	8.7	28.4	**0.4**	13.6	38.2
0.1	5.0	24.9	**0.2**	8.9	28.9	**0.4**	14.0	39.1
0.1	5.2	24.9	**0.2**	9.2	29.3	**0.4**	14.4	40.1
0.1	5.5	25.0	**0.3**	9.5	29.9	**0.4**	14.8	41.1

Table 5. Weights associated with the time in months from the last negative HIV test to the first positive HIV test (μ = 184 days is the mean window period).

T	W_{10}	T	W_{10}
0	1.00	**13**	2.26
1	1.00	**14**	2.41
2	1.01	**15**	2.57
3	1.03	**16**	2.73
4	1.09	**17**	2.89
5	1.17	**18**	3.05
6	1.27	**19**	3.21
7	1.39	**20**	3.37
8	1.52	**21**	3.54
9	1.66	**22**	3.70
10	1.80	**23**	3.86
11	1.95	**24**	4.03
12	2.10	**>24**	T / μ

Guidance for the Transportation of Remnant HIV-Positive Specimens to the CDC STARHS Laboratory from Private or Public Testing Laboratories

Purpose

This guidance describes two possible specimen transport models that originating laboratories may use to ship remnant diagnostic serum specimens to the CDC STARHS laboratory for testing for recent HIV-1 infection using the serologic testing algorithm for recent HIV seroconversion (STARHS). Originating laboratories may choose to select either model, but must clearly communicate their choice to and coordinate with the state / local HIV Incidence Surveillance Coordinator (ISC) who will be responsible for managing the results.

Introduction

In December 2004, an expert consultation was convened by the Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories (APHL). The purpose of the 5th HIV Incidence Consultation on Laboratory and Specimen Transport was to discuss the best approaches for transporting remnant HIV positive sera from private and public laboratories to the CDC STARHS laboratory for testing using STARHS. The consultation participants included HIV Incidence Surveillance staff from CDC and state / local areas, personnel from commercial, private, university, and public health laboratories, APHL, and the American Clinical Laboratory Association. The goal for the meeting was to gather input from stakeholders for the development of an infrastructure for shipping specimens from private (including university and/or medical center), commercial, and public health laboratories to the CDC STARHS laboratory for STARHS.

The discussions concluded that two models were acceptable for shipping specimens from testing laboratories to the CDC STARHS laboratory. This guidance describes both specimen transportation models. The models differ in: 1) the extent of the testing laboratories involvement in aliquoting / labeling samples for STARHS; 2) the physical storage location of the samples until specimen disposition (to be tested using STARHS or to be discarded) is determined by the ISC; and 3) the frequency of shipments to the CDC STARHS laboratory.

Each testing laboratory may choose either model, but this choice should be clearly communicated to the ISC.

Laboratory Types

For the purposes of this guidance, there are three laboratory types. While each testing laboratory may independently decide which specimen transport model will work best for that facility, CDC has provided suggestions based on the type of laboratory and that facility's relationship with the state / local public health laboratory.

Laboratory Types:

1) **Commercial laboratories** that process samples from many states and/or jurisdictions (included in this category are: Quest Diagnostics Inc, Laboratory Corporation of America [LabCorp], ARUP Laboratories, Specialty Laboratories, and Mayo Clinic)
2) Smaller **private / university / hospital or medical center laboratories** that provide service primarily at the state or local level, but may also process samples for more than one state and/or jurisdiction
3) **Public Health Laboratories** (PHL)

Specimen Information

Type of Specimens Shipped to CDC STARHS Laboratory - HIV positive serum from Western Blot (WB) or Immunofluorescence Assay (IFA) confirmed diagnostic samples will ultimately be shipped to the CDC STARHS laboratory, depending on the specimen transport model chosen by the originating laboratory. Detailed information about which samples will be shipped is included in the model descriptions of this guidance (Specimen Transport Options).

Specimen Volume - The optimal quantity of serum required for STARHS testing is 0.5ml per aliquot. However, if less than 0.5ml of the remnant sample is available for testing using STARHS, the sample should still be sent to the CDC STARHS laboratory. The CDC STARHS laboratory is the only laboratory that should determine if a sample is rejected due to insufficient quantity.

Sample Storage - Short-term (less than one week) storage of samples in the refrigerator (2 – 8°C) is acceptable, but for long-term storage (more than one week), samples must be frozen at negative (-)20°C or colder. This includes any period of time that the samples are kept at the originating / testing laboratory or the "pass through" public health laboratory prior to shipment to the CDC STARHS laboratory or the interim period while STARHS disposition is being determined. Effort should be made to avoid repeated freezing and thawing of samples, as this may give erroneous results.

- It is recommended that, if not already in practice, a daily temperature log be kept to ensure the freezer is operating properly.
- The freezer should be housed in a location with proper ventilation to avoid overheating and freezer failure.
- The freezer must contain adequate space to store specimens.

Specimen Numbering - The specimen number on the samples shipped to the CDC STARHS laboratory will either be the original laboratory-assigned specimen accession number or the STARHS identification number, depending on the transport model selected by the originating laboratory. Detailed information about specimen numbering is included in the model descriptions of this guidance (Specimen Transport Options).

Specimen Retention - The ISC must coordinate with the laboratory storing HIV positive remnant sera (the CDC STARHS laboratory and/or their state / local PHL) to identify samples that should be tested using STARHS. However, not all stored samples will be tested using STARHS, and those that will not be tested will have to be identified for disposal. The ISC should regularly notify the storage laboratory of which samples should be tested using STARHS and which should be disposed of by submitting a list of laboratory-assigned specimen accession numbers with "test" or "toss" for each specimen according to the decision reached. The state / local ISC and the storing laboratory should communicate regularly (every 1-3 months) to discuss any specimens for which no disposition has been communicated to determine if the sample can be disposed of or if further investigation is needed. Samples should not be destroyed or disposed of until the disposition is definitively determined.

Packaging and Shipping Procedures

Shipping Guidance - Shipping procedures are described in detail in the CDC document *<Guidance for Processing, Storage, and Shipping to the CDC STARHS Laboratory>*. Specimens may be shipped from originating laboratories to the state PHL as a "pass-through" facility or to the CDC STARHS laboratory as 'Diagnostic Specimens. However, due to the requirement for dry ice, all laboratories shipping HIV positive samples must be certified to ship dangerous goods.

Frequency of Shipments - The frequency of specimen shipments to the CDC STARHS laboratory or the pass-through facility will be determined by the shipping laboratory, considering factors such as specimen retention policies and freezer / storage space, and in consultation with the ISC and the receiving laboratory.

Shipping Couriers - Specimens must be shipped on dry ice by same-day or overnight delivery service to ensure that specimens do not thaw in transit. The shipping laboratory may decide which courier service to use for specimen transport.

Additional Information for Commercial Laboratories Only - APHL has set up a Federal Express billing account for the large commercial laboratories to defer costs of shipping samples to the CDC STARHS laboratory.

Additional Information for All Other Private Laboratories - Intra-state shipments from private laboratories to the PHL may be shipped by Federal Express (or a similar commercial courier) or an established local courier service. Funding permitting, states may elect to set-up a billing account with Federal Express (or a similar commercial courier) to pay for shipping costs incurred by the private laboratory to either the state / local PHL or the CDC STARHS laboratory (see Funding for Specimen Handling).

Tracking Shipments - The shipping laboratory should notify the receiving laboratory (state PHL or CDC STARHS laboratory) by fax or email when specimens are shipped, *including the name of the courier and the tracking number of the shipment*. The receiving laboratory will be responsible for tracking the shipments and will notify the originating laboratory if the specimens are not received

Additional Information Related to Commercial Laboratories Only - As part of the contract between APHL and the large commercial laboratories, APHL will track shipments from the commercial laboratories to the CDC STARHS laboratory. Commercial laboratories must provide APHL with a list of sample numbers sent to the CDC STARHS laboratory. The CDC STARHS laboratory must notify APHL of any shipments sent from a commercial laboratory to the CDC STARHS laboratory that are received. This notification is needed for billing reconciliation purposes at APHL.

Sample Rejection Criteria - Sample rejection due to thawing, breakage, insufficient quantity, or lost-in-transit will be determined and recorded by the CDC STARHS laboratory.

Confidentiality and HIPAA Regulations

STARHS must ensure that confidentiality is protected and maintained to meet standards for HIV surveillance. The Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA) regulations permit protected health information to be shared for the purposes of public health surveillance activities (1). This protection allows the originating laboratories to send specimens labeled with their laboratory-assigned accession number to either the state PHL or the CDC STARHS laboratory, where samples to be tested using STARHS will be re-assigned a unique STARHS identification number prior to testing. This process will minimize re-labeling errors and simplify the shipment procedures for private laboratories. However, the state / local public health department must have the laboratory accession number to link the test result to the patient information in the surveillance record. Therefore, the laboratory accession number must be included on the HIV laboratory report sent to the state / local public health department by the originating laboratory.

Funding for Specimen Handling

As a rule, surveillance is not a remunerated activity. However, through a Cooperative Agreement with APHL (# U60/CCU303019-17), a pre-determined fee to offset personnel, administrative, and handling costs incurred by the high volume, multi-jurisdictional commercial laboratories (Section 3, Laboratory Type 1) will be reimbursed for an initial start-up period. The APHL Cooperative Agreement is effective through June 2006, but may be renewable. Reimbursement for other private laboratories is not covered by the APHL Cooperative Agreement; funding for specimen handling costs may be made available through the state's Cooperative Agreement with CDC for HIV/AIDS Incidence Surveillance (Program Announcement 04017), but handling fee reimbursement is not recommended.

Specimen Transport Options

Option A: Specimen Originated at Private Laboratory and is Sent Directly to the CDC STARHS Laboratory

Transportation Overview - In this transportation model, the originating private laboratory performing the confirmatory testing will send ***all*** confirmed HIV positive diagnostic specimens directly to the CDC STARHS laboratory (bypassing the state / local PHL) by overnight shipping in accordance with the procedures described in the document <*Guidance for Processing, Storage, and Shipping to the CDC STARHS Laboratory*>. The CDC STARHS laboratory will store specimens until specimen disposition is determined by the state / local ISC, at which point, the CDC STARHS laboratory will pull samples to be tested using STARHS, aliquot, re-label them with a STARHS identification number, and perform STARHS. All samples that should not be tested using STARHS (i.e., samples that are not the diagnostic specimen) will be discarded.

In this model, the originating laboratory would continue to submit laboratory report information in the current manner to the appropriate jurisdiction, but must also include the laboratory-assigned specimen accession number and the collection date on the report.

Figure 1 graphically depicts the flow of specimens and reports when samples originate at a private laboratory and are then shipped directly to the CDC STARHS laboratory.

Procedures for Specimens Sent Directly from a Private Laboratory to the CDC STARHS Laboratory

- The ISC notifies the CDC HIV Incidence Surveillance (HIS) Coordinator about each private laboratory that plans to send specimens directly to the CDC STARHS laboratory. The ISC should send the following information to the CDC HIS Coordinator for each laboratory:
  - Name of laboratory and laboratory point of contact,
  - Full contact information, including mailing address, phone number, fax, and email
  - Estimated number of positive samples expected per year.
- The CDC HIS Coordinator will contact the CDC STARHS laboratory with this information from private laboratories. This information is important for the CDC STARHS laboratory to plan for storage capacity.
- The state/local ISC should provide the private laboratory with a copy of the <*HICSB Incidence Surveillance STARHS Specimen Submission Form*>. The form should be pre-filled with the laboratory contact information, the name and address of the person who will receive the STARHS results (ISC), and the appropriate check box marked for Incidence Surveillance:

  ☑ **INCIDENCE SURVEILLANCE (HICSB)**

- The submitting private laboratory must include a copy of the <*HICSB Incidence Surveillance STARHS Specimen Submission Form*> with a list of all laboratory-assigned accession numbers included in the shipment. If more than one specimen box is included in the shipping container, then each box should contain its own STARHS Specimen Submission Form. If possible, an encrypted electronic version of the list of specimen accession numbers should also be included in the

shipment; this version will help the CDC STARHS laboratory log the samples with minimal chance of entry errors. ***Note: the manifest should not contain any patient identifiers other than specimen accession numbers.*** At the time of shipment, the submitting laboratory should also mail a copy of the shipping manifest to the ISC, notifying him/her of the shipment. This notification is critical for the ISC to be able to track specimens. As previously noted, identifying information for specimens should not be faxed or e-mailed, even if encrypted.

- The CDC STARHS Laboratory will not provide the private laboratories with any shipping materials, labels or cryovials, but will return the shipping container if a prepaid return air bill is included in the shipment. Surveillance sites may provide the private laboratories with prepaid shipping labels or shipping account numbers (i.e., Federal Express) to cover shipping expenses.
- Specimens shipped from private laboratories directly to the CDC STARHS laboratory will be stored frozen, indicated only by their original laboratory-assigned accession number. The ISC will send to the CDC STARHS laboratory a written list of specimens (identified by the original laboratory-assigned accession number, and, if known, the name of the originating lab) that are to be tested using STARHS (test list) or to be disposed of (toss list). The CDC STARHS laboratory will not assign a STARHS identification number unless the ISC notifies the laboratory that the sample is to be tested using STARHS. The CDC STARHS laboratory will continue to hold specimens that are not on one of these two lists.
- The CDC STARHS laboratory will test the specimens and send the STARHS results back to the designated ISC listed on the <*HICSB Incidence Surveillance STARHS Specimen Submission Form*>. Samples will be tested and reported by the newly assigned STARHS identification number.
- Periodically the CDC STARHS laboratory will review the stored specimens to reconcile the status of any samples that have been stored for a lengthy period of time. This will reveal any specimens that the ISC never ordered to be tested or discarded. The length of time specimens must be held will vary widely by surveillance site depending on such factors as reporting delays, etc.

Roles of Parties Involved

Role of Private Laboratories - The private laboratories are responsible for forwarding two items for HIV incidence testing: (1) a laboratory report to the public health surveillance department per local requirements, including the collection date, the laboratory-assigned specimen accession number, and identification information about the testing facility; (2) remnant HIV positive serum from WB or IFA confirmed diagnostic samples labeled with the laboratory-assigned specimen accession number.

The private laboratories may elect to aliquot 0.5 ml of the remnant sera for shipment to the CDC STARHS laboratory so that any additional portion of the remnant sera may be stored at their facility, or they may send the entirety of their remnant sera, without any further manipulation, to the CDC STARHS laboratory.

Prior to sending shipments to the CDC STARHS laboratory, private laboratories should carefully review the <*Guidance for Processing, Storage, and Shipping of Specimens to the CDC STARHS Laboratory*> to ensure proper shipping and handling of specimens.

Role of CDC STARHS Laboratory - The CDC STARHS laboratory must store all remnant HIV positive serum samples received until specimen disposition has been determined by the appropriate jurisdiction's ISC. The ISC will provide the CDC STARHS laboratory with a list of all samples to be tested using STARHS (test list) and a list of all samples to be discarded (toss list), listed by specimen accession number. The samples on the toss list should be discarded according to established laboratory methods.

The CDC STARHS laboratory will pull all samples on the test list and aliquot them into the designated cryogenic vial for testing. The CDC STARHS laboratory will simultaneously re-label the samples to be tested using STARHS with a STARHS identification number. The CDC STARHS laboratory must provide the appropriate ISC with a link between the STARHS identification number and the original specimen accession number. After the ISC has been provided with the linkage information, the CDC STARHS laboratory will destroy the laboratory copy of the specimen accession information.

The CDC STARHS laboratory will test all samples on the test list by the STARHS identification number and send results to the ISC from the appropriate jurisdiction. The STARHS results are for surveillance purposes only therefore results will not be reported back to the originating laboratory, provider, or client.

Role of the State / Local HIV Incidence Surveillance Coordinator - The ISC from the jurisdiction where the specimen originated will determine the disposition of the specimen and coordinate with the CDC STARHS laboratory to ensure that the specimen is either tested or discarded as appropriate. The ISC will also maintain the link between the original specimen accession number and the STARHS number, and will manage the STARHS results.

Specimen Numbering - Specimens will be stored at the CDC STARHS laboratory by the original laboratory-assigned specimen accession number. Once a specimen appears on the test list the sample will be assigned a unique STARHS identification number and will be tested using STARHS. All subsequent procedures use only the STARHS identification number.

Theoretical Laboratory Types for this Transportation Model - The laboratories that would best use this model are high volume, multi-jurisdictional commercial laboratories. However, other private laboratories may also choose to elect this specimen transport model.

Note: The testing laboratory may choose either of the two transport models. With the exception of public health laboratories, the examples listed in this section are merely suggestions, not requirements, for the types of laboratories that may choose to elect this model.

Option B: Specimen Originated at or Sent Via State / Local Public Health Laboratory

Transportation Overview - In this transportation model, confirmatory testing will have been performed at either the PHL or a private laboratory. For samples originating at a private laboratory, that laboratory will send ***all*** confirmed HIV positive diagnostic specimens to the state / local PHL. The state / local PHL will store all specimens received from the private laboratories until sample disposition is determined by the ISC. All specimens on the test list (those to be tested using STARHS) will be pulled, aliquoted into the designated cryogenic vials provided by the CDC STARHS laboratory, relabeled with a STARHS identification number, and shipped to the CDC STARHS laboratory by overnight shipping in accordance with the procedures described in the document <*Guidance for Processing, Storage, and Shipping to the CDC STARHS Laboratory*>. All specimens that are on the toss list (those that are not to be tested using STARHS) will be pulled and discarded according to existing laboratory procedures.

In this model, the originating laboratory would continue to submit laboratory report information in the current manner, but must also include the laboratory-assigned specimen accession number, other relevant specimen identifiers, and testing laboratory identification on the report.

Many laboratories send enzyme immunoassay (EIA) positive specimens to a reference laboratory for confirmatory WB or IFA, which usually results in different laboratory accession numbers. In this case, care must be taken to ensure that the appropriate specimen accession numbers are associated with the correct surveillance report.

Figure 2a graphically depicts the flow of specimens and reports when samples originate at the PHL and are then shipped to the CDC STARHS laboratory. **Figure 2b** describes the flow of specimens and reports when samples originate at a private laboratory and are sent to the PHL for storage prior to shipment to the CDC STARHS laboratory.

Procedures for Specimens Sent from a Private Laboratory through a State Public Health Laboratory to the CDC STARHS Laboratory

- The ISC works with each private laboratory to set up procedures for shipping specimens to the state PHL.
- The ISC should provide the private laboratory with a copy of the <*HICSB Incidence Surveillance STARHS Specimen Submission Form*>. The form can be pre-filled with the state PHL contact information, or a new form may be developed in agreement with the PHL. Some private laboratories already have existing mechanisms for transporting specimens to the PHL. These procedures may also be used.
- The submitting private laboratory must include a list of all laboratory-assigned specimen accession numbers included in the shipment to the PHL. At the time of shipment, the private laboratory will mail a copy of the list to the ISC, notifying him/her of the shipment. The private laboratory should also notify the PHL of the

shipment by calling or emailing the PHL with the shipment tracking number, if applicable, and the number of samples sent. This information is critical for both parties to be able to track specimens.

- The PHL will store the specimens from the private laboratory, holding them until specimen disposition is determined by the ISC. Specimens should be stored frozen by the original laboratory-assigned specimen accession number. On a regular basis, the ISC will notify the PHL which specimens they are storing should be pulled for STARHS testing (test list) and those that can be discarded (toss list).
- The PHL will discard all specimens on the toss list and will prepare all specimens on the test list for testing using STARHS.
    - All specimens to be tested using STARHS will be pulled, thawed, and aliquoted into the designated cryovials provided by the CDC STARHS laboratory.
    - The PHL will re-label the samples to be tested using STARHS with a unique STARHS identification number using labels provided to the PHL by the CDC STARHS laboratory.
    - The PHL will send the ISC the linkage information between the original laboratory-assigned specimen accession number and the new unique STARHS identification number.
    - The PHL will ship all re-labeled specimens to the CDC STARHS laboratory according to the procedures described in the document <*Guidance for Processing, Storage, and Shipping to the CDC STARHS Laboratory*>.
    - The PHL should provide the CDC STARHS laboratory with a completed <*HICSB Incidence Surveillance STARHS Specimen Submission Form*>, listing all samples in the shipment by the newly-assigned STARHS identification number. The PHL should also include an encrypted electronic version of the specimen list in the shipment; this version will help minimize data entry errors at the CDC STARHS laboratory. The list of STARHS identification numbers on the <*HICSB Incidence Surveillance STARHS Specimen Submission Form*> serves as verification from the ISC that all samples in the shipment are to be tested using STARHS.
    - A copy of the completed <*HICSB Incidence Surveillance STARHS Specimen Submission Form*> should also be mailed to the ISC as notification of the shipment.
    - The PHL should also notify the CDC STARHS laboratory of the shipment by calling or emailing the laboratory to provide the shipment tracking number and number of samples sent.
- The CDC STARHS laboratory will test all samples received from the PHL with a pre-assigned and labeled STARHS identification number and send STARHS results back to the designated ISC listed on the <*HICSB Incidence Surveillance STARHS Specimen Submission Form*>.

- Periodically the PHL should review their stored specimens to reconcile the status of any samples that have been stored for a lengthy period of time. This review will reveal any specimens that the ISC did not order to be tested or discarded. The length of time specimens must be held will vary widely by surveillance site depending on such factors as reporting delays, etc.

Roles of Parties Involved

Role of Private Laboratories - The private laboratories are responsible for forwarding two items for HIV incidence testing: (1) a laboratory report to the public health surveillance department per local requirements with specimen identifiers, the laboratory-assigned specimen accession number, and identification information about the testing facility; (2) remnant HIV positive serum from WB or IFA confirmed diagnostic samples labeled with the laboratory-assigned specimen accession number and testing laboratory identification information.

The private laboratories may elect to aliquot 0.5 ml of the remnant sera to send to the PHL so that any additional portion of the remnant sera may be stored at their facility, or they may send the entirety of their remnant sera, without any further manipulation, to the PHL.

Prior to sending shipments to the CDC STARHS laboratory, private laboratories should carefully review the *<Guidance for Processing, Storage, and Shipping of Specimens to the CDC STARHS Laboratory>* to ensure proper shipping and handling of specimens.

Role of Public Health Laboratories - The PHL must store all remnant HIV positive serum samples (tested in their own facility or shipped from a private laboratory) until specimen disposition has been determined by the ISC. The ISC will provide the PHL with a list of all samples to be tested using STARHS (test list) and a list of all samples to be discarded (toss list) listed by specimen accession number.

The PHL will pull all samples that will not be tested using STARHS and discard them according to existing laboratory procedures.

The PHL will pull all samples to be tested using STARHS and aliquot them into the designated cryogenic vial provided by the CDC STARHS laboratory. The PHL will simultaneously re-label the samples with a STARHS identification number using labels provided to the PHL by the CDC STARHS laboratory. The PHL must also provide the ISC with a link between the STARHS identification number and the original specimen accession number. The PHL will ship all samples to be tested using STARHS, labeled only with the STARHS identification number, to the CDC STARHS laboratory according to the procedures described in the document *<Guidance for Processing, Storage, and Shipping to the CDC STARHS Laboratory>*.

Role of State / Local HIV Incidence Surveillance Coordinator - The state / local ISC from the jurisdiction where samples originated will determine the disposition of all samples stored at the PHL and coordinate with the PHL to ensure that only specimens to be tested

using STARHS are shipped to the CDC STARHS laboratory and all specimens that will not be tested using STARHS are discarded. The ISC will also maintain the link between the original specimen accession number and the STARHS number, and will manage the STARHS results.

Role of CDC STARHS Laboratory - The CDC STARHS laboratory will test all samples received from a PHL using the STARHS identification number. Once testing is complete, the CDC STARHS laboratory will return results to the appropriate jurisdiction's ISC.

Specimen Numbering - Specimens will be stored at the PHL labeled with the original laboratory-assigned specimen accession number. Once specimen disposition is determined, each sample to be tested using STARHS will be assigned a unique STARHS identification number by the PHL prior to shipment to the CDC STARHS laboratory. All subsequent procedures use only the STARHS identification number.

Theoretical Laboratory Types for this Transportation Model - The laboratory types that would best use this model are single-jurisdiction laboratories such as hospital, medical center, university, small independent reference laboratories, or local branches of large commercial laboratories. In many cases, these laboratories already have working relationships and established procedures for submitting samples to their state and/or local PHL and would prefer not to change their existing practices. All state / local PHL performing confirmatory testing for HIV also fall into this category, except they would simply hold samples until the ISC determines specimen disposition.

Note: The testing laboratory may choose either of the two transport models. With the exception of public health laboratories, the examples listed in this section are merely suggestions, not requirements, for the types of laboratories that may choose this model.

Responsibilities

Private Laboratories

Select a Model Type - Each private laboratory performing confirmatory testing of HIV diagnostic specimens must select one of the two specimen transport model types and inform the ISC which model was chosen. The private laboratory must send remnant sera from confirmed HIV-seropositive samples to either the state / local PHL or to the CDC STARHS laboratory.

Additional Laboratory Report Information - The private laboratory must include the laboratory-assigned specimen accession number on the laboratory report form sent to the HIV surveillance department, per state / local disease reporting requirements.

Many laboratories send EIA positive specimens to a reference laboratory for confirmatory WB or IFA. In this case, care must be taken to ensure that the appropriate specimen accession numbers are associated with the correct surveillance report.

Public Health Laboratories

Sample Storage and Retention - The PHL will often serve a dual function as a testing laboratory or a "pass through" facility for private laboratories. The PHL will store (Section 4.3) all WB or IFA confirmed positive samples and/or all samples received from private laboratories until sample disposition is determined by the ISC.

Aliquoting and Sample Shipment - Once sample disposition has been determined by the ISC, the PHL will be responsible for pulling the identified samples, aliquoting samples into the appropriate tubes, and re-labeling the samples with a STARHS identification number for testing. The PHL will send the ISC the linkage information between the laboratory-assigned specimen accession number and the STARHS identification number. The PHL will ship all samples to be tested using STARHS (test list) to the CDC STARHS laboratory and discard all samples on the toss list according to existing laboratory procedures.

State / Local HIV Incidence Surveillance Coordinator

Sample Disposition - The ISC will determine sample disposition for all HIV seropositive diagnostic samples tested in the jurisdiction. The ISC will coordinate with the PHL and/or the CDC STARHS laboratory to ensure the proper samples are tested.

Data Management - The ISC will retain the linkage information between the laboratory-assigned specimen accession number and the STARHS identification number to ensure that STARHS results can be matched to surveillance data. The ISC will send incidence data to CDC on a monthly basis on or before the 15th of each month. If the ISC is in a local jurisdiction, then results should be sent to the state ISC for matching purposes before submitting data to CDC.

CDC STARHS Laboratory

Sample Rejection Criteria - Sample rejection due to thawing, breakage, insufficient quantity, or lost-in-transit will be determined and recorded by the CDC STARHS laboratory.

Sample Storage and Retention - All samples that are shipped directly from a private laboratory and not a state PHL must be stored (Section 4.3) at the CDC STARHS laboratory until sample disposition is determined by the ISC. Storage time may vary from state-to-state depending on the state's surveillance practices. Once sample disposition has been determined by the ISC, the CDC STARHS laboratory will be responsible for pulling all samples on the test and toss lists from the ISC. The samples on the toss list will be discarded. The samples on the test list will be aliquoted into the appropriate tubes and re-labeled with a STARHS identification number for testing. The CDC STARHS laboratory will apply a label to the sample tube and then to a line listing of specimen accession numbers received from the ISC or PHL for those samples to be tested using STARHS. The CDC STARHS laboratory will send the ISC the linkage information and then destroy the linkage information held at the CDC STARHS laboratory. All subsequent testing and results will only refer to the STARHS identification number and will no longer include the original specimen accession number.

Result Reporting - The CDC STARHS laboratory will report STARHS results by the STARHS identification number only to the ISC with jurisdiction over the sample as designated by the <*HICSB Incidence Surveillance STARHS Specimen Submission Form*>. The results reporting mechanism will adhere to the methods agreed upon between CDC and the CDC STARHS laboratory.

References

1. CDC. HIPAA Privacy Rule and Public Health: Guidance from CDC and the U.S. Department of Health and Human Services. MMWR, April 11, 2003; 52, 1-12. Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/m2e411a1.htm.

Figure 1. Specimen Originates at National Commercial Laboratory or Private Laboratory and is Sent Directly to the CDC STARHS Laboratory

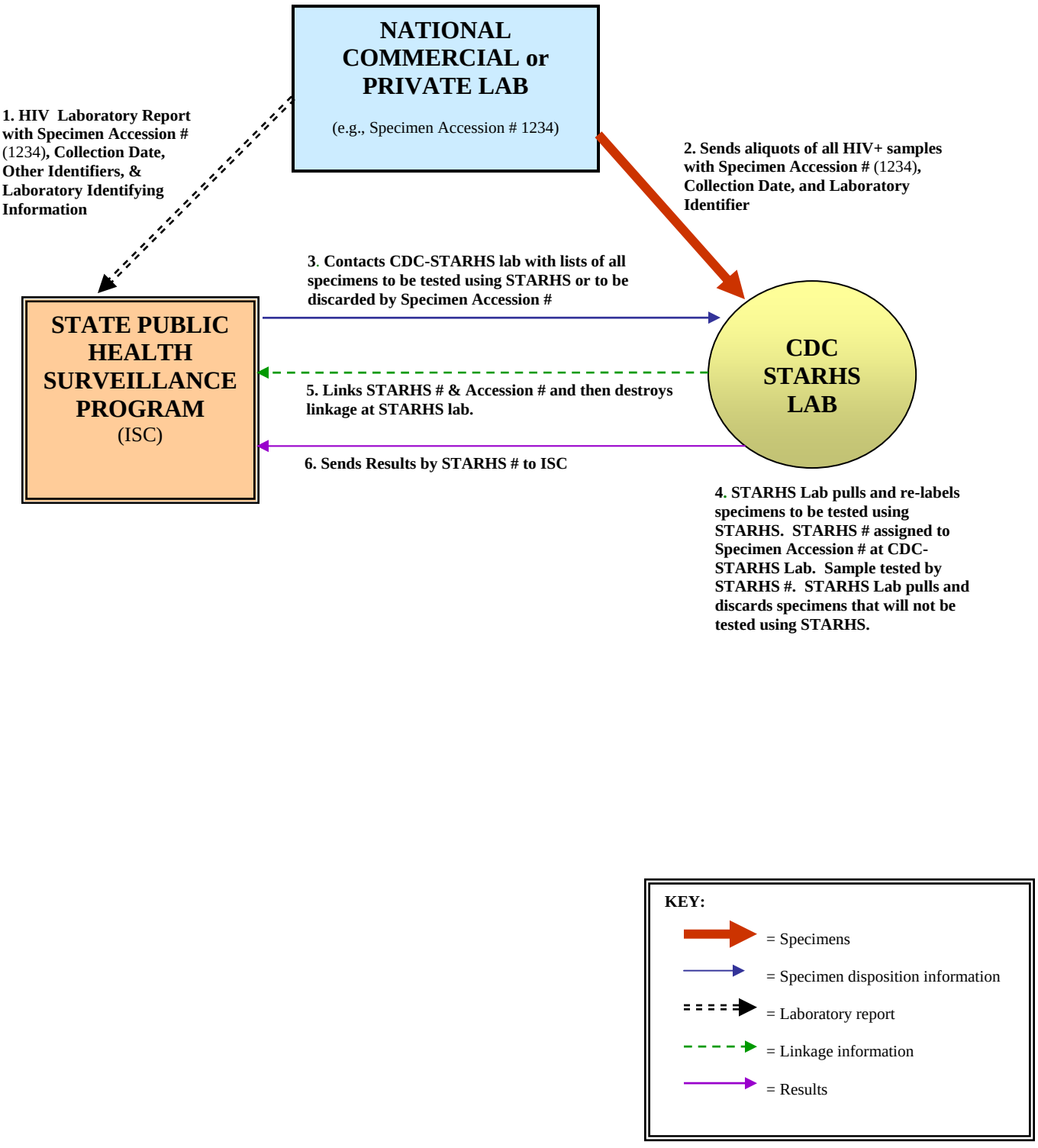


Figure 2a. Specimen Originates at a Public Health Laboratory (PHL Performed the Confirmatory HIV Testing)

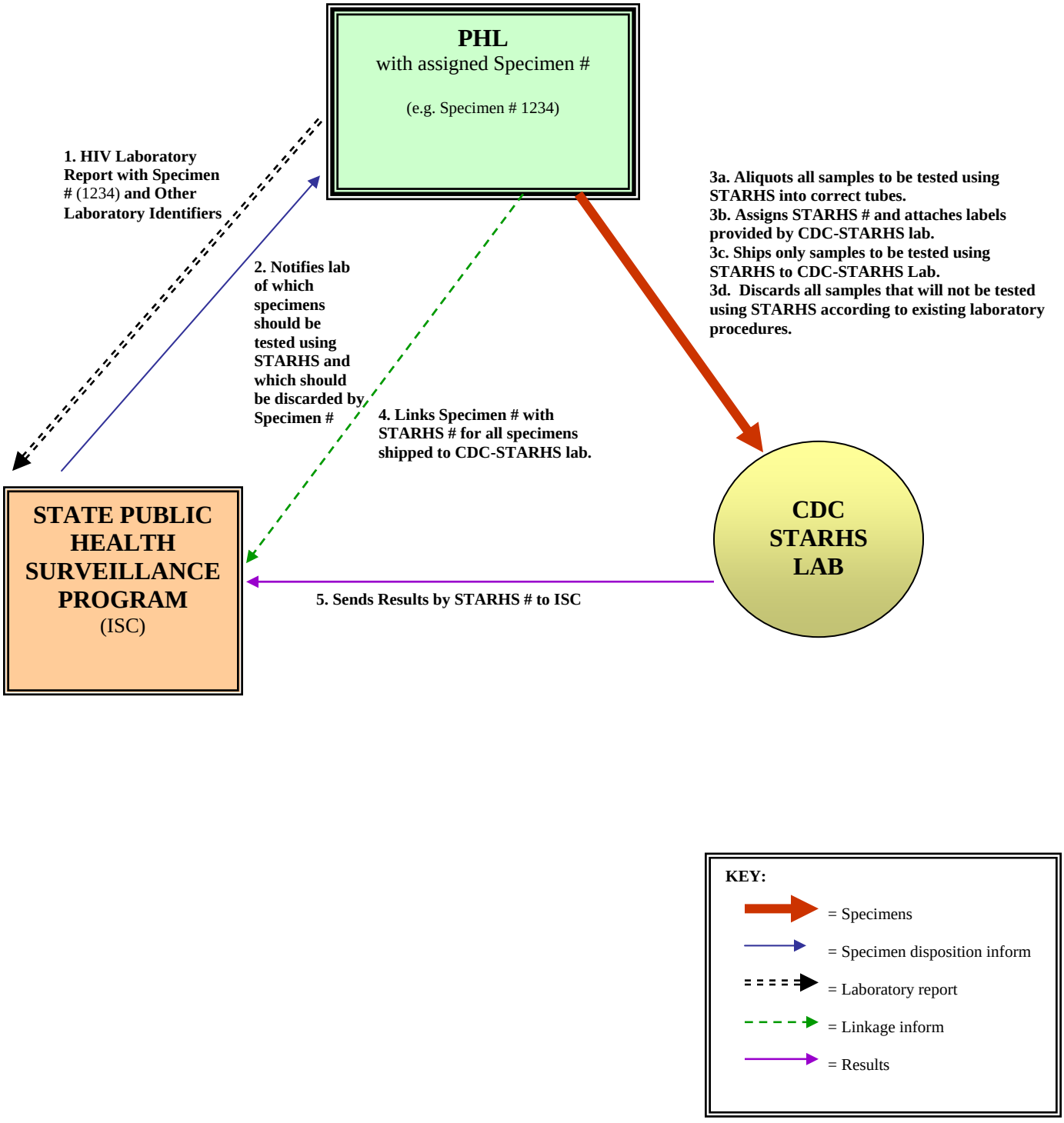
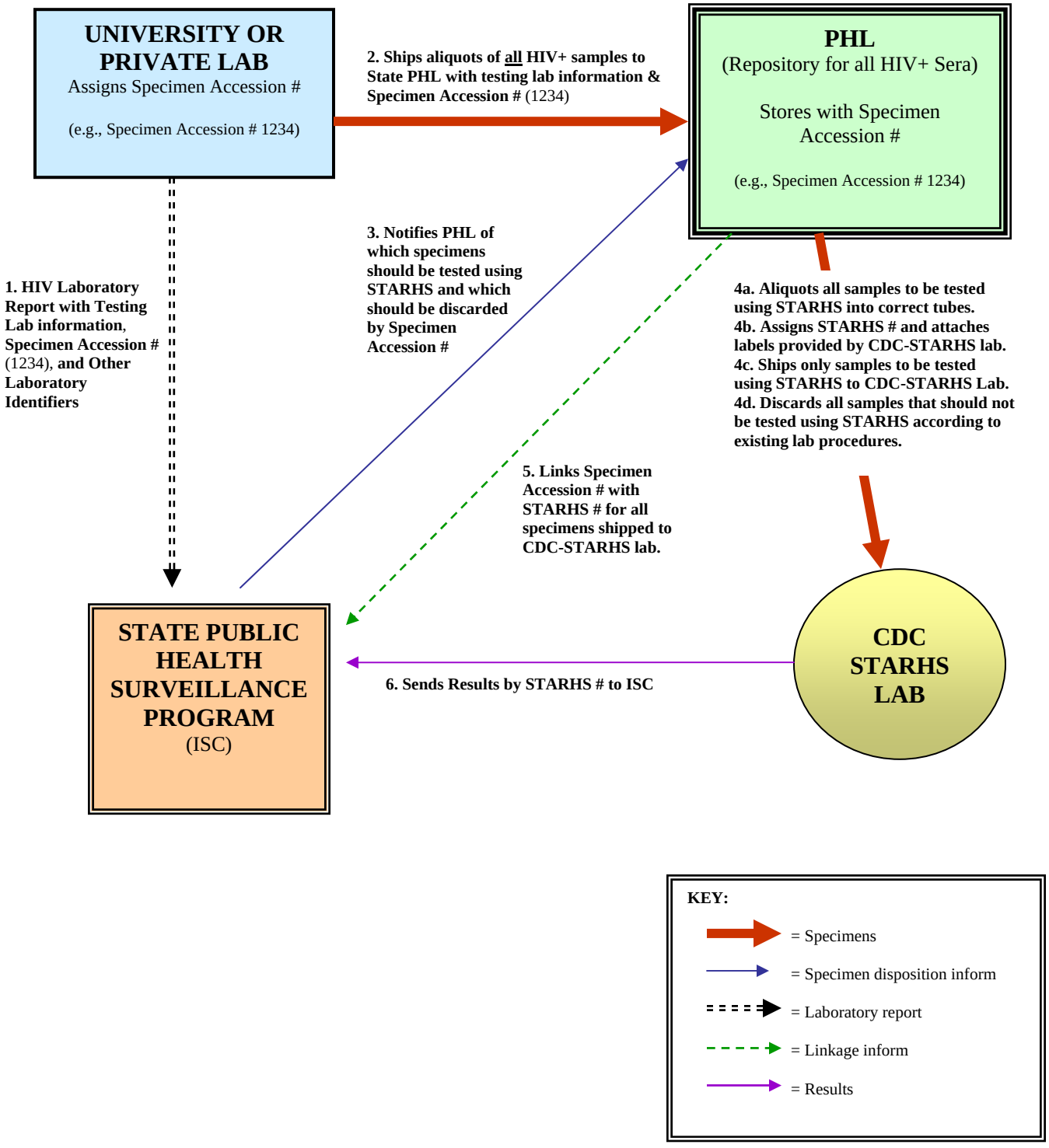


Figure 2b. Specimen Originates at a Private Laboratory (for example, a University Hospital Laboratory, Regional or Local Independent Commercial Laboratory) and Sends Sample to State Public Health Laboratory (serves as a pass-through facility)



HICSB Incidence Surveillance
STARHS SPECIMEN SUBMISSION FORM

Please complete this form and send it with each shipment. Specimens should be sent to:

NYSDOH Wadsworth Center
Axelrod Institute
Diagnostic HIV Testing Lab: STARHS
120 New Scotland Avenue
Albany, NY 12208

SHIPPING FACILITY INFORMATION:

Name:_____

Address:_____

_____

Phone Number:_____

Fax:_____

Email:_____

Contact Person:_____

RESULTS SENT TO:

Name_____

Address_____

_____

Phone Number:_____

Fax_____

Email:_____

- ☐ **INCIDENCE SURVEILLANCE (HICSB) - List of eligible specimens sent separately**
- ☐ **INCIDENCE TESTING FOR HIV DRUG RESISTANCE SURVEILLANCE (HRS)**
- ☐ **BEHAVIORAL SURVEILLANCE (BSCB)**
- ☐ **EVALUATION OF DRIED FLUID SPOT SURVEILLANCE (DFS)**

RANGE OF SPECIMEN NUMBERS SENT (OR ATTACH LIST):

_____

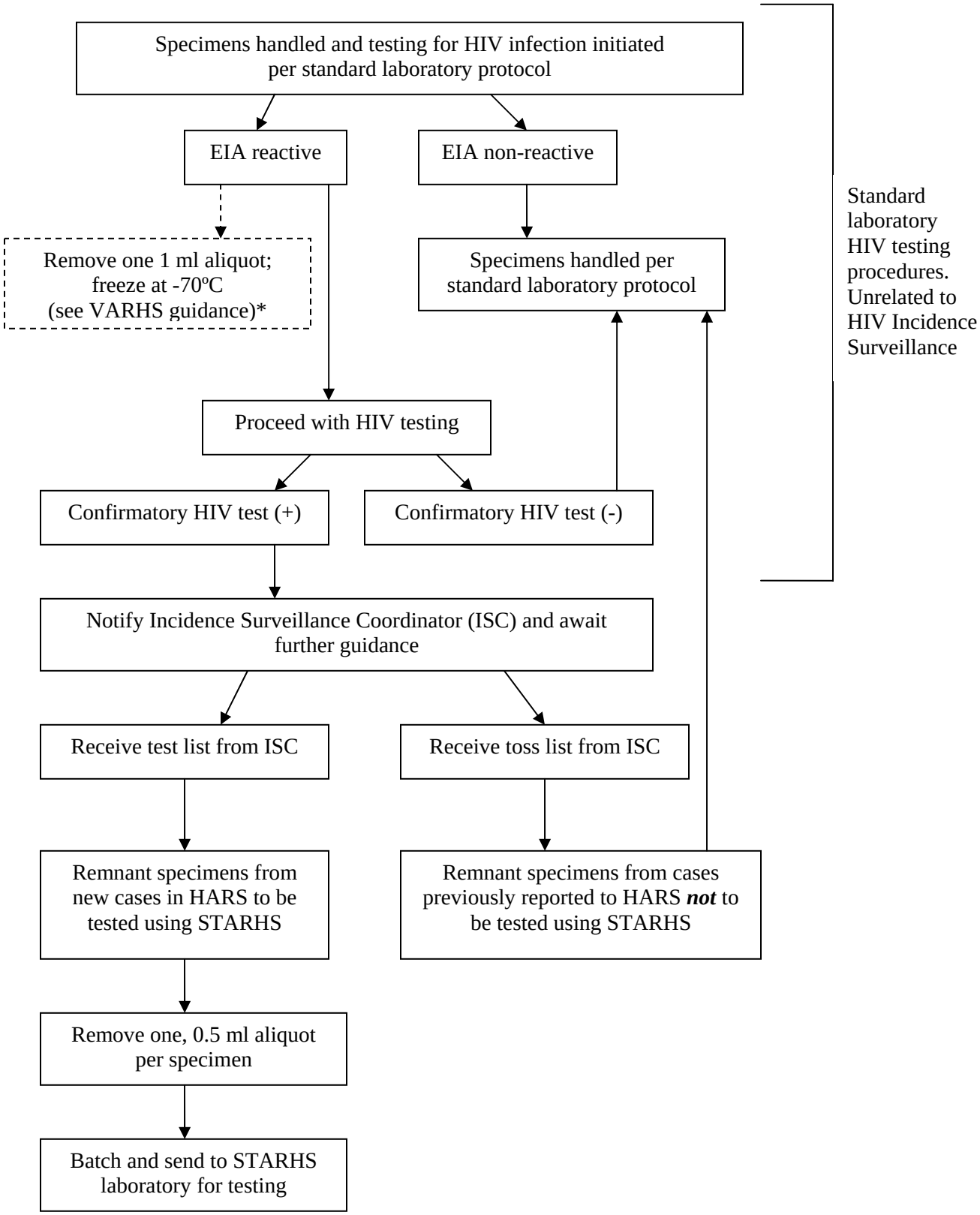
_____

_____

_____

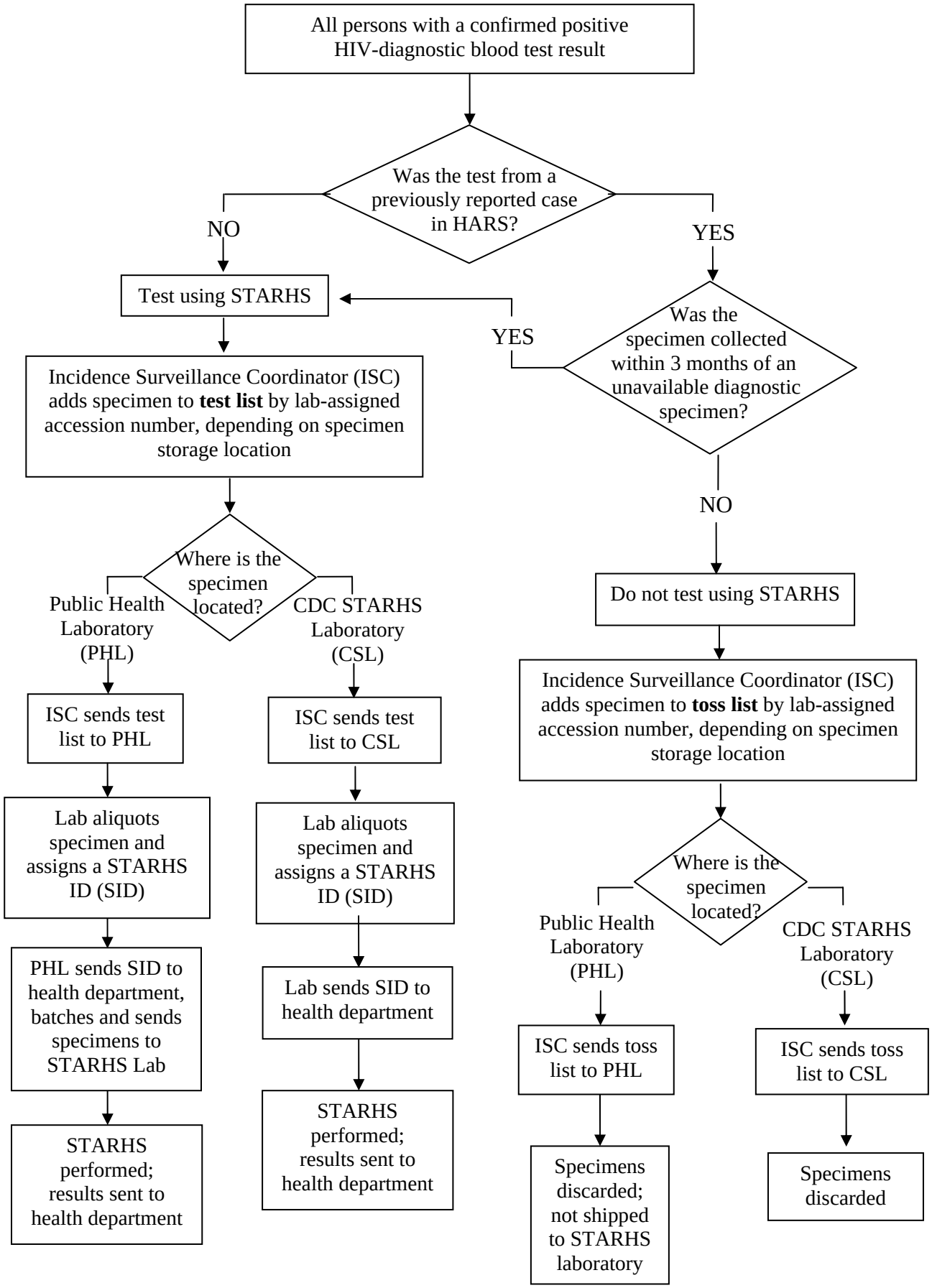
Please identify any specimens above that are not collected under the Standard Procedures and should be tested using the Vironostika HIV-1 Less Sensitive Assay.

Operational Public Health Laboratory Flow Chart for HIV Incidence Surveillance



*Applies only to laboratories participating in VARHS

Epidemiologic Flow Chart for HIV Incidence Surveillance



Training and Certification for Shipping Infectious Substances

FedEx 800-GO-FEDEX 3 day IATA based training Covers all hazardous materials Cost is $550

Saf-T-Pak 800-814-7484 Specifically for infectious and diagnostic substances, and dry ice 3 options--- One day seminar, On-site programs, or Interactive CD For interactive CD: for one sitting, can be done in 3-5 hours Certificate good for 2 years OR until regulations change Cost is ~$250

Viking Packaging (Oklahoma) 800-788-8525—David Weilert Seminars monthly in Tulsa/ $300 per person Covers all nine classes of hazardous materials Covers shipping under IATA Certificate good for 2 years Will do group classes in local area---$3,000 plus travel costs

These are some companies that provide training for dangerous goods shipping. The Centers for Disease Control and Prevention does not endorse any particular company.

Guidance for Processing, Storage, and Shipping of Specimens to the CDC STARHS Laboratory

(Revised: 8/2006)

Purpose

This standard operating procedure describes methods for the handling, storage, and shipping of serum specimens that will be tested for recent HIV-1 infection using STARHS. Results from these tests will help estimate HIV incidence.

Introduction

Remnant serum from positive HIV diagnostic specimens is to be collected and frozen using vials and labels specified or supplied by the CDC STARHS laboratory. Ideally, 0.5 ml should be collected for each aliquot. Frozen serum will be shipped to the CDC STARHS laboratory for testing.

CDC STARHS Laboratory

The CDC STARHS laboratory is the Wadsworth Center Retroviral Immunology Diagnostic HIV Testing Laboratory which is part of the State of New York Department of Health. Frozen aliquots will be shipped to:

NYSDOH Wadsworth Center
Axelrod Institute
Diagnostic HIV Testing Lab: STARHS
120 New Scotland Avenue
Albany, New York 12208
Attn: Brian Granger

Setting and personnel for specimen processing

- Centrifugation, aliquoting, and shipping should be performed at or under the auspices of a laboratory that is CLIA-certified for handling HIV+ specimens.
- All personnel handling specimens should receive blood borne pathogens training. See the **Occupational Safety and Health Association (OSHA) Occupational Exposure to Bloodborne Pathogens Standard:**

  http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10051.

- Personnel handling or processing specimens should have appropriate laboratory training in the relevant laboratory techniques for handling HIV+ specimens and for performing the specific tasks required.
- The setting in which centrifugation, aliquoting, and shipping occurs should meet Biosafety level 2 specifications required by the U.S. Department of Health and Human Services for handling of

specimens containing HIV:

- [http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm, Biosafety in Microbiological and Biomedical Laboratories (BMBL) 4th Edition (4th%20BMBL.pdf), pages 20-27, 171-175].

Materials

- Cryogenic vials - Supplied by CDC STARHS Laboratory
- Specimen labels - Supplied by CDC STARHS Laboratory – Label will identify sample (barcode, number, etc) by STARHS identification number
- Cardboard storage boxes for cryogenic vials – Can be supplied by CDC STARHS Lab if requested
- Freezer—STARHS samples can be refrigerated at 2-8^{o}C, but for long term storage and shipping, samples should be frozen at -20^{o}C
  - It is recommended that, if not already in practice, a daily temperature log be kept to ensure the freezer is operating properly
  - The freezer should be housed in a location with proper ventilation to avoid overheating and freezer failure.
  - Staff must be certain there is adequate space in freezer to store specimens.
- A supply of dry ice in pellet form
- Insulated shipping containers certified to ship frozen diagnostic specimens (HIV+ serum and dry ice)
- Shipping courier air bills
- Materials for shipper packing—See Packing procedures for shipping to the CDC STARHS laboratory later in this document
- *<HICSB Incidence Surveillance STARHS Specimen Submission Form>*

Specimen Collection and Processing

All processing of specimens should be done by personnel qualified to handle HIV+ specimens under the auspices of a laboratory equipped for the handling of HIV + specimens [http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm, Biosafety in Microbiological and Biomedical Laboratories (BMBL) 4th Edition (4th%20BMBL.pdf), pages 20-27, 171-175].

- Aliquot the serum (0.5 ml per cryogenic vial). Use labels to identify the specimen and record this information in the proper setting. (Specimen log for eventual transfer to HIV Incidence Surveillance database.)
- Store aliquots in refrigerator or freezer until specimen disposition has been determined and scheduled shipping date has arrived.

Shipping

- Specimens for STARHS should be sent to CDC STARHS laboratory using the address written on the <*HICSB Incidence Surveillance STARHS Specimen Submission Form*> and in the "CDC STARHS Laboratory" section in this document. All specimens will be shipped as diagnostic specimens using IATA (International Air Transport Association) Packing Instructions 650. Dry ice will be included with each shipment using IATA Packing Instructions 904.
  - Because samples will be shipped using dry ice, shipping personnel must be trained and certified to ship dangerous goods. See **Appendix 7.1.B** for a list of companies that provide training.
  - Establish contact with Lea N'ko Ali-Napo (nla01@health.state.ny.us) at the CDC STARHS laboratory.
  - Ensure that adequate STP320 or equivalent shipping containers are available. The CDC STARHS Laboratory will return them to the submitting laboratory if a return air bill is included in the shipment. The shippers are expensive and need to be re-used.
  - Ensure that you have an adequate supply of shipping courier air bills which can be obtained free of charge from most couriers.

- Packing procedures for shipping to the CDC STARHS laboratory - It is recommended that all of these steps are read and understood **before** starting the preparation of the actual shipment
  - Bring the STP320 shipper or equivalent that is to be used for the shipment and materials needed for packing the specimens into the area in which the shipment will be prepared.
  - If the shipper is new and being used for the first time, check to be sure that it includes the following items:
    - Two (2) sheets of bubble wrap
    - Two (2) STP 710 or equivalent certified secondary containers
    - Two (2) 250 ml absorbent strips
    - Class 9 label and dry ice quantity label
    - Other hazard and handling labels
    - One (1) instruction sheet
  - For a diagram of the above contents, refer to the SaftPak catalog.
  - Use only what is needed of the above contents for each individual shipment. Save left over supplies for future shipments.
  - If the shipper is being re-used, the proper labels will already be in place on the outer cardboard container. Ensure that adequate supplies of the other materials listed above are on hand.
  - Put on personal protective equipment.
  - Remove cryogenic vials from freezer and accurately record the specimen accession or STARHS identification numbers. The specimen numbers can either be written directly onto

the STARHS Specimen Submission Form or on a separate list that will be attached to the form. Return them to the freezer. Repeat the process until all specimen numbers have been recorded for each vial that is going to be shipped.

- **These specimens should remain frozen at all times and therefore should not be removed from a frozen environment for more than a few minutes**.
- Prepare 3 copies of the STARHS Specimen Submission Form (Appendix 7.1.A) — listing or attaching the specimen number on each vial to be shipped.
  - Copy 1 (original) will be sent with the specimens in the shipment.
  - Copy 2 should be mailed to ISC as notification of shipment.
  - Copy 3 will be retained by the submitting laboratory for their records.
- If possible, on a floppy disk or CD, also include an encrypted electronic version of the list of specimen numbers in the shipment. This will help the CDC STARHS laboratory minimize the amount of data entry they have to do when logging in the samples, thereby minimizing errors.
- Prepare the Shipping courier air bill that the CDC STARHS laboratory will use to return the shipper back to the submitting laboratory for re-use. The air bill MUST be completely filled in with the return address, the CDC STARHS laboratory address, and the proper billing number.
- If dry ice is in another location which requires leaving the area in which the shipment is prepared, use a separate container to bring the dry ice that is needed for shipping back into the shipping area at this time.
- Bring the specimens to the area in which the shipment is prepared. Work quickly, keeping in mind that **these specimens should remain frozen at all times and therefore should not be removed from freezing temperature environment for more than a few minutes.**
- Re-check the screw-cap lids on the specimen vials—tighten if necessary.
- Place the specimens into the secondary leak-proof container and make sure samples are surrounded by bubble wrap and absorbent strips. The vials should not move around or rattle inside the vessel.
- Place the secondary vessel into the inner box and place the inner box into the polystyrene cooler.
- Pack dry ice pellets in the shipper and around the inner box. The STP320 shipper will hold ~8 kg of dry ice (~10lbs) and, if packed completely, will keep the contents frozen for greater than 80 hours.
- DO **NOT** PUT DRY ICE INSIDE THE INNER BOX
- Place the lid on the polystyrene cooler
- Place one copy of the completed <*HICSB Incidence Surveillance STARHS Specimen Submission Form*> on top of the shipping box return form with the completed *return* FedEx air bill stapled to it. Fold in half and place on top of the polystyrene lid.
- Fold over the top flaps and seal the shipping container with clear shipping tape.

- The outer box must have a mark in the form of a square set at an angle of 45^{o} (diamond shaped). The mark must be at least 2 inches by 2 inches and include the UN 3373 designation. The proper shipping name "Diagnostic specimens" must be marked on the outer package adjacent to the diamond shaped mark. Labels can be purchased to place on the outer box that fulfill this requirement.
- Apply the Class 9 Hazard Label over the lower diamond shaped outline on the box.
- Apply the net quantity dry ice label to the outlined area adjacent to the Class 9 Hazard Label. Write the approximate amount (in kg) of dry ice you used to pack the container.
- Prepare the shipping courier paper work addressed to the CDC STARHS laboratory. Select the overnight shipping option.
- Call or email the CDC STARHS laboratory to notify them of the shipment. Provide the CDC STARHS laboratory with the shipment tracking information and the total number of samples in the shipment. ***Note: Do not fax or email laboratory-assigned specimen accession numbers or STARHS identification numbers.***