ID: 2001-ID-03 **Committee:** Infectious Disease

Title: The impact of new technologies and therapies on HIV/AIDS surveillance: routine nationwide reporting of CD4, STAHRS, antiretroviral resistance, and viral load test results.

Statement of Problem:

CD4 and viral load reporting:

Over the course of the HIV/AIDS epidemic, surveillance practices have reflected changes in understanding of HIV disease and evolving medical practices for diagnosis and treatment of HIV infection and AIDS. The HIV/AIDS surveillance case definitions have been revised periodically to ensure that surveillance programs accurately monitor the extent of morbidity and mortality associated with HIV in the U.S. In 1993, the AIDS case definition was revised to include CD4 t-lymphocytes <200 cells/µL or <14%.

Subsequently in 1996, CSTE recommended that all states and territories implement laboratory-initiated reporting of immunologic AIDS cases to assist in more timely and comparable ascertainment of cases across states. Although many states have implemented laboratory reporting of CD4 counts, the level of reportable CD4 counts varies. A 1997 survey of HIV/AIDS surveillance coordinators indicated at least 27 states had some reporting requirements for CD4 counts, of which 4 states required reporting of results <500 cells/µL, 1 required reporting of results <800 cells/µL, and 4 require reporting of all CD4 test results to the health department. States with HIV infection reporting that require reporting of CD4 counts > 200 cells/µL have found that this reporting practice enhances the reporting of HIV infection cases as well as of AIDS cases.

Obtaining data on CD4 levels among persons diagnosed with HIV infection is becoming increasingly important for monitoring the impact of advances in antiretroviral therapy, evaluating new treatment guidelines, and meeting the increasing need for epidemiologic data on persons at all stages of HIV disease for allocation of resources for treatment services and evaluating public health interventions. As more states implement HIV infection reporting, reporting of CD4 results will remain an important benchmark of disease progression and morbidity and enable systematic assessment of the proportion of HIV cases that have received follow-up medical assessment. Further, evaluation of CD4 counts near the time of HIV diagnosis has been described as a "snapshot" method for estimating HIV incidence, and was recommended to CDC as an approach for estimating incidence of HIV infection during a CDC consultation on methods to estimate incidence of HIV infection in the United States held in Atlanta, February 27-28, 2001

In January, 2000, the surveillance case definition of HIV infection was expanded to include HIV nucleic acid (DNA or RNA) detection tests that have become standard of care for the clinical management of HIV infection in the U.S. Some states have incorporated laboratory reporting of these detection tests into existing surveillance practices. Increasingly, HIV/AIDS surveillance programs in the United States,

especially in states newly initiating reporting of HIV infection, will rely heavily on laboratory reporting of viral load test results to identify reportable HIV cases among previously diagnosed persons who are receiving routine monitoring of viral loads.

STARHS testing:

Recently developed technologies permit the identification of very recently infected persons among persons with serologic evidence of HIV infection by using a less sensitive EIA followed by a more sensitive EIA, i.e., the so-called Serologic Testing Algorithm for Recent HIV Seroconversion (STARHS) or "detuned" test. Routine detuning of all new positive HIV tests in the U.S. was recommended as a primary approach for estimating incidence of HIV infection during the recent CDC consultation on methods to estimate incidence of HIV infection in the United States. To accomplish this, state and territorial health departments would need to require routine systematic detuned testing of specimens from all residents who are newly diagnosed with HIV as part of their HIV case reporting requirements. Inclusion of consent for detuned testing as a routine part of consent for HIV testing would expedite surveillance of HIV incidence.

There are several challenges to implementation of a STARHS-based strategy for surveillance to estimate HIV incidence in the population. Currently there is FDA IND approval for use of detuned testing for research purposes. This requires anonymization of specimens in most cases; this current approval would need to be modified to allow confidential STARHS testing. Also, it will be important for States to understand what proportion of positive HIV tests are currently done using non-serum specimens (e.g., oral mucosal transudate or dried blood spots), which could not be subjected to detuned testing. Also, it will be important to anticipate the need for adequate supplies of reagents for more broadly implemented detuned testing strategies; recent FDA IND approval of a second test kit (e.g., Organon Teknika kit) should help to address this concern. Expertise in conducting detuned testing is currently concentrated in selected reference labs and issues of transport of specimens and reporting of detuned test results across jurisdictions need to be considered.

At this time, STARHS testing has been evaluated as a means to predict recent infection on a population basis, but has not been characterized or licensed for use on an individual basis. For this reason, in most circumstances the results of STARHS testing have not been returned to clients or to health care providers. If, in the future, detuned testing were determined to have clinical utility, it would be important to reconsider the surveillance strategy of routine detuning for public health surveillance purposes without return of test results.

Resistance monitoring:

Other changes in technologies used for clinical management of HIV infection that should be considered by surveillance programs relate to monitoring drug resistence in infected persons. Recently updated guidelines on clinical practices for the treatment of HIV infection, entitled "Guidelines for the Use of Antiretroviral Agents in HIV Infected

Adults and Adolescents." provided by the U.S. Department of Health and Human Services and the Henry J. Kaiser Family Foundation state that both genotype and phenotype drug resistance assays are recommended in certain circumstances. Over time, these newer tests will likely be incorporated as standard of care for infected persons and there will be increased need for surveillance data to describe the impact of drug resistence on the epidemic in the United States.

Thus, all states and territories should be encouraged to adopt laboratory reporting of CD4 t-lymphocyte counts and viral load results to meet increasing needs for epidemiologic data and provide complete and accurate case counts. States should identify new HIV positive tests among all HIV positive tests (e.g., those matching to HIV case reports) and require that public and private licensed laboratories forward an aliquot of the positive sample to a reference laboratory capable of performing the detuned EIA. Routine consent for detuned testing as part of consent for HIV testing should be adopted. In addition, there is a need to standardize reporting practices, including the levels at which CD4 results are reportable across states and the data elements that are reportable. Standardization of the reporting of results will facilitate progress towards electronic laboratory reporting, which is an important means of increasing the efficiency of surveillance programs. CDC has been working in collaboration with the Food and Drug Administration (FDA), the Association of Public Health Laboratories (APHL), and the American College of Pathology (ACP) and other experts to develop guidelines for standardized reporting of viral load test results to health care providers and facilities and for the purpose of public health reporting of notifiable diseases. A MMWR Recommendations and Reports is currently being drafted on these standards.

Specific Statement of Desired Action:
CSTE Recommends:
1) All states implement laboratory reporting of CD4 t-lymphocyte test results and consider reporting all CD4 tests, including those CD4 counts >200 cells/µL, conducted by laboratories in their jurisdiction. CDC should facilitate the management and use of such data by developing standards for laboratory reporting, promoting electronic laboratory reporting of CD4 test results, and developing surveillance software systems to automate or improve efficiency of matching high volumes of CD4 reports. Until such data management systems are operational, States should determine the reportable level based on capacity of surveillance programs, capabilities of currently available software, and their data needs to determine the reportable level for CD4 tests.

2) States should implement laboratory reporting of HIV nucleic acid (DNA and RNA) detection tests.

3) States should develop and implement procedures to identify, among newly reported HIV infection cases, which persons are very recently infected by using the detuned assay. States should consider including detuned testing as part of HIV testing in counseling and testing settings and incorporate consent for detuning into routine consent procedures for HIV testing. CSTE recognizes that full implementation of this recommendation will be dependent upon FDA approval of and availability of test kits for the detuned procedure,CSTE and CDC guidelines for detuning as a routine part of HIV surveillance practices, and adequate funding.

4) States should consider laboratory reporting of tests of drug resistence for persons reported with HIV infection or AIDS. In addition, states in the process of revising HIV reporting requirements should consider the use of broad language that will allow reporting of additional tests (e.g. hepatitis) that may become important in the management of HIV infection in the future.

5) CDC should provide technical assistance and adequate funding to states to conduct these additional surveillance functions and to standardize data elements for CD4, viral detection tests, detuned EIA tests and tests for drug resistence. In addition, CDC should provide guidance on implementing electronic reporting procedures and enhance the capacity of state surveillance programs to manage electronic laboratory data.

Fiscal impact:
Initiation of laboratory reporting in some areas may result in a data management burden on surveillance staff. Electronic reporting can ease the paper burden and assist areas in handling large numbers of test results more efficiently. Some programs may need additional computer or personnel support to implement a laboratory reporting system.

Probable impact on Public Health:
Public health programs will benefit from the data available for planning for treatment and care services as well as additional epidemiologic data for describing the spectrum of HIV infection in infected individuals in the U.S., and estimating HIV in states and nationally.

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