CDC's Model Performance Evaluation Program: Assessment of the Quality of Laboratory Performance for HIV–1 Antibody Testing

WILLIAM O. SCHALLA, MS
THOMAS L. HEARN, MS
ROGER N. TAYLOR, PhD
ELOISE EAVENSON, PhD
RONALD O. VALDISERRI, MD, MPH
JOYCE D. K. ESSIEN, MD, MBA

Mr. Schalla, Research Microbiologist, Mr. Hearn, Health Scientist, and Dr. Taylor, Microbiologist, are with the Model Performance Evaluation Program (MPEP), Division of Laboratory Systems (DLS), Public Health Practice Program Office (PHPPO). Dr. Eavenson is a Health Scientist, DLS, and Dr. Valdiserri is Director, DLS. Dr. Essien is Acting Director, PHPPO.

Tearsheet requests to William O. Schalla, MS, Model Performance Evaluation Program, DLS, PHPPO, Bldg. 6, Rm. 315, CDC, 1600 Clifton Rd. NE, Atlanta, GA 30333.

Synopsis

In 1986, the Centers for Disease Control (CDC) implemented the Model Performance Evaluation Program (MPEP) to evaluate the performance of laboratories that test for antibody directed against human immunodeficiency virus type 1 (HIV–1). The impetus for developing this program came from the recognition of a need to assess the quality of existing and changing laboratory technology and to ensure that the quality of testing was sufficient to meet medical and public health needs. To develop the program, CDC chose HIV–1 antibody testing as the first specific application for assessing the quality of laboratory performance because (a) *of the importance of accurate and reproducible test results for acquired immunodeficiency syndrome (AIDS) surveillance, prevention, and treatment programs;* (b) *HIV–1 testing technology is new to many laboratories; and* (c) *HIV–1 testing practices and applications continue to evolve.*

Unlike proficiency testing programs, the MPEP is not limited to assessing quality in the analytical step, alone. It will also assess quality in the preanalytical and postanalytical steps of the testing process, that is, from the time a test is requested until the clinician who ordered the test takes an action based on the test result.

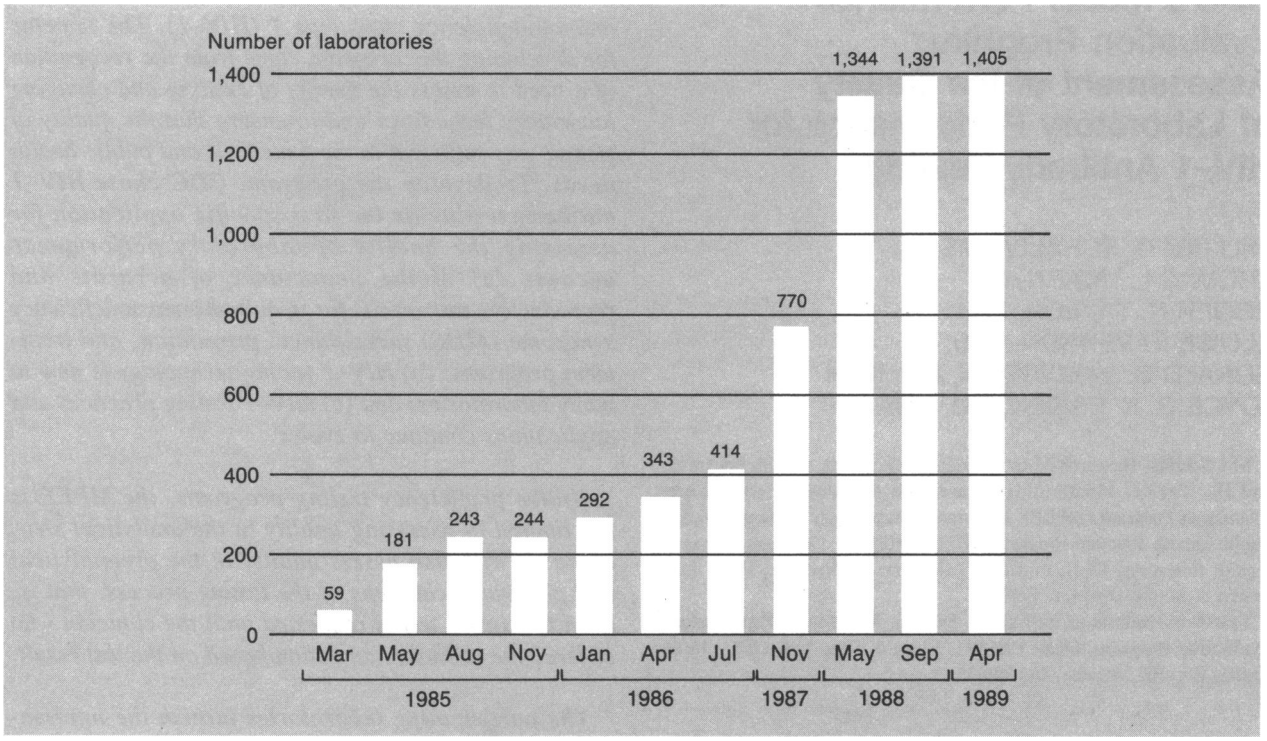
The participating laboratories furnish the information needed for the performance evaluation program by (a) *completing questionnaires designed to describe HIV–1 testing laboratories and their testing practices,* (b) *analyzing specially prepared sample panels for HIV–1 antibody reactivity, and* (c) *reporting results to CDC.*

TO DATE, about 1,400 laboratories that perform human immunodeficiency virus type 1 (HIV–1) testing have voluntarily participated in activities of the Model Performance Evaluation Program (MPEP). Because of the importance of reliable HIV–1 test results to Centers for Disease Control's (CDC) family of HIV seroprevalence surveys, laboratories supporting those surveys are required to participate in the MPEP.

Laboratory testing in general has long played an essential role in medical diagnosis, patient care management, identification of risk factors for disease, and disease surveillance. During the last 20 years, laboratory testing procedures have changed considerably. Substantial technologic improvements have made tests more sensitive and specific today. Testing, which years ago was confined to the clinical laboratory, is now done in physicians' offices, in shopping centers, and at home. Perhaps the greatest change in testing is the greater frequency of tests ordered and the increased demand for a faster turnaround time. Twenty years ago, tests were performed only by specially trained medical technologists; many tests today are performed by technicians, nurses, physicians, and even patients themselves. Many of these changes have prompted the laboratory community and the general public to ask, "What is the quality of testing and test results in terms of their utility, timeliness, and cost?" (Cost includes not only monetary cost but also cost to patient and public health.)

In response to these concerns and because high quality in laboratory testing is a valuable component of disease prevention and surveillance programs, the CDC has developed the MPEP, using testing for antibody directed against HIV–1 as its first application. The goals of the program are (*a*) to develop appropriate methods for defining and evaluating quality in laboratory testing systems (including test selection, sample collection, and reporting and interpreting test results); (*b*) to determine the analytical quality of HIV–1 antibody testing, as currently practiced in private and pub-

Growth of laboratory participation in CDC's performance evaluation surveys for human immunodeficiency virus type 1 testing, March 1985–April 1989



lic health laboratories; (*c*) to evaluate the effect of testing quality on patient and public health (that is, to determine if the test results meet physicians' and public health officials' needs); and (*d*) to develop strategies for identifying and correcting both errors and impediments to achieving high quality.

Relationship of MPEP to HIV–1 Testing

After HIV–1 was recognized as the etiologic agent of AIDS (*1–5*) and with the subsequent licensing of the first enzyme immunoassay (EIA) for detecting HIV–1 antibody in 1985, there was a dramatic increase both in the variety of test kits used for detecting antibody directed against HIV–1 and in the number and types of laboratories that conduct such tests (*6, 7*). Within the United States, HIV–1 antibody testing has presented the health community with many challenges, including the need to develop and implement systems for assuring high quality and reliability of HIV–1 test results. In the absence of clinical disease, physicians and public health officials usually rely on antibody test results to confirm infection by HIV–1. Consequently, reliable HIV–1 antibody test results are essential to the success of surveillance and prevention programs.

The assurance of quality in laboratory testing for HIV–1 antibody depends on the intrinsic quality of the test, actual test performance characteristics, test result interpretations, and appropriate clinical application of the testing information (*7*). Monitoring the quality of laboratory testing over time is important because of the expansion and changes in (*a*) the types of facilities that provide HIV–1 antibody testing (blood banks, State health laboratories, hospital laboratories, independent laboratories); (*b*) the reasons that tests are performed (screening of blood products, diagnosis, surveillance, evaluation of behavioral intervention studies); (*c*) the knowledge about the clinical manifestations of HIV–1 infection; and (*d*) the way HIV–1 tests are performed (enzyme immunoassay (EIA), Western blot (WB), indirect immunofluorescence, dried blood spots, polymerase chain technology, and DNA or RNA probes). However, the expanding role of these test methods and the new technology that will be used for screening or diagnosis require that any testing information be not only accurate and precise but both reliable and consistent over time. Only when these conditions exist will the objectives of the surveillance studies be met.

Description of the Program

In 1985, CDC established the first proficiency testing program for laboratories conducting HIV–1 antibody testing (*6*). In the first such program, CDC mailed 10

Summary of CDC's Model Performance Evaluation Program (MPEP) (human immunodeficiency virus type 1 testing) activities from November 1987 to May 1989

Date	Event	Number of laboratories	Percentage[1]	Comments
November 1987	Sample panel	684	89	One vial each of a positive and negative reference sample mailed to all MPEP-enrolled laboratories
February 1988	Sample panel	144	99	Panel of 22 samples mailed to candidate reference laboratories and laboratories supporting CDC's family of surveys
May 1988	Sample panel	1,249	93	Panel of 22 samples mailed to all MPEP-enrolled laboratories
May 1988	Questionnaire	1,181	88	Questionnaire mailed to all MPEP-enrolled laboratories
September 1988	Sample panel	1,203	90	Panel of 22 samples mailed to all MPEP-enrolled laboratories
October 1988	Questionnaire	1,075	79	Questionnaire mailed to all MPEP-enrolled laboratories
April 1989	Sample panel	1,248	88	Panel of 22 samples mailed to all MPEP-enrolled laboratories

[1]Percentage of laboratories furnishing sample results or completed questionnaires before the final CDC reporting date.

samples (later decreased to 6 samples) that were selected for their positive, weakly positive, and negative antibody activity, which would mimic actual patient specimens. The laboratories were requested to analyze these samples by their usual testing procedures and report their results to CDC. The CDC then compared the laboratories' results with reference laboratories' interpretations for the samples.

Proficiency testing results are a useful indicator of the analytical capability of the laboratory performing the test. In the aggregate, proficiency testing results have been used for tracking changes in testing methods and test performance and for identifying problems in testing. In addition, proficiency testing programs provide information that laboratories use for self-improvement. All these outcomes of the proficiency testing programs are important in assessing and improving testing quality. However, proficiency testing focuses only on the analytical step of the total testing process and provides little information about the preanalytical and postanalytical steps of testing.

The Institute on Critical Issues in Health Laboratory Practice has defined six functional steps in the testing process (*8*). They are (*a*) formulation of the clinical question, (*b*) collection and management of specimens, (*c*) technology and methodology development and transfer, (*d*) analysis of specimens, (*e*) results validation and reporting, and (*f*) results interpretation and application. High quality in laboratory testing can be achieved only if this quality is maintained in each of the six steps of the testing process. From that perspective, CDC implemented the MPEP (HIV–1 testing) in 1986, building from its experience with proficiency testing. The concern of the program is the assessment and improvement of laboratory testing quality throughout the entire testing process.

The objectives for the first phase of the program, from 1986 through 1989, were to (*a*) identify and describe laboratories conducting HIV–1 antibody testing, (*b*) describe their testing practices, (*c*) evaluate their analytical performance, (*d*) develop better methods for evaluating quality of testing, (*e*) identify problems in HIV–1 antibody testing, and (*f*) develop strategies for improving HIV–1 antibody testing. To accomplish these objectives, CDC has requested that HIV–1 antibody testing laboratories voluntarily participate in activities of the model program.

Participants were requested to complete questionnaires designed to describe their laboratories; their HIV–1 test methods and procedures; and their testing process, which includes the purpose of testing (for example, screening, diagnosis, research, organ donation); the sources of specimens; how specimens are treated; and how test results are reported to the clinician. They also are requested to test sample specimens for HIV–1 antibody.

To maintain confidentiality of the data, laboratory-identifying information such as name and address is not linked, at CDC, to the data obtained from either the questionnaires or the sample analyses. For those laboratories experiencing testing difficulties, subsequent followup by CDC occurs before delinkage is initiated. The data do, however, contain unique code numbers that are necessary for trend analyses and for any subsequent studies.

About 1,400 laboratories currently participate in the CDC MPEP (figure). The March 1985 through July 1986 data in the chart represent participants in CDC's HIV–1 proficiency testing program, which preceded the implementation of the current model performance evaluation program. The extent of participation in the MPEP activities, to date, is shown in the table. Approximately 90 percent of all laboratories receiving sample panels or questionnaires voluntarily returned results.

'Accurate and reproducible laboratory test results are essential for surveillance and detection of HIV–1 infection. The purpose of CDC's family of HIV seroprevalence surveys is to monitor levels and trends of HIV–1 infection in sentinel subgroups of the U.S. population.'

(All laboratories supporting the CDC family of seroprevalence surveys are required to participate in the MPEP). Such a high rate of participation suggests strong support for the goal of improving the quality of HIV–1 antibody testing.

Survey Questionnaires

The MPEP questionnaires are designed to create a profile of HIV–1 antibody testing laboratories and their testing practices. Types of information obtained include the number of personnel involved in HIV–1 testing, educational level of the personnel, types of specimens tested, treatment of specimens before testing, specimen storage conditions, testing methods, testing algorithms, manufacturers of kits used in daily HIV–1 testing, WB bands detected, WB interpretative criteria used, number of specimens tested, and the number of specimens that contain HIV–1 antibody as detected by screening and supplemental or confirmatory tests. The resulting profiles will be used to help document and understand changes and trends in HIV–1 testing occurring over time. By correlating the data obtained from the questionnaires with the results of the sample analyses, CDC will look for variables that might be used to independently predict testing quality.

Candidate Reference Laboratories

The performance evaluation component of the program uses a number of laboratories that volunteered to serve as candidate reference laboratories and were selected from the laboratories participating in the program. When the MPEP was first implemented, candidate reference laboratories were selected according to laboratory type (that is, blood bank, State health department, hospital, independent, or other), past testing history (if this information was available), and their willingness to serve as a candidate. Since the MPEP has been implemented, the performance evaluation panels and survey forms have provided the program with more information about each laboratory and, now, candidate reference laboratories are selected according to laboratory type, testing volume, testing practices, and individual capabilities. Candidate reference laboratories are used on a rotating basis to take advantage of their individual capabilities and testing practices.

The candidate reference laboratories serve more than one purpose in the evaluation program. Their primary function is to test all the donor specimen material that will be used to compose the evaluation panels for the participating laboratories. The MPEP is examining the performance of the candidate reference laboratories that test the donor specimen material in order to recognize specific performance patterns. By comparing the results of the participating laboratories with the results from the candidate reference laboratories and from CDC laboratories, the performance of the program laboratories can be examined to determine which ones have performed well and which have performed poorly.

Evaluation Panels

Performance evaluation surveys are conducted by using specially designed panels of sample plasma specimens. Before including the sample specimens in the performance evaluation surveys, CDC and a group of candidate reference laboratories test them to determine the HIV–1 antibody reactivity of each sample. The surveys are not designed as a regulatory proficiency testing mechanism, although individual laboratory participants should find the results beneficial in comparing their own performance with that of other laboratories.

The performance evaluation surveys also serve as a vehicle to evaluate the most suitable sample panel configurations and the limits of testing performance and technology. Each survey panel contains sample specimens with HIV–1 antibody reactivity ranging from negative through weakly positive to strongly positive. In addition, each of the survey panels, to date, contained both single and pooled donor-derived samples. The results obtained from analyzing these samples are used to evaluate the utility of pooled donor samples in performance evaluation surveys.

Several different blinded sample panel configurations have been used in each survey; not all laboratories receive the same samples. In testing the samples, each laboratory is requested to treat the samples the same way that they treat patients' specimens (that is, to use the same testing method, the same manufactured or in-house prepared kit and reagents, and the same testing personnel). The CDC furnishes forms for reporting results, kit or test used, results for any quality control samples analyzed with survey samples, and final interpretation (HIV–1 antibody reactivity) for the survey samples.

Reporting Results to Participants

After each survey, CDC compiles laboratory test results and furnishes aggregate reports to the laboratories. The first report comprises candidate reference laboratory results, grouped by test method. This report is sent to candidate reference and participating laboratories shortly after all test results are received. A subsequent aggregate report includes an analysis of participating laboratory results grouped, for each evaluation sample, by test kit manufacturer, test method, testing algorithm, and WB band patterns. Additionally, laboratory results from the MPEP questionnaires are tabulated and aggregate results are sent to all participants.

Assessing Steps in the Total Testing Process

In order to assess barriers to high quality HIV–1 antibody testing in the preanalytical and postanalytical steps of the testing process, CDC collaborates with the Association of Schools of Public Health, at the San Diego State University, Graduate School of Public Health, to develop systematic analyses for identifying important variables in those steps. The CDC staff and San Diego State University staff are field-testing methods for performance analyses by cataloging events that occur in the total testing process—from the time HIV–1 antibody tests are requested in various settings (for example, public health clinic, hospital, or blood collection facility) through specimen collection, laboratory analyses, and reporting results to the clinician or person who requested the test.

In addition to the types of analyses just mentioned, blind and open proficiency testing are conducted in laboratories serving the facilities from which specimens for HIV–1 antibody tests originate to provide other measurements of quality (for example, analytic accuracy). Also, this testing is done to evaluate differences in testing methods and in formats for reporting HIV–1 antibody test results.

MPEP and CDC's HIV Seroprevalence Surveys

Accurate and reproducible laboratory test results are essential for surveillance and detection of HIV–1 infection. The purpose of CDC's family of HIV seroprevalence surveys is to monitor levels and trends of HIV–1 infection in sentinel subgroups of the U.S. population. The success of the seroprevalence surveys will depend, in large part, on the quality of the laboratory test results (*9*). Consequently, all laboratories conducting HIV–1 testing for the facilities that participate in the family of surveys are required to meet several criteria, including (*a*) participating in the CDC MPEP (HIV–1 testing), (*b*) using Food and Drug Administration-licensed EIA and WB kits, (*c*) retesting samples that are repeatedly reactive by EIA with a licensed supplemental test (WB test), (*d*) adhering precisely to instructions described in the test kit's package inserts, and (*e*) using internal quality control samples. The CDC has an additional study requirement to validate the results obtained by laboratories supporting the family of surveys: that the participating laboratories store all of the patients' specimens, some of which will be retested by another laboratory at a future date. Collectively, these requirements should provide the data necessary for assessing the analytic quality of testing and for identifying problems that could arise in testing.

Fulfilling all of these requirements and following good laboratory practices provide a quality assurance model for the participating laboratories and enhance the standardization of testing necessary to achieve the family of surveys' objectives. Telephone and onsite consultations, if necessary, are conducted with family of surveys' laboratories where there are indications of performance problems.

References

1. Barre-Sinoussi, F., et al.: Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). Science 220: 868–870, May 20, 1983.
2. Gallo, R. C., et al.: Isolation of human T-cell leukemia virus in acquired immune deficiency syndrome (AIDS). Science 220: 865–867, April 19, 1983.
3. Gallo, R. C., et al.: Frequent detection and isolation of cytopathic retrovirus (HTLV–III) from patients with AIDS and at risk for AIDS. Science 224: 500–503, May 4, 1984.
4. Broder, S., and Gallo, R. C.: A pathogenic retrovirus (HTLV–III) linked to AIDS. N Engl J Med 311: 1292–1297, Nov. 15, 1984.
5. Curran, J. W., et al.: Epidemiology of HIV infection and AIDS in the United States. Science 239: 610–616, Feb. 5, 1988.
6. Taylor, R. N., and Przybyszewski, V. A.: Summary of the Centers for Disease Control human immunodeficiency virus (HIV) performance evaluation surveys for 1985 and 1986. Am J Clin Path 89: 1–13, January 1988.
7. Schalla, W. O., Hearn, T. L., Griffin, C.W., and Taylor, R. N.: Role of the Centers for Disease Control in monitoring the quality of laboratory testing for human immunodeficiency virus infection. Clin Microbiol Newsletter 10: 156–159, October 1988.
8. Proceedings of the 1986 Institute on Critical Issues in Health Laboratory Practice: Managing the quality of laboratory test results in a changing health care environment. The Du Pont Company, Wilmington, DE, 1986, pp. 55–67, 99–110, 115–192.
9. Dondero, T. J., Pappaioanou, M., and Curran, J. W.: Monitoring the levels and trends of HIV infection: the Public Health Service's HIV surveillance program. Public Health Rep 103: 213–220, May–June 1988.