Analysis of the June 23, 1997 Performance Evaluation
HIV-1 RNA Determinations (Viral Load) Results
Reported to the Centers for Disease Control and Prevention
by Laboratories Participating in the Model Performance Evaluation Program

This report is an analysis of results reported to the Centers for Disease Control and Prevention (CDC) by laboratories participating in the Model Performance Evaluation Program (MPEP) after they performed viral ribonucleic acid (RNA) determinations on human immunodeficiency virus type 1 (HIV-1) performance evaluation samples shipped to them June 23, 1997. The newly implemented viral load project of the MPEP commenced with this panel shipment and testing results were reported by 148 (89%) of the 167 laboratories who were sent sample panels.

Samples used in the MPEP HIV-1 RNA determinations performance evaluation survey are undiluted, unpooled plasma obtained from individual donors who are HIV-1 infected or non-infected. Before shipment, the CDC tested each donor with at least three test kits which included the viral RNA test kit approved by the Food and Drug Administration (FDA), and two test kits not approved by the FDA and designated for research use only.

The second page following the report title page, Table 1, lists the CDC panels for this shipment, the labeled vials contained in each panel, the CDC donor numbers, the CDC results obtained with each test kit manufacturer, and the CDC interpretation of the results based on the manufacturers' criteria. For all the HIV-1 infected donors, HIV-1 RNA was detected by all the test kits used and the CDC interpretation for these donors was positive for RNA. Conversely, the donors not infected with HIV-1 did not have HIV-1 RNA detected consistent with the criteria contained within the test kit manufacturer's insert. Based upon the lower limits of the test kit sensitivities, these donors were interpreted by CDC as negative for HIV-1 RNA.

Summary of Results

Figure 1 shows the cumulative frequency of test results reported by laboratories for those donors who were HIV-1 infected and had detectable HIV-1 RNA, and for those donors not infected with HIV-1 and in whose donor plasma HIV-1 RNA was not detectable. For the three donor samples (Donor 1, Donor 1 duplicate, and Donor 2) that were infected with HIV-1, 491 (97.8%) of the results detected HIV-1 RNA, while 11 (2.2%) of the results did not detect HIV-1 RNA. Conversely, of the 338 results reported for the two donors not infected with HIV-1, laboratories reported 329 (97.3%) results not detecting HIV-1 RNA, yet 9 (2.7%) reported results detecting HIV-1 RNA.

Types of Laboratories Performing HIV-1 RNA Determinations

The types of laboratories reporting results are shown in Figure 2. Each laboratory type is listed by decreasing frequency. Approximately 50% of the laboratories that reported results are hospital laboratories.

Types of Test Kits Used by Laboratorians

The types of test kits used by laboratories performing viral RNA determinations are shown in Figure 3 and are listed by decreasing frequency. The Roche Amplicor HIV-1 Monitor™ test kit, approved by the FDA, was used by 67% of the laboratories reporting results.

Aggregate Testing Results Reported by Donor

Aggregate testing results, for each donor by test kit, reported by participant laboratories, are shown in Table 2. Since the lower limit sensitivities of the reported test kits ranged from <20 RNA copies/ml to <500 RNA copies/ml, the results are shown for each individual donor by test kit and listed according to the minimum, maximum, and median values reported. Information listed in the results section for each individual donor also includes the HIV-1 infection status of the donor and which panel vials contained the donor material. The first page of Table 2 shows the laboratory test results reported for CDC Donor 1 and the laboratory test results reported for the duplicated sample of Donor 1. For this shipment, Donor 1 was the only sample that was duplicated in each panel providing participant laboratories the opportunity to review their intra-shipment reproducibility for that donor sample.

Please note that in Table 2, the columns under each donor sample provide the number of laboratory results detecting HIV-1 RNA or not detecting viral RNA, followed by the minimum, median, and maximum result value listed for each test kit manufacturer.

In general, laboratories performed well in testing these performance evaluation samples. Most laboratories detected HIV-1 RNA in those samples obtained from donors infected with HIV-1 and in which CDC detected viral RNA. Of the eleven testing results reported by laboratories not detecting viral RNA in these HIV-1 RNA positive samples, 3 incorrect results were reported for Donor 1, 3 were reported for the duplicate sample of Donor 1, and 5 incorrect determinations were reported for Donor 2.

Similarly, most laboratories did not detect viral RNA in samples obtained from donors who were not infected with HIV-1. Of the laboratories detecting viral RNA in these two donor samples, 5 incorrect determinations were reported for Donor 3 with values ranging from 2,000 to 9,787, and 4 incorrect determinations were reported for Donor 4 with values ranging from 500-2,500 RNA copies/ml.

Use of Quality Control Testing Material

Information was collected on the use of quality control (QC) samples in addition to the controls contained in the test kits. Depending on the manufactured test kit used, positive and negative test controls, test standards, or test calibrators are internal kit control samples used to validate a test run and to quantitate HIV-1 RNA copies/ml, and may not validate the analytic testing process which may include testing problems related to pipetting, inadequate incubation conditions, inadequate washing, or variability in kit lot sensitivity. Of the 148 laboratories that reported results, 145 (97%) laboratories provided information on their use of QC samples other than the controls contained in the test kit. Of these, 38 (26%) indicated they used QC samples other than those contained in the test kit. Among these 38 laboratories, 23 (60%) indicated they obtained their QC material from an in house source, 10 (26%) obtained their QC material from a commercial source, 4 (10%) used VQA standards obtained through AIDS Clinical Trial Group (ACTG) participation, and 2 (5%) laboratories did not provide a source for their QC samples. Although various combinations of QC materials were used, e.g., high RNA copies plus a negative control or low RNA copies plus a negative control, 13 (34%) laboratories indicated they used a high RNA copy control, low RNA copy control, and negative control all in combination. Of the 38 laboratories using QC material in addition to that contained in their test kit, 23 (60%) used their QC material with each set of tests and 15 (40%) used QC material only with each new test kit.

Conclusion

The results of this first performance evaluation shipment for HIV-1 RNA determinations showed that most laboratories correctly detected HIV-1 RNA in those samples from donors infected with HIV-1. Only a few laboratories did not detect HIV-1 RNA. Similarly, most laboratories did not detect HIV-1 RNA in the samples from donors not infected with HIV-1 RNA, while only a few laboratories did detect HIV-1 RNA in these donor samples. For the samples from donors infected with HIV-1, the overall analytic sensitivity for the results reported was 97.8%. For the samples from donors not infected with HIV-1, the overall analytic specificity was 97.3%.