

Assumes tests per analyzer: TDM = 2, Chemistry = 15, Hematology = 1, Ligands, Reproduction & Immunology = 5

Assumes reagent cost per test: TDM = \$2.88, Chemistry = \$0.40, Hematology = \$0.90, Ligands = \$3.00, Reproduction = \$2.38, Immunology = \$2.38

Reliability of Estimates

The impact of method verification on any particular laboratory will depend on how many tests are introduced in any given year. The impact will be more on laboratories that are frequently expanding test menus, replacing test methods or test systems rather than those maintaining test menus and test systems. Obviously, any start-up laboratory performing nonwaived testing would be verifying the entire test menu. Nearly two-thirds of the laboratories in the Pacific Northwest Sentinel Network introduced no test systems during the 2-year interval and none introduced more than five (LaBeau, et al, 1999). Therefore, we believe while our estimates may accurately describe the impact on the universe of affected laboratories, for any particular laboratory, we may have underestimated or overestimated the consequences.

Discussions with manufacturers revealed that assistance with method verification is often included in the cost of buying or leasing an instrument or other new test system, regardless of the size of the laboratory. Regardless of whether the manufacturer assists in the verification process, the laboratory or the manufacturer or both will incur costs. What is relevant to the impact is whether the frequency of the method verification will change. Since method verification already frequently occurs in the absence of regulation and manufacturers often provide assistance, our estimate of the total cost of method verification probably overstates the incremental impact of the new requirement. However, we were unable to quantify how frequently method verification is performed currently, thereby preventing us from precisely estimating the incremental change in the frequency of method verification when this regulation becomes effective. Therefore, we may have overstated or understated the number of assays that laboratories will actually do to verify performance.

d. Calibration Verification

Rationale

During the phase-in period, laboratories performing unmodified moderate complexity testing cleared by

the FDA performed testing without meeting the calibration verification requirement. On April 24, 2003, the phase-in period ends, and all laboratories must perform calibration verification at least every 6 months for each quantitative nonwaived test, as appropriate. Calibration verification is done to ensure that the test results are accurate throughout the reportable range of patient results for each test system.

Methodology

To determine the impact, we estimated the number of laboratories these changes will affect, their current menus of quantitative tests for which calibration verification would be applicable, the number of data points needed for verification and the costs in terms of labor, verification materials and reagents.

Number of Laboratories This Change Will Impact

We assumed that this QC change will affect all 29,601 laboratories, since Certificate of Compliance and COLA laboratories perform some moderate complexity testing. In addition, we assumed these laboratories have not been performing calibration verification on commercial, unmodified moderate complexity test systems.

Laboratory Menus of Tests With Verifiable Calibration

Calibration verification is performed for quantitative testing. For this analysis, we focused on multi-test clinical analyzers for which calibration verification materials are commercially available. Specifically, we estimated the fraction of laboratories that have analyzers for performing quantitative tests for chemistry, therapeutic drug monitoring, ligands, reproductive hormone testing, hematology, and immunology. By "ligands" we mean analytes measured by immunoassay, for example carcinoembryonic antigen, cortisol, and folate.

Number of Analytes Per Analyzer

For the purposes of estimating reagent consumption, we estimated the number of analytes being done by multi-test analyzers. We assumed that the variability of laboratory types and sizes would affect the number of different tests being performed; however, we were unable to account for the variability in this model. Because POLs comprise the largest portion of the laboratories that these changes will affect and POLs tend to have relatively limited test menus, we assumed most laboratory menus to be minimal among

those laboratories that these changes will affect.

In order to estimate the number of analytes per laboratory, we analyzed data from three proficiency testing programs that target POLs (Medical Laboratory Evaluation, American Proficiency Institute, and College of American Pathologists' Excel) as a gauge of the numbers of tests offered among those laboratories these changes will affect. From these data, we estimated average test menus of fifteen chemistry analytes, two therapeutic drugs, one hematology analyte, and five for each ligand, immunology, and reproductive testing analyzer. Using this model, the specific number of analytes that must be verified has little impact on the estimates because most of the expense is in the verification kits.

Number of Data Points To Verify Calibration

At a minimum, laboratories must check three points in the reportable range to verify calibration, that is, the low, mid, and high points of the range. Although there is no requirement to perform duplicate testing at each level, it adds information about precision while adding very little to the cost of the procedure. Therefore, we included duplicate testing. We estimated that six data points are the minimum for adequate calibration verification, three concentrations in duplicate. Since calibration verification must be performed at least twice yearly, laboratories must collect a total of at least twelve data points for each analyte every year.

Benefits

We believe that calibration verification can reduce errors in patient testing by periodically providing information on the accuracy of an assay after it is calibrated, after any major maintenance or after problems are detected in routine QC. However, we are not aware of any studies demonstrating the affect of calibration verification on error rates.

Labor Costs

For estimates of labor costs, we assumed that 2 hours per year will be sufficient for each analyte for both performing the assay and inspecting the results for acceptable performance. This estimate may be too low in some instances and too high in others. The cost of the analyst time, \$17.90 per hour, is the 2000 mean wage per hour for a staff medical technologist from Ward-Cook and Tannar (2001). In addition, we assumed that the labor cost of calibration verification per year is the