Teaching and Assessing New Method Verification Skills Using Interactive Simulations

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ABBREVIATIONS: CLIA = Clinical Laboratory Improvement Amendments; CLS = clinical laboratory science; CMS = Centers for Medicare and Medicaid Services; WSU = Weber State University.

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Since the introduction of the Clinical Laboratory Improvement Act of 1988 every laboratory has faced new regulatory compliance challenges including Clinical Laboratory Improvement Amendments/Centers for Medicare and Medicaid Services (CLIA/CMS) pre-use verifications of the manufacturer's performance claims of each new instrument and method used in the laboratory. Skills in planning and conducting such verification studies are among those which should be taught to students preparing for careers as clinical laboratory scientists.

I present a method to teach and assess student skills in planning and conducting a new method verification that is being successfully utilized in my CLS-3314 Advanced Clinical Chemistry course of Weber State University's (WSU) CLS program, both on-campus and online. The method, which does not impact actual patient care or the laboratory workflow or significantly affect program budget, uses an interactive simulation approach in which each and every student has the opportunity to design and direct a customized verification study. In a prerequisite course, the students first define the components of method verification prescribed by the current CLIA/CMS regulations.[2] They learn the requirements for verifying accuracy, precision, analytical measurement range, sensitivity, and that the reference range used is appropriate for the patient population being served. Next, in the Advanced Clinical Chemistry course these verification skills are assessed and enhanced. The course requires that student assume the role of a technical consultant to a laboratory, plan and design each verification experiment, and create explicit written instructions on how each experiment should be conducted.

This simulation follows this concept: "If one can teach someone else to do something, then the teacher has mastered the task" (source unknown). As a former technical consultant to a large reference laboratory who has directed and designed numerous instrument and method verifications, I rarely performed the actual testing. Rather, I developed very detailed experimental designs and assay instructions that allowed others to perform it. After the actual testing had been performed, I evaluated the results of each experiment using appropriate statistical analyses, and then made the appropriate decisions or recommendations regarding the use of the method for patient care. I believe that the most critical method verification skills involve:

- knowing exactly what experimental studies must be done.
- carefully designing each verification experiment.

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- developing explicit written instructions for others to follow.
- evaluating the test data and performing appropriate statistical analyses on that data.
- drawing the appropriate conclusions about each verification experiment.
- documenting the verification process and conclusion as a formal report.

Actually performing the analytical testing is the least significant of all the method verification skills. During this simulation the students follow the critical steps outline above. The students are assigned to serve as a "technical consultant" to some hypothetical laboratory in this simulation exercise. They develop very detailed experimental design instructions that are submitted to a fictitious bench technologist who supposedly actually performs the testing according to those experimental designs. The test results are then returned to the student, who must evaluate the results of each experiment using appropriate statistical methods, and then make appropriate decisions or recommendations regarding the adoption of the method for patient care.

VERIFICATION TOOLS

During the simulation, both the students and the teacher use Microsoft Excel™ and Microsoft Word™ for the simulation.[3] Excel is used for the statistical analysis using the Analysis ToolPak library, and Word is used to generate the experimental designs and assay instructions, method performance summary, and the final validation report. Alternate spreadsheet and word-processing software can be used, as well as specialized tools such as EP Evaluator™ if desired.[4] For simplicity the simulation involves verifying an alternate commercial reagent to be used on a specific analyzer platform for a specific analyte, such as magnesium. In our simulations we use the Roche Cobas Mira S™ platform since these instruments are used in our student laboratories.[5]

PERFORMING THE SIMULATION

In the simulation, a new hypothetical reagent ("NuLab" magnesium reagent, as an example) is being considered for use on the analyzer, and the students are told that it has already been Food and Drug Administration/CMS-approved for use on that analyzer. The students are given the pertinent manufacturer's performance claims for this reagent, and the verification involves documenting that the new reagent meets or exceeds the Food and Drug Administration-approved minimum performance criteria as specified in the manufacturer's package insert. If so, the use of the new reagent can be implemented. If not, adoption of the reagent must be rejected.

The students must develop clear, detailed experimental designs for each validation experiment addressing accuracy (by recovery, calibration verification, and correlation with a reference method), analytical measurement range, within-run and run-to-run precision, minimum detection limit, and reference range (transference of an existing range or a reference range study, if required). The student's instructions are then sent to the fictitious bench technologist. The teacher uses a spreadsheet to generate representative test results for each experiment, based upon each student's experimental design. The raw data (test results) are returned to the student for review. Each student then evaluates the data from each experiment and performs the appropriate statistical analysis. The experimental results from each experiment are then compared to the performance specifications of the reagent manufacturer. At the completion of the simulation, each student must generate and submit a method performance summary sheet (to be an appendix to the method's standard operating procedure), and a final verification report, for use during laboratory inspections to document the entire validation. The final verification report must summarize the experimental design of each experiment and the experimental findings. Each experiment must be included as an attachment to the report, complete with statistical analysis conclusions and charts, when appropriate. The students are instructed to format their spreadsheet printouts so that they are "report quality" in order to earn maximum points.

DISCUSSION

This simulation provides each student with all the challenges of an actual verification study, with the exception that the student does not actually perform analytical testing. This simulation is "interactive" from the standpoint that the faculty must generate raw data in accordance each student's unique experimental design. Unfortunately, there can be considerable variation in acceptable designs among students. Some students may choose to follow Clinical and Laboratory Standards Institute (formerly the National Committee for Laboratory Standards)[6] evaluation protocols, while others may follow alternate protocols. The students are given the charge to perform the verifications under conditions that maximize the efficiency of the verification (minimize reagent and labor costs while maintaining acceptable sample sizes, etc.), and complete sufficient studies so that the verification would ultimately "pass" an actual College of American Pathologists[7] laboratory accreditation inspection. If a student submits an experimental design which is inappropriate or incomplete, the teacher should generate the corresponding data for the student. The teacher should then consult with the student in order to cor-

rect the mistake and provide retraining. Appropriate points may be deducted from the student's project grade under the rationale of "unnecessary reagent/labor costs" at the discretion of the teacher. The written instructions for each experiment must be absolutely clear and complete to the extent that any technologist or technician could follow the instructions and correctly perform all necessary testing, which reinforces the need for developing excellent technical writing skills. If the instructions are not of sufficient quality, the instructions are returned to the student for clarification, and points may be deducted from the student's final project score.

Since there can be a wide variation in experimental designs for each experiment, data sets for several common variations may be created ahead of time (for good designs as well as common substandard designs). For example, for the within-run precision study, several sample size variations might be specified by the students (n = 20, n = 30, n = 40). Additionally, there are several acceptable ways to assess accuracy. With expected variations such as these, the creation of additional data sets ahead of time will allow giving raw data back to the students in a timely manner. If the student's design differs from those already created (forbid the thought), existing data sets may be modified quickly to match the student's experimental design. Our CLS program uses simulations for 16 different analytes which allows every student to have their own "customized" verification project. While this approach requires considerable "up-front" developmental work by the teacher, our program's faculty believes that the quality of the individualized learning process makes the extra effort worthwhile.

Grading each verification experiment is accomplished by the teacher's assessing the appropriateness of each experimental design and performing the statistical analysis and evaluation in tandem with the student. This assesses (1) the student's skills in method verification and (2) the student's correct performance and interpretation of the statistical analyses.

CONCLUSION

The simulation presented is one tool which can be used to teach and assess new method verification skills. In the past our CLS program utilized student verification projects that involved actual assay work using our instrumentation, involved considerable reagent, control, calibrator, and disposable costs, and included the need to acquire large numbers of human serum or plasma specimens from our affiliated hospitals and clinics. After using this interactive verification simulation process, we have found it also to be effective in assessing and documenting CLIA/CMS pre-use verification skills. The costs for the simulation process are minimal since there are no reagent, control, calibrator, or disposable costs, nor is there any need to acquire actual human specimens. Even when done in an actual hospital setting, the simulation process causes no interference with actual patient care, since no "real-time" analyzer use is required. Equally important is the fact that each and every student has the unique opportunity of designing and directing a customized verification study.

My previous work experience in performing new method/instrument validations and verifications in actual hospital laboratories has contributed to the success of this validation simulation at WSU. Faculty interested in using a simulation process such as the one presented are encouraged to network with those in actual clinical laboratories who are conducting ongoing pre-use verifications. Such collaboration can generate a source of verification data and experimental design information from which to develop future simulations for student use.

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