Development of a Coagulation Factor Testing Autoverification Method in a Clinical Reference Lab

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I. Introduction

Coagulation factor testing by a one stage method requires multiple dilutions be assayed and analyzed to produce a single result. Samples producing results on initial dilution falling outside the analytic measurement range (AMR) must be tested at additional dilutions.

The aim of the study was to develop advanced computer algorithms with automated reflex testing rules. Development of the rules would allow laboratories to perform complete coagulation factor analysis utilizing autoverification procedures as outlined in the Clinical Laboratory Standard Institute (CLSI) AUTO-10A guideline (1) and in compliance with the College of American Pathologists (CAP) Hematology Checklist (2).

II. Methods

In fig. 1, a typical calibration curve and multiple dilutions of a hemophilia (or other factor deficient) patient sample are shown, with the concentration of undiluted calibrator defined as 100%. A horizontal line with a y-axis value of 100% reflects the linear regression of the dilution-corrected calibrator activities vs. the corresponding dilution (referred to as predefined Multidilution Management Criteria, MMC). A second parallel line represents the linear regression of the dilution-corrected patient activities vs. their corresponding dilutions.

The presence of a factor inhibitor (either specific or non-specific) in patient samples results in under-recovery of factor levels in clot-based assays (fig. 2). Dilution of the patient sample in the presence of a non-specific inhibitor tends to diminish the extent of inhibition. Non-parallelism causes the slope of the line defined by the dilution-corrected patient activities versus dilution to be different from the slope of a similar line produced the calibrator which is devoid of inhibitor.

Prospective validation of the expert rules was accomplished using 552 different anonymized FVIII deficient plasma samples each tested at 1:10, 1:20, and 1:40 dilutions giving a total of 1,656 individual results on an automated coagulation analyzer using the STA Coag Expert data manager system. All dilutions were performed in an automated fashion on the STA-R Evolution. Reagents used for testing included the STA-PTT A as the aPTT reagent along with the STA-Deficient VIII immunodepleted plasma following automated programming of standard factor VIII testing procedures as supplied by the manufacturer into expert rules format (Diagnostica Stago Inc., Parsippany, NJ).

III. Results

The rules schematic for factor assays programmed into the STA Coag Expert data manager is displayed in fig. 3. Starting from the top left point of the flow chart, where the test is ordered through the laboratory information system (LIS; Factor assay ordered); initial testing at three different dilutions (1:10, 1:20 and 1:40) is performed. The mean of three dilutions is used to determine the next step, followed by subsequent steps as shown.

Fig. 3: Factor Testing Expert Rules Flow Chart Schematic

IV. Conclusion

When properly implemented, expert rules utilizing autoverification procedures can 1) handle the mundane and error prone task of result verification, allowing medical technologists to focus on the true problem samples, 2) improve the consistency in the quality of test results, and 3) reduce staff fatigue, improving the work environment in the process. As a scalable solution, the rules reported here can be utilized in a variety of low to high volume settings. The CET staff estimated that implementation of the expert rules has reduced overall labor expenditure by 2.4%. Given the varied test menu and high workload in the CET, saving labor expenditures by implementation of expert rules for the coagulation factor testing represents a key institutional win, allowing users to concentrate on inconclusive specimens and results which require greater levels of attention. Importantly, the rules are flexible enough to be implemented across a wide variety of instrument/reagent systems.

V. References