

Laboratory Issues in the Management of Anticoagulation Clinics

Point of Care Testing: From the Professional to the Patient Self Tester

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OBJECTIVES

- Select
- Implement
- Troubleshoot



Cost

■ POC-

- Typically more expensive per unit cost, but total cost is less expensive.
- Lab pay or site pay?
 - Reagent rental, purchase, gratis devices w/ lg reagent purchase?

■ PST-

- The burden of cost is on the patient to either pay out of pocket or support with insurance approval.

Instrument Selection

- Go to each vendor website or operator's manual to get instrument specifications.
- Take this information and drop it into an Excel spreadsheet.
- Have the clinic highlight those criteria most important to them and then the POCC should do the same.

PST- instrument selection is at the discretion of the prescribing health care provider. The laboratory should feel comfortable making recommendations for testing devices.

CLIA Certificate

- CLIA Waived?
- CLIA Moderately Complex?

Who's your daddy?

Method Validation-CLIA

CLIA WAIVED

The minimum requirement for waived testing is to follow the manufacturers directions. There are no recommendations for method validation.



MODERATE COMPLEXITY

- Comparison of methods to estimate inaccuracy or bias,
- Replication to estimate imprecision,
- Linearity to determine reportable range
- Verify that the manufacturer's reference intervals (normal values) are appropriate for the laboratory's patient population.

Periodic Validation

“If a laboratory performs the same test using different methodologies or instruments, or performs the same test at multiple sites, the laboratory must have a system that twice a year evaluates and defines the relationship between test results using different methodologies, instruments or testing sites.”

Method Validation-JCAHO

Waived



Moderately Complex

JCAHO recognizes the waived tests as defined by CLIA '88, but requires more than just following manufacturer's directions. JCAHO's waived testing standard WT.1.3, "policies and procedures governing specific testing-related processes are current and readily available," includes equipment performance evaluation.

For JCAHO, it is only necessary to evaluate the method, not all instruments.

QC.1.2-

"before a new test method is used to report patient results, the laboratory must verify that the method will produce accurate results on a consistent and reliable basis...the laboratory at least verifies accuracy, precision, and reportable range for a patient-testing procedure that is an approved, unmodified test of moderate complexity for which the manufacturer has established the performance specifications. The laboratory also ensures that the reference range applies to the specific patient population (s) tested."

JCAHO

- WT.1.10** -- Organization defines use of waived test results in patient care (definitively or only as a screen).
- WT.1.20** -- Organization identifies staff responsible for performing and supervising waived testing.
- WT.1.30** -- Staff performing tests have adequate, specific training and orientation to testing and demonstrate satisfactory levels of competence.
- WT.1.40** -- Approved policies and procedures governing testing processes are current and readily available.
- WT.1.50** -- QC checks, as defined by the organization, are conducted on each procedure.
- WT.1.60** -- Appropriate QC and test records are maintained.

Method Validation- CAP

CAP's philosophy is that all clinical laboratory testing, including even CLIA waived tests, essentially need to meet the requirements defined under Section §493.1253(b)(2) of CLIA '88.

- Procedure manual (§493.1251)
- Test systems, equipment, instruments, reagents, materials, and supplies (§493.1252)
- Establishment and verification of method performance specifications (§493.1253)
- Equipment maintenance and function checks (§493.1254)
- Calibration and calibration verification procedures (§493.1255)
- Control procedures (§493.1256)
- Specialty and subspecialty requirements (§493.1261-1278)
- Comparison of test results (§493.1281)
- Corrective actions (§493.1282)
- Test records (§493.1283)
- Analytic systems assessment (§493.1289)



CAP

Does the system for validating and revalidating the analytical specifications for each procedure include:

- Calibration and recalibration?
- Quality Control?
- External validation- PT program?
- Inter-instrument comparability assessment (for each analyte)?
- Analytical Measurement Range determination?
- Clinically Reportable Range determination?
- Interference Assessment?
- The ID of the employee who performed the analysis?

“THE” Correlation Study

The correlation should encompass 20 + data points that cover the range of the instrument. (e.g. INR 1-7).

➤ Linear Regression

- **Slope** describes the angle of the line that provides the best fit. A perfect slope would be 1.0. Deviations from 1.0 are proportional systematic errors.
- The **y intercept** describes where the “line of best fit” intersects with the y-axis. Ideally, the y intercept should be 0.0. Deviations from 0.0 are an indication of constant systematic error.
- The **correlation coefficient** describes how well the results between the two methods change together. An r of 1.00 indicates perfect correlation. The lower the r value, the more scatter in the data. What is acceptable to your institution?
- Comparison Plot (i.e. Bland Altman) should be used to display the data from the comparison of methods.
 - Constant bias- data points on one side of the line of best fit. What do you do?
 - Proportional bias- data points evenly distributed around the line of best fit.

INR

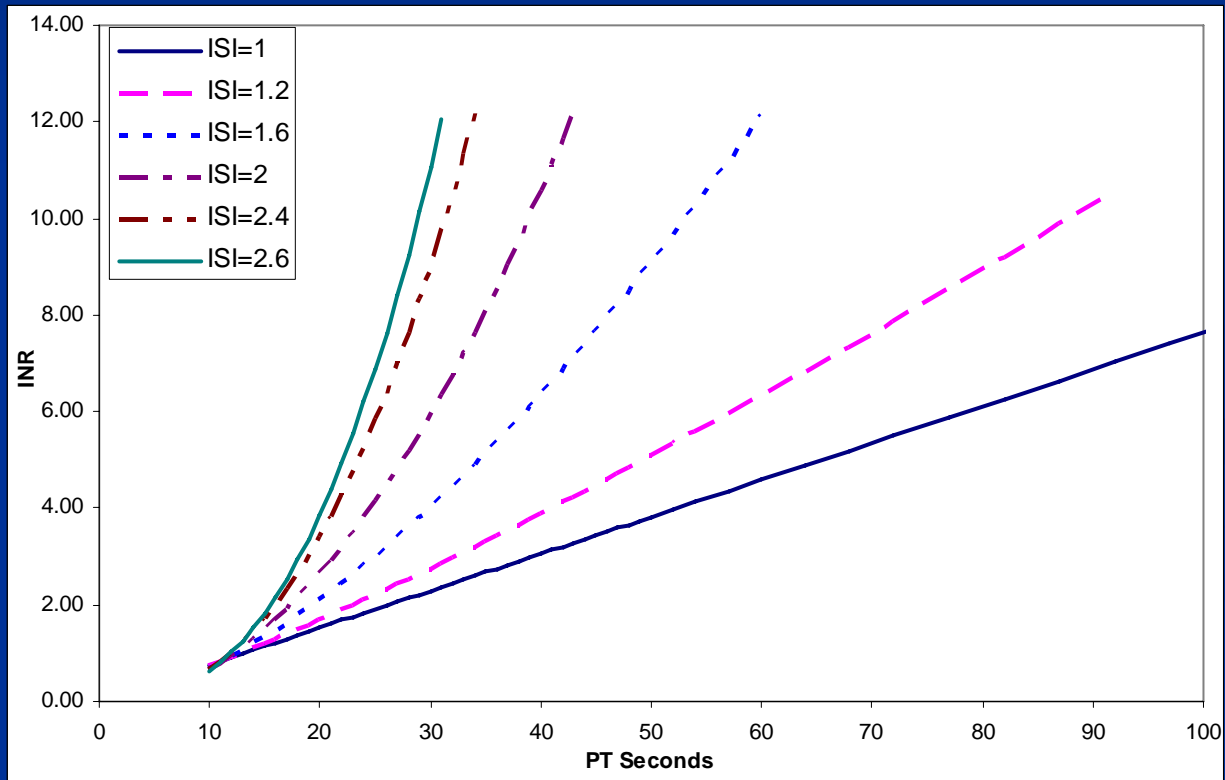
- International Normalized Ratio (INR)
 - ISI -> International Sensitivity Index
 - INR target ranges are specified by patient populations
 - DVT, Afib, Atrial MHV: INR= 2.0 - 3.0
 - Mitral mechanical heart valve: INR= 2.5 – 3.5
 - Individual variation

$$INR = \left(\frac{PT_{patient}}{PT_{meannormal}} \right)^{ISI}$$

Thromboplastin

- Thromboplastin reagents are used to monitor oral anticoagulant therapy with vitamin K antagonists for patients with thromboembolic disorders. Currently, three thromboplastins are available:
 - a recombinant human thromboplastin;
 - a native IS of rabbit and
 - a native IS of bovine origin.
- The contribution of the thromboplastin international sensitivity index (ISI) to the interlaboratory coefficient of variation (CV) of the international normalised ratio (INR) with individual reagents was assessed. The precision of the INR should increase with lower ISI values. *Journal of Clinical Pathology* 1989;42:92-96

Effect of ISI on INR



Implementation

1. Make at least one person responsible for the POC process.
2. Provide a notebook with SOP, QC logs, reagent logs, package inserts, POCC business card, etc.
3. Ensure QC program understanding with proper documentation
4. Organize a maintenance program and provide logs
5. Ensure method of result recording and documentation retention
6. Order Proficiency Testing material (when available)

KEY TO SUCCESS STARTS HERE:

TRAINING

Training

Training of individuals should include the following:

- Theory of the instrument
- Specimen collection and application
- Instrument calibration
- Quality Control principles and procedures
- Patient Testing
- Instrument Maintenance
- Troubleshooting

Training

■ Sources of Training

- POCC taught in service.
- Manufacturer's on-site training (Sales Rep. or Technical Specialist).
- Manufacturer's web based training modules.
- Train the Trainer (POCC-> MA -> Nurse -> Provider)
- PST-Patients phone trained/live in service by nurse

■ Content of Training

- Direct Observation Competency
- Knowledge Based Competency

Training

■ Direct Observation

- Patient Preparation
- Specimen Collection
- Specimen Application
- Testing
- Recording/reporting of results
- QC Testing
- Instrument maintenance
- Testing assessment through:
 - Internal blind samples, PT

■ Knowledge Based

- Theory of instrument
- Storage Requirements
- QC Requirements
- Troubleshooting

Process Improvement Initiative- Competency should be adjusted periodically to account for observed errors, FAQ and package insert changes.

Procedure

- Purpose
- Clinical Significance
- Forms and Records
- Specimen Collection
- Equipment and Materials
- Calibration
- QC
- Steps in the Patient Testing
- Calculations
- Reporting of Results
- Procedure Notes
- Limitations

Including a section on troubleshooting/error codes can be very insightful to clinic personnel. This can be copy/pasted from the manufacturer operator's manual.

Quality Control

The manufacturer should develop system-specific QC recommendations that are consistent with the robustness and stability of the test system, its intended use, and with the device's process controls and available QC modalities.

NACCLS (CLSI) H49-A

Quality Control Options

- Internal Control (on board)
- External Control (liquid)
- Equivalent Quality Control (EQC)



Maintenance

- Follow manufacturer recommendations.
 - Cleaning
 - Temperature verification
 - Battery Replacement/charging

Connectivity

Connectivity can be achieved many ways:

- RALS (mod complex devices)
- Telcor (mod complex devices)
- Standing Stone-CoagClinic (all devices)
- QAS PPM (all devices)

Some of the above software connect to the LIS/HIS and some require manual entry.

“GUILTY UNTIL
PROVEN INNOCENT”

Troubleshooting

1. Pre-analytical Error

- Hand warm?
- Lancing performed correctly?
- No over manipulation of the collection site?
- One, large drop of blood collected?

2. Medication interference

- Bridging Therapy (Heparin/LMWH)
 - Many PT/INR measurement systems (both lab and POC) are sensitive to Heparin and LMWH to varying degrees.

3. Disease interference

- Antiphospholipid antibodies

POC versus Laboratory

■ Point of Care

- Whole Blood
- No Added Anticoagulant
- No Dilution
- No Preanalytical Delay

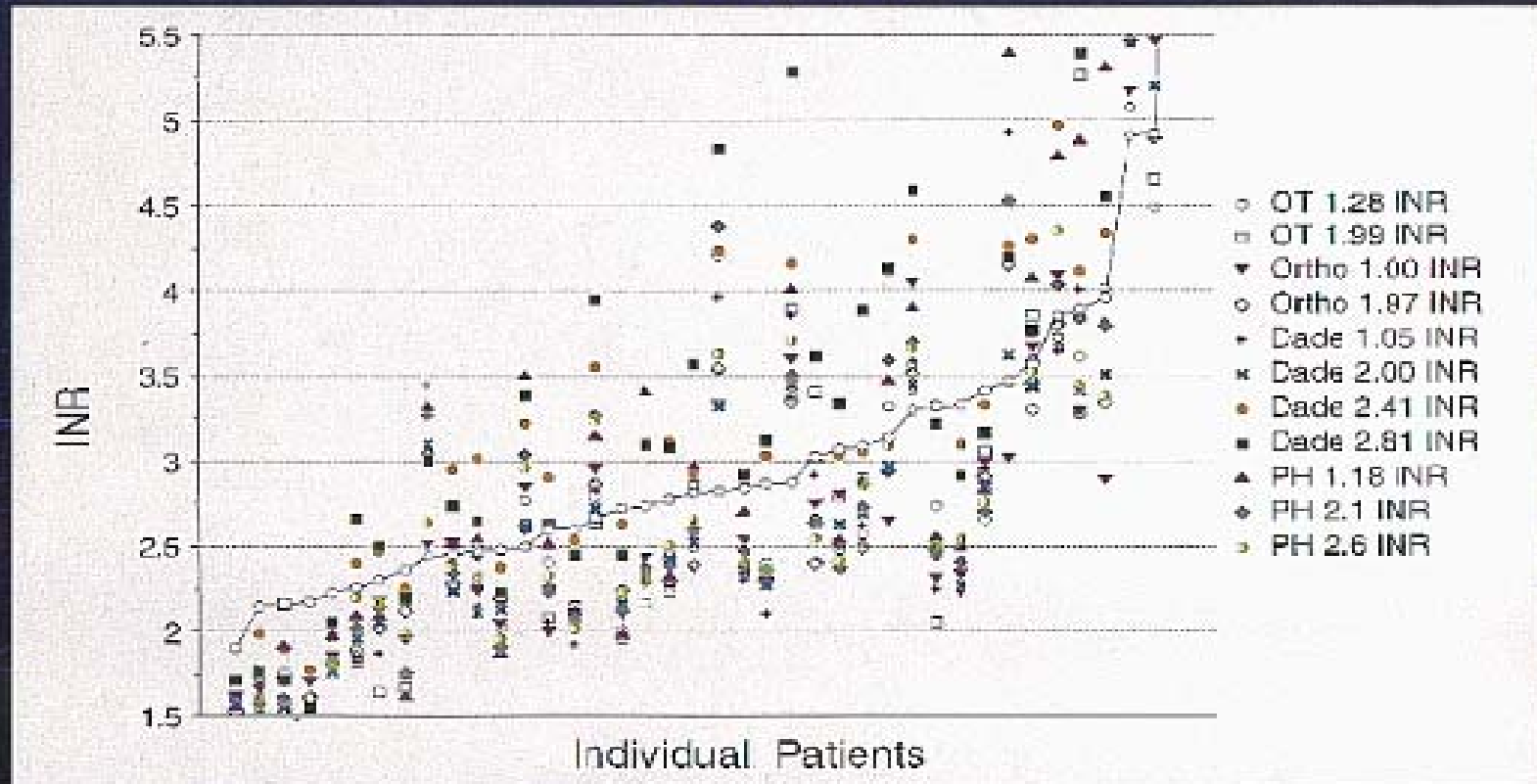
- Reagent
- Instrument
- Clot detection

■ Standard Laboratory

- Platelet Poor Plasma
- Sodium Citrate Anticoagulant
- 1:9 Dilution
- Variable Preanalytical Delay

Variability of INR across Laboratory Systems

Results



Differences observed between POC and lab are similar to those seen lab to lab.

POC versus Laboratory

Anderson's Criteria states that agreement is achieved if any one of these three clinically relevant conditions is met:

- both measurements are within the patient's therapeutic range;
- both measurements are either above or both below that range; and
- that the measurements are within 0.4 units of each other.

Anderson D, Harrison L, Hirsch J. Evaluation of a portable Prothrombin Time monitor for home use by patients who require long-term oral anticoagulant therapy. Arch Intern Med. 1993;153:1441-1447.

Bottom line

- Repeat any patient result not consistent with patient clinical presentation and history. If POC repeats and concern still exists, send to the laboratory for confirmation.
- When the result is above the “cut off”, then the result **SHOULD** be verified by the laboratory.

Case Studies

Patient Self Testing

“Physicians in charge will be able to cope with the increasing numbers of patients on oral anticoagulants. Laboratory workers now engaged in such huge routine may be available for other tasks. Health services may save considerable amount of economic resources now spent in the management of patients on oral anticoagulants. Patients themselves may benefit by spending less time to attend overcrowded waiting rooms.

"Control of Oral Anticoagulant Therapy with Whole Blood Prothrombin Time Devices: the Future Has Begun." Tripodi, Armando *Thrombosis and Haemostasis* Vol. 84 (2000): 362-363

Patient Self Testing

Not all patients requiring oral anticoagulant therapy are candidates for PST.

➤ Patient Selection:

- Adequate understanding
- Physical/mental ability to perform test
- Willingness to perform test
- Willingness to comply with requirements for SOP, QC and maintenance and communicating results to health care provider
- History of compliance with medical recommendations
- Adequate insurance coverage or willingness and ability for self pay.

Patient Self Testing

- Training- more comprehensive than a professional.
 - Basic disease and anticoagulation information
 - Blood collection technique
 - Performance of POCT
 - Data management and communication of the result to the health care provider.
 - Communicate to the physician office (call, email, fax)
 - Telemedicine (QAS, Raytel, etc.)

Patient Self Testing

Lab Issues:

- Correlation (different devices) ?
 - Meter choice (provider prescribed)?
 - Reagent storage?
 - QC, Calibration?
 - Maintenance?
- Documenting of result (is it a lab result)?
- Patient training and competency assessment?
- No payment!

Conclusions

POC is a key part of an A/C clinic. Collaboration between the clinic and laboratory is essential for successful patient care and compliance.

PST is expanding. The laboratory needs to understand the process and work with the clinic to ascertain the best program for patient training and support of the devices.

Q & A

Thank you!

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