

CLIA Corner

State Hygienic Laboratory at The University of Iowa

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Iowa CLIA Surveyors:

Nancy Grove, BS, MT(ASCP)

Kristine Rotzoll, BS, MT(ASCP)

Melinda Bochmann, BA, MT(AMT)



In This Issue of the CLIA Corner we address:

• CLIA Updates for Prothrombin Time & INR Testing

Can you believe it's been over ten years since we published the *CLIA Corner* on prothrombin times and INR testing (Third Quarter 2006)? With the CLIA Interpretative Guidelines revisions in January 2016, it's definitely "prothrombin" time for an update.

Although there are other oral anticoagulant drugs on the market, warfarin (i.e. Coumadin) is still the most commonly used one. The proper therapeutic dosage is vital to the health and well-being of the patient. Administering too little may not prevent blood clotting, while administering too much could cause excessive bleeding.

The prothrombin Time (PT) is the test that measures how long it takes for a patient's blood specimen to clot. PT test methods vary from point-of-care devices to automated instrumentation. Automated coagulation test systems sample the plasma, combine the plasma with the reagents, detect an end point or clot formation, and display the test results without operator intervention. The International Sensitivity Index (ISI) is the correction factor for variable sensitivities of thromboplastins (PT reagent).

Most laboratories report the PT test results as the International Normalized Ratio or INR. The INR is a calculation primarily used for monitoring a patient's oral anticoagulant therapy. The INR corrects for the variability in PT results attributable to the ISI. Therefore, this allows all PT's to be corrected to an international standard.

The laboratory must meet any and all regulatory requirements and comply with the manufacturer's requirements when performing PT and INR

testing. Laboratories should also comply with the manufacturer's recommendations for testing. These include, but are not limited to:

- Handling reagents, materials, and supplies;
- Adhering to conditions for storage and testing; and
- Performing equipment maintenance and function checks

Compliance is critical to ensure accurate and reliable test results.

TEST REQUESTS-STANDING ORDERS

Many patients who are on oral anticoagulant therapy have standing orders from their physician for the PT/INR testing. The laboratory must have a policy regarding standing orders which defines the frequency these orders need to be reviewed and renewed by the ordering physician.

SPECIMEN COLLECTION AND PROCESSING

As with any laboratory test, it all begins with the specimen. The laboratory must follow the manufacturer's instructions and good laboratory practices and procedures for the collection and processing of whatever type of specimen is required.

For devices that use a capillary whole blood sample, following the manufacturer's collection guidelines is extremely important. Most of these devices operate without external quality controls, so if you do not collect the specimen properly, it is likely the test results will be erroneous or inaccurate. This means the patient's anticoagulant dosage could be determined by

inaccurate results, thus potentially causing harm to the patient.

For instruments that use a plasma sample, the laboratory must review the operator's manual and package inserts to determine the correct procedures for specimen collection and processing. The laboratory must establish the optimal speed and time for each centrifuge used to process coagulation specimens. Generally, the recommended centrifugation speed and time is 1500g for 15 minutes at room temperature or for a speed and time that produces platelet-poor plasma. Platelet-poor plasma is defined as plasma with a platelet count of less than 10,000/ μ L. Once the speed and time is determined, the laboratory must perform a periodic check to ensure an acceptable specimen is achieved.

PROCEDURES

Review your laboratory's procedures for performing coagulation testing, including specimen collection, labeling, storage, preservation, handling, and rejection criteria. If your laboratory is using the operator's manual and/or package insert as its procedure, anything pertinent to your laboratory that is not included in the operator's manual (i.e. specific control and calibration testing, reporting patient results, corrective action for unacceptable controls or calibrations, etc) must also be included in a procedure. All procedures, including operator's manuals and package inserts, must be approved, signed, and dated by the current laboratory director.

Equipment Maintenance and Function Checks

- Follow and document all manufacturer requirements for equipment maintenance and function checks.
- For maintenance and function checks not defined by the manufacturer, the laboratory must establish protocols and frequency of checks.
- Monitor and document temperatures where necessary: equipment, reagent refrigerator, room temperature, etc.
- Check and document centrifuge speed and timers as well as other timers.

Controls

For all *non-waived, non-manual* coagulation test systems, the lab must include two levels of control materials each eight (8) hours of operation and each time a reagent is changed. For *waived* devices, follow the manufacturer's instructions for control testing.

Calibration and Calibration Verification

Follow the manufacturer's calibration guidelines for your test system. If calibration is required, the laboratory may also be required to perform calibration verification procedures. *CLIA does not require calibration verification for test systems which include instruments that cannot be adjusted or calibrated because they are factory or manufacturer calibrated (e.g. unit use devices). This would include prothrombin time procedures on a fibrometer, or instruments that utilize a whole blood specimen and single unit use cartridge (PT/INR, Activated Clotting Time).*

The remainder of this issue pertains to the non-waived automated coagulation test systems.

PT Testing and INR Calculations

The following CLIA regulations and interpretative guidelines contain specifics for PT/INR coagulation testing (refer to Appendix C-Survey Procedures and Interpretative Guidelines for Laboratories and Laboratory Services at https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/App-C_Survey-Procedures-IGs-for-Labs-Labs-Svcs-Final.pdf):

D5411 - §493.1252 Standard: *Test systems, equipment, instruments, reagents, materials, and supplies;*

(a) *Test systems must be selected by the laboratory. The testing must be performed following the manufacturer's instructions and in a manner that provides test results within the laboratory's stated performance specifications for each test system as determined under §493.1253.*

D5545 - §493.1269 Standard: *Hematology*

(b) *For all non-manual coagulation test systems, the laboratory must include two levels of control material each 8 hours of operation and each time a reagent is changed.*

INR Calculation: The INR is equal to the ratio of

the patient's PT (in seconds) to the laboratory's established normal mean PT (in seconds), then raised to the power of the ISI.

$INR = (\text{Patient PT} \div \text{Mean Normal Range PT}) \text{ ISI}$

NOTE: A scientific calculator is needed to calculate the INR.

Example:

Patient PT (in seconds) = 18.5
Normal mean PT (in seconds) = 12.9
ISI value (obtain from the package insert of the laboratory's current lot of thromboplastin reagent) = 2.002

$$18.5 \div 12.9 = 1.434 \text{ (Patient Ratio)}$$
$$1.434^{2.002} = 2.056 \text{ (INR Result)}$$

Report the INR as: INR = 2.1

For **International Normalized Ratio (INR) calculations**, the laboratory must perform the following:

- **Establish a normal patient PT mean with each new thromboplastin lot number.**
Establishing a new normal patient PT mean is important because the value is used to calculate the INR results. The laboratory collects specimens from a minimum of 20 normal individuals (check the manufacturer's guidelines for the specific criteria and exclusions for the "normal" pool of individuals) and performs a PT using the new lot of thromboplastin reagent. Using these results, the laboratory calculates an average PT, thus establishing a new normal patient PT mean. Check the manufacturer's guidelines for exceptions to this. Each laboratory must establish its own normal patient mean with each lot of reagent even if the same equipment and lot numbers of reagent are used in multiple laboratory locations.
- **Verify that the normal patient PT mean study has been performed according to the manufacturer's instructions.**
- **Incorporate the current and pertinent normal patient PT mean and ISI value for each lot of thromboplastin (manual, instrument, or LIS).**
When the new lot of thromboplastin is placed into use, the newly established normal PT mean and ISI value for the lot number are programmed

into the coagulation analyzer or laboratory information system, whichever system is used to calculate the INR result. Each new lot number of PT reagent is assigned a specific ISI value based on the manufacturer and model of coagulation analyzer, so it is the laboratory's responsibility to use the correct value.

- **Document the manual check of the INR calculation for each new lot number.**

A manual check of the INR calculation can be accomplished by using a scientific calculator or the chart provided with the thromboplastin reagent package insert. If the manual calculation does not match the one from the instrument or LIS, then double check to make sure the correct normal patient mean and ISI value is programmed into the analyzer or LIS system. *Select an abnormal low or abnormal high prothrombin time result and verify the calculation.*

- **Document each thromboplastin lot number, with the normal patient PT mean and the ISI value provided by the manufacturer (manual or instrument).**
Check out our updated sample worksheet – this could be your laboratory's means of completing this requirement. (This is NOT a CMS/CLIA sanctioned form.)
- **Periodically verify, for each thromboplastin lot number in use, the correct normal patient PT mean and the International Sensitivity Index (ISI) value are being used for calculating the INR value.**
Verify that the ISI used in the calculation correlates with the ISI specified in the reagent package insert. *It is up to the laboratory to determine the frequency for performing these periodic checks.*
- **Periodically verify the accuracy of the INR calculation (manual, instrument or LIS).**

Again, it is up to the laboratory to determine the frequency for performing these periodic checks.

In summary, the importance of ensuring compliance with the CLIA regulations and good laboratory practices throughout the entire testing process cannot be stressed enough for not only PT/INR testing, but for all laboratory testing. The overall quality of patient care greatly benefits when the laboratory produces accurate and reliable test results.

New Lot of PT Reagent Worksheet

Date: _____

Reagent: _____ Lot #: _____ Exp Date: _____

Establishing Normal Patient Mean

Review manufacturer's instructions for normal patient selection.

<u>Normal Patient Mean PT</u> <u>results</u>					<u>New Patient Mean</u> <u>Value</u>
1	5	9	13	17	
2	6	10	14	18	
3	7	11	15	19	
4	8	12	16	20	

New ISI value: _____

Date normal patient mean and ISI programmed into analyzer/LIS: _____

***Manual INR Check:**

Select normal and abnormal (high and low) patient

Date	Patient's Name or Accession Number	Automated INR Result	Manual INR Result

Platelet Poor Plasma Check

Spin down 5 Sodium Citrate (blue top) tubes and verify platelet count <10,000/ μ L

Date	Platelet Count				
	1	2	3	4	5

Periodic Checks – Verifying PT Reagents

To be performed every six months until reagent expiration or new reagent is implemented.

Date	Verified correct Normal PT mean and ISI	Verification of INR value Patient's Name or Accession Number	Automated INR Result	Manual INR Result

Laboratory director or designee signature: _____

Date reviewed: _____

*INR = (Patient PT \div Normal Patient Mean PT) ^{ISI}