

# CLIA Corner

The University of Iowa Hygienic Laboratory

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## In This Issue...

### Prothrombin Time & INR Testing

Did you know that there are over two million Americans who are currently on oral anticoagulant (Coumadin) therapy? For each of these patients, the Prothrombin Time (PT) and/or International Normalized Ratio (INR) are the laboratory test(s) performed to monitor the medication dosage. Once the patient's PT/INR values are within the therapeutic range; the patients are usually monitored with PT/INR testing every three-six weeks. That equals more 26 million PT/INR results being reported out each year, and this only includes patients being monitored on oral anticoagulant therapy!

This edition of the CLIA Corner will focus on PT and INR testing, including the steps your laboratory must take in order to be in compliance with the CLIA regulations.

*NOTE: For single-use devices (e.g. Roche Diagnostics CoaguChek, ITC ProTime Microcoagulation System, etc.), the laboratory should refer to the manufacturer's instructions for specimen and quality control requirements.*

**Specimen Collection:** Obtaining reliable and accurate PT and INR results starts with good specimen collection. PT/INR samples should be drawn in a sodium citrate anticoagulant tube, with the blood to anticoagulant volume being 9:1. Follow the manufacturer's recommendations for obtaining the correct volume of whole blood in the sodium citrate tube. Other specimen collection factors that will lead to erroneous results include clotted and hemolyzed specimens. Be sure to stress the importance of good sample collection to your facility's phlebotomists.

**Specimen Processing:** Once an acceptable specimen has been collected, it is important that the specimen be processed correctly to ensure accurate PT/INR results. The laboratory should review the operator's manual for the coagulation analyzer and the reagent package insert to determine the optimal speed and time to process specimens. The Clinical Laboratory Standards Institute (CLSI) recommends centrifuging specimens at 1500g for 15 minutes at room temperature or for a speed and time that produces platelet poor plasma. CLSI defines platelet poor plasma as plasma with a platelet count of less than 10,000/ $\mu$ L. In order to determine if the plasma is indeed platelet poor, the laboratory should centrifuge the specimen for a given amount of time and then run the plasma portion of the sample through the hematology analyzer to determine the platelet count. If the platelet count is higher than 10,000/ $\mu$ L, the sample should be centrifuged for a longer period of time. Once the laboratory establishes the optimum time and speed to process the specimen, a periodic check should be performed from time to time to ensure that the platelet count is still acceptable.

*With each new lot number of PT reagent, there are certain CLIA requirements that must be met. These requirements include: establishing a new normal patient mean, programming the correct ISI (International Sensitivity Index) into the coagulation analyzer; comparisons between the new and old lot numbers of PT reagent, and documenting the manual check of the INR calculation.*

**Establishing a new normal patient mean:** Establishing a new normal patient mean is important because the value is used to calculate INR results. To establish the new normal patient mean, the laboratory collects specimens from 20 normal patients and performs a Prothrombin Time (PT) using the new lot of thromboplastin reagent. Using these results, the laboratory calculates an average PT, thus establishing a new normal patient mean. The newly established patient normal mean should then be programmed into the laboratory's coagulation analyzer or

laboratory information system, whichever system is used to calculate INR results. Please note that certain substances such as: alcohol, antibiotics, aspirin, oral contraceptives, and Vitamin K are known to interfere with Prothrombin Time results. Do not select patients taking any of these substances for your pool to establish the new normal patient mean.

**Programming the correct ISI into the coagulation analyzer:** The ISI value is also used in calculating INR results. Therefore, in order to provide accurate and reliable results it is important that the correct ISI value be programmed into the laboratory's coagulation analyzer. Each new lot number of PT reagent is assigned a specific ISI value based on the manufacturer and model of coagulation analyzer. If an ISI value has not been assigned to the laboratory's coagulation analyzer, the laboratory will need to contact the manufacturer to determine which ISI value to use.

**Comparisons between the new and old lot numbers of PT reagent:** The laboratory should draw patients with PT/INR results within the therapeutic range and abnormal patients in order to perform comparison studies. This is done to verify the consistency of the new PT reagent. After analyzing the data, if it appears that the PT/INR results are running higher or lower with the new reagent, it may be necessary to inform physicians of the change in reagent and the effects on patient PT/INR results.

**Documenting the manual check of the INR calculation:** A manual check of the INR calculation should to be performed with each new lot number of PT reagent and periodically thereafter. The INR calculation is as follows:  $INR = (Patient\ PT / Mean\ Normal\ Range\ PT)^{ISI}$

**Worksheet:** A worksheet is provided with this issue for the laboratory to document the testing results when switching to a new lot of PT reagent. (Please note that this is NOT a CMS/CLIA sanctioned form.)

### **Miscellaneous information:**

***Policies and Procedures:*** Review your laboratory's policies and procedures for performing coagulation testing. Verify that the specimen collection policy is up to date including specimen labeling, storage, preservation, processing, and rejection criteria. If the laboratory is using the coagulation analyzer operator's manual as the procedure it must be signed by the laboratory director. The operator's guide must include specific quality control policies, calibration policies, and the laboratory's system for entering patient results. If the operator's guide does not contain all of the necessary information, it is the laboratory's responsibility to include this information in their procedures.

***Quality Control:*** The CLIA regulations state, "For all non manual coagulation test systems, the lab must include two levels of control material each 8 hours of operation and each time a reagent is changed."

***Calibration and Calibration verification:*** Remember to follow the manufacturer's calibration guidelines for your coagulation analyzer. If a calibration is required for your coagulation analyzer, then the laboratory must also perform calibration verification procedures in order to be in compliance with the CLIA regulations.

***Test Requests-Standing Orders:*** Many patients who are on oral anticoagulant or Coumadin therapy have standing orders from their physicians for Prothrombin Time/INR testing. The laboratory should have a written policy clearly defining the use of standing orders, describing which tests may be covered by standing orders and at what intervals standing orders should be reconfirmed with the physician.

### **References:**

1. Clinical Laboratory Institute Standards (CLSI); H21-A4, *Collection, Transport, and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays*; Approved Guideline-Fourth Edition.
2. Clinical Laboratory Institute Standards (CLSI); H47-A, *One-Stage Prothrombin Time (PT) Test and Activated Partial Thromboplastin Time (APTT) Test*; Approved Edition.
3. Centers for Medicare & Medicaid Services; *Appendix C – Survey Procedures & Interpretative Guidelines for Laboratories & Laboratory Services*; January 12, 2004.

A special thanks to Jeanne Eitzmann, MT(ASCP), Laboratory Manager, Shenandoah Medical Center, Shenandoah, Iowa, for sharing her "New Lot of PT Reagent Worksheet".

# New Lot of PT Reagent Worksheet

Date(s) of Testing: \_\_\_\_\_ Date of Initial Use: \_\_\_\_\_

Reagent: \_\_\_\_\_ Lot #: \_\_\_\_\_ Expiration Date: \_\_\_\_\_

New ISI Value: \_\_\_\_\_ Date ISI Programmed in Analyzer: \_\_\_\_\_ Tech: \_\_\_\_\_

## Establishment of Normal Patient Mean w/New Reagent Lot

<u>Normal Patient PT Results</u>					<u>New Patient Mean:</u>
1	5	9	13	17	Analyzer Programmed: _____  Date / Tech: _____
2	6	10	14	18	
3	7	11	15	19	
4	8	12	16	20	

## Comparison of Patients' PT/INR Results

<u>Patients in Therapeutic PT/INR Range</u>				<u>Patients w/Abnormal PT/INR Results</u>			
Old Lot Reagent		New Lot Reagent		Old Lot Reagent		New Lot Reagent	
PT	INR	PT	INR	PT	INR	PT	INR
1				1			
2				2			
3				3			
4				4			
5				5			

## Crossover Quality Control (QC) PT Study w/Old & New Reagent Lots

<u>Control Level 1 Range:</u>				<u>Control Level 2 Range:</u>			
Old Lot	New Lot	Old Lot	New Lot	Old Lot	New Lot	Old Lot	New Lot
1		6		1		6	
2		7		2		7	
3		8		3		8	
4		9		4		9	
5		10		5		10	

### Manual INR Check

INR = (Patient PT/Mean Normal Range PT)<sup>ISI</sup>

Patient ID #	Analyzer Results	Manual Calculation
1		
2		
3		

### Platelet Poor Plasma Check

Centrifuge RPM/Time: \_\_\_\_\_

Platelet Count (less than 10,000)
1
2
3
4
5

Supervisor's Review: \_\_\_\_\_ Date: \_\_\_\_\_