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Area	Laboratory-Hematology
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Coagulation New Reagent Lot Number Rollover

Document Type: Procedure

I. PURPOSE AND OBJECTIVE:

Currently, all 11 hospitals are on the same instrument platform (ACL TOP) and they all have transitioned to the same lot number of Prothrombin (PT) and Activated Partial Thromboplastin Time (APTT). This procedure will establish the protocol utilizing five representative hospitals (RYO, TRY, FMH, WYN, and DBN) to standardize the new reagent lot rollover.

II. ACRONYMS:

A. Abnormal Control 3 (ABN 3)
B. Activated Partial Thromboplastin Time (aPTT)
C. Disseminated Intravascular Coagulation (DIC)
D. Dilute Russell's viper venom time confirm (dRVVT C)
E. Dilute Russell's viper venom time screen (dRVVT S)
F. Fibrinogen QFA (QFA)
G. Information Technology (IT)
H. International Normalized Ratio (INR)
I. International Sensitivity Index (ISI)
J. Laboratory Information System (LIS)
K. Laboratory Test Directory (LTD)
L. Low Fibrinogen Control (Low Fib)
M. Normal Control 1 (Normal 1)

N. Prothrombin Time (PT)

O. RecombiPlastin 2G (RP2G)

P. Royal Oak (RYO)

Q. Troy (TRY)

R. Farmington Hills (FMH)

S. Wayne (WYN)

T. Dearborn (DBN)

III. ESTABLISH A HEPARIN THERAPEUTIC RANGE:

A. **For RYO Only:**

1. Obtain two lot numbers of aPTT reagents from the manufacturer to perform the cumulative summation study (see steps 2-4). Once complete, the coagulation medical director will select the preferable lot number to send to each of the five representative hospitals.
2. Obtain 15 -20 patient samples as described in Section B below.
3. One cumulative summation document will be prepared to send to all hospitals. The 15 - 20 frozen samples will be used for Ex-vivo studies if the cumulative summation study fails or is deemed inadequate.
4. Plot the comparison data obtained with the current lot of aPTT reagent on the x-axis and the data obtained with the new lot of aPTT reagent on the y-axis.
5. Determine the mean and standard deviation for the current and new aPTT reagent lot.
6. The difference between the means and standard deviations is recorded for future reference.
7. Prepare a cumulative summation of differences.
   NOTE: See CAP Survey 2007 CG2 Participant Summary.
8. Within one month run the anti-Xa test on the frozen samples (if needed).

B. **For 5 hospitals (RYO, TRY, FMH, WYN, and DBN):**

1. **Please review the screening criteria for Heparin patients-each sites:**
   a. On continuous infusion of unfractionated heparin.
   b. INR <1.3.
   c. Only received a one-time dose of warfarin.
   d. Not receiving anticoagulant in the past 48 hours.
   e. Not receiving concomitant hormone therapy and not pregnant.
   f. Do not save hemolyzed samples.
2. Utilizing the list of patients obtained daily from the pharmacy, run a PT and aPTT on 15-20 patients at each of the five representative hospitals using a current lot of PT/aPTT reagent and a new lot number of aPTT reagent.

3. Double-spin the specimen before saving the aliquot. Save plasma on 10-15 heparin patients after the ordered test is completed and print the patient's result ***(preferably within one hour or ASAP).***
4. **Please use only the approved aliquot tubes (Screwcap tube, 5 ml, 75 x 13 mm, round base, polypropylene).**
5. Place samples in the -70 freezer and compile all patient results for transcription into the electronic file.
6. Complete all columns in the Heparin Sample Worksheet (this document will be sent every year by the coagulation supervisor) by typing and sending the electronic document to RYO by email.
7. Once all samples have been completed and are frozen, send them to RYO.

C. **For the other locations (Canton, Grosse Pointe, Lenox, Livonia, Taylor, and Trenton)**

1. Reconstitute each vial of the calibrator according to the package insert
2. Prepare the mixtures at the end of 30 minutes of reconstitutions:

Test	Run Heparin Calibrators Per Mixtures Below
Heparinized APTT Samples	0.0 Heparin Calibrator
	300µL 0.0 Calibrator + 100µL 0.8 Calibrator
	200µL 0.0 Calibrator + 200µL 0.8 Calibrator
	0.8 Heparin Calibrator
	200µL 0.0 Calibrator + 200µL 2.0 Calibrator

3. Perform all testing within 30 minutes. Run samples as soon as the mixtures are made up and in the extended mode to avoid further delay in actual testing times between analyzers. Time is critical so you will not have degrading heparin in the mixtures.
4. Run samples on the fresh current lot & new lot on the reference analyzer
5. Move the new lot to the other IL ACL TOP and repeat testing on the same samples.
6. Complete all columns in the worksheet (this document will be sent every year by the coagulation supervisor) by typing and sending the electronic document to RYO by email.

IV. ISI (ALL SITES):

A. Enter the ISI value provided on the package insert of the RP2G from the Material List window.

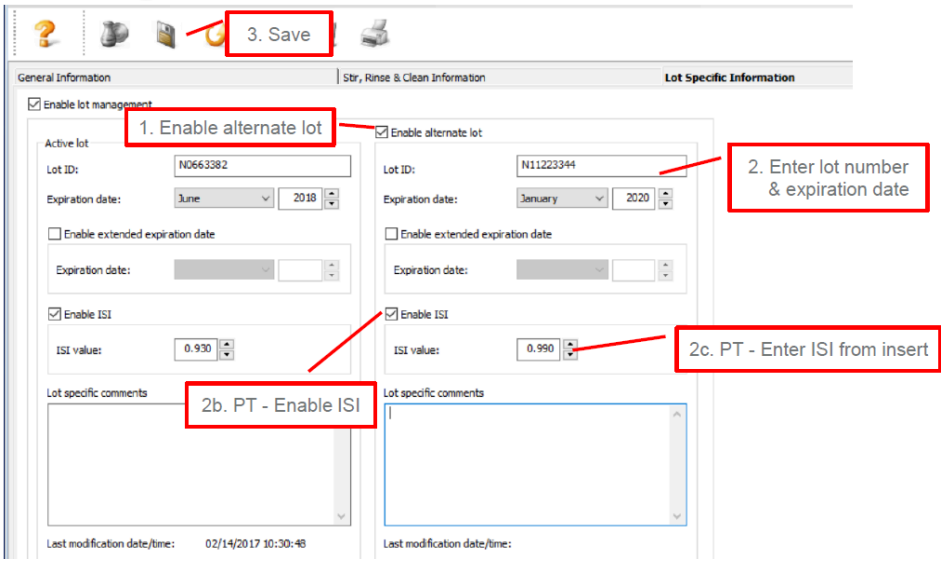
B. The ISI is specific to each lot number and describes the reagent's sensitivity and the geometric mean used to calculate the INR.

C. It is imperative to enter the geometric mean (established from the normal patient population studies) when the new lot is activated.

V. PROCEDURE:

A. **All Sites:**

1. **Program for new lots:** Program all ACL TOP analyzers for new lots of the following:
    a. Reagents: APTT, PT, QFA (if applicable), and DDHS 500 (may be performed at a different time than the system rollover. IL does not allow annual sequestration of DDHS 500).
    b. Controls: Normal 1, ABN 3, Low Fib (if applicable), and DDHS 500.
    c. Calibrators: HemosIL Calibrator Plasma (if applicable).
2. **How to program for a new lot:**
    a. Remove all materials (reagents, quality controls, and calibrators) from the analyzer.
    b. Choose **Setup> Materials List.**
    c. Choose the **Lot Specific Information tab** > **Enable Lot Management** > **Alternate Lot** button.
    d. Enter the lot number and expiration date for each reagent and control and select the **Save** icon to store the information.
    e. Enter the control ranges established by IL and reflected on the package insert for each quality control (QC) material while gathering data to determine your site-specific QC ranges
    f. Enter HemosIL Calibrator Plasma lot numbers and expiration dates.
    g. Select the **Save** icon to store the information. Once the lot number is saved, the **Assigned Values** icon becomes available to enter the calibrator target value.
    h. Enter the calibrator value from Calibrator Plasma and DDHS 500 package insert, and Choose **OK.**
    i. Choose the **Previous Screen** icon to exit.



3. **Prepare Standard Curve:** Always start with **fresh Factor Diluent**, verify all maintenance is up to date, and perform the Enhance Clean for all Probes **with fresh Clean B** before calibration.

a. **Prepare a standard curve for the new lot of QFA (if applicable):**

i. Load the QFA Thrombin, Calibration Plasma, Diluted Clean B, and Factor Diluent onto the ACL TOP.

ii. Select **Calibration> Status List**.

iii. Double-click on the QFA Thrombin test code to open the **Calibration Details** screen.

iv. Choose the **Run** icon.

v. Select **OK** at the "Do you confirm the operation?" prompt.

vi. Choose the **Previous Screen** icon to return to the **Calibration Status List.**

vii. Verify the Job Status for the QFA. Notice that the QFA low test code now says **Active**.

4. **Reviewing the Calibration:**

a. Once the calibration is complete, review the calibration results. The calibration must be validated before usage for calculating results.

i. Verify the **Calibration Status List** is displayed or choose **Menu Bar, Calibration, Status List**.

ii. Double-click on the QFA and QFA low test code to open the Calibration Details.

iii. Choose the **Calibration Information** tab to verify that no errors or warnings occurred during the calibration. Errors will be posted within the Calibration Information tab.

iv. If the calibration is acceptable, choose the Validate icon to validate the calibration curve. The lettering of the calibration tab will change to blue.

b. **Troubleshooting failed calibrations:**

i. If any Data Reduction (DR) rules fail the calibration will also fail and "Failed" will be posted in the Job.

ii. Using the calibration curve tab review the data for outliers by checking the CV and replicate values. Omit a random outlier if needed.
Note: If more than one replicate is an outlier, you may have a precision issue. If this happens, start with steps iii & iv below and then recalibrate.

iii. Always start with fresh Factor diluent.

iv. Verify all maintenance is up to date. Consider performing the Enhanced Clean for All Probes with fresh Clean B before calibrating

5. **Establish New Control Ranges**:

a. Using the new lot number of reagents, run the new lot numbers of controls for several days utilizing several operators.

i. For the PT and APTT: Run 20 points for the new control levels on

each IL ACL TOP(s) analyzer.

ii. For QFA (If applicable): Run 20 points for level 1 and Low Fib.

iii. For Thrombin Time: Run 20 points for the new control level 1 and low abnormal assay on all core lab routine coagulation analyzers. **(RYO Only)**

b. At least 20 data points must be run before establishing a new control range. Once 20 points have been run the new quality control (QC) range can be established utilizing the data obtained.

i. To determine the mean and SD for each specific QC filter the data to include all the points and select the target icon from the toolbar to set the mean and SD

6. **Perform Patient Correlation Studies: Use the reference (primary) analyzer:**

a. **PT and aPTT (All Sites)**:

i. Run a minimum of 20 patient correlations. Run 10 normal patients and 10 abnormal patients using both the current and new lot of reagents.

b. **QFA (Except Canton,Taylor, Livonia and Lenox):**

i. Run a minimum of 10 patient correlations. Run 5 normal patients and 5 abnormal patients using both the current and new lot of fibrinogen reagent.

c. **Thrombin Time: (RYO Only):**

i. Run a minimum of 10 patient correlations. Use 5 normal patients and 5 abnormal patients using the current and new lot of reagents.

7. **Verify Reference Ranges (All Sites):**

a. Verify reference ranges for the PT, aPTT, and QFA (if applicable). Draw at least 20 (Canton, Lenox, Livonia, Taylor, and Trenton may draw 10 at each site) normal donors with a mixture of females and males. Avoid using donors that are on anticoagulants. (**See Attachment B**)
NOTE: PATIENTS MUST NOT BE USED FOR THE STUDY ONLY NORMAL DONORS.

b. Run the normal donors on the primary analyzer for the current and the new lot of reagents, and run the normal donors on the rest of the analyzers and alternate methods if available only for the new lot of reagents.

c. Verify that the blood donors fill out a form listing any anticoagulant medications taken in the last 7 to 10 days. (**See Attachment B**)

d. Combine all site data for reference ranges.

e. Protime geometric mean is to be calculated for all sites.

B. **(RYO Only):**

1. **Perform Factor Sensitivities Individually for All Factors Tested for in Our Laboratory:**

a. Load the Precision Biologic reference plasma in a 2 mL cup in the sample

rack.

b. Load the factor-deficient plasma in the diluent rack in lane D1 or D2 and assign it as Factor Sensitivity Diluent.

c. Enter the reference plasma factor value specific to the factor you are testing, converted to a % (refer to the package insert for directions on conversion if needed), into the Calibrator Target Value field on the Calibration screen. (Setup>Test List>Select your test>Calibration>Automatic Dilution)

d. Select Calibration, Status List.

e. Double-click on the **INFacSen/ExFacSen** test code to open the Calibration details screen.

f. Choose the **Run** icon

g. Select **OK** at the "Do you confirm the operation?" prompt.

h. Choose the Previous Screen icon to return to the Calibration Status List.

2. **Start4 Analyzer:**

a. Prepare a standard curve for the new QFA reagent. Refer to STart4 Quantitative Fibrinogen procedure.

b. Run new controls over several days utilizing several operators. Run 20 data points for each level of QC Normal1, and ABN 3 for the PT and PTT tests.

c. Run 20 data points Normal 1, and Low Fib for the QFA test.

d. Run 20 normal donors for the PT test to establish the geometric mean.

VI. NEW LOT OF dRVVT SCREEN AND dRVVT CONFIRM - RYO ONLY:

A. For each new lot of dRVVT S and C, normal ranges should be determined; collect 20 normal donor samples.

B. Determine the mean of each normal range in seconds.

C. The mean of each normal range will be used as the constant denominator in the calculations of the ratio.

1. **dRVVT Screen:**

a. The patient sample result in seconds is divided by the Mean of the dRVVT S normal range

$$\textbf{dRVVT Screen Ratio} = \frac{\textbf{Patient dRVVT Screen results (in seconds)}}{\textbf{Mean of dRVVT Screen normal Range (in seconds)}}$$

2. **dRVVT Confirm:**

a. The patient sample result in seconds is divided by the mean of the dRVVT C normal range

$$\textbf{dRVVT Confirm Ratio} = \frac{\textbf{Patient dRVVT Confirm results (in seconds)}}{\textbf{Mean of dRVVT Confirm Normal Range (in seconds)}}$$

3. **Normalized dRVVT Ratio:** The ratio results from the dRVVT S is divided by the ratio result from dRVVT C.
    a. **Normalized dRVVT Ratio= $\frac{\text{dRVVT Screen Ratio}}{\text{dRVVT Confirm Ratio}}$**

VII. BEFORE THE GO-LIVE DATE:

A. **LIS:**
1. Submit an Information Technology (IT) ticket to update reference ranges for the PT, aPTT, QFA, and Thrombin time (if needed).
2. Submit an IT ticket to update the auto-verification run for the INR.
3. Submit an IT ticket to update the Heparin Therapeutic Range (if needed).
4. Submit an IT ticket to update the dRVVT reference ranges (if needed).

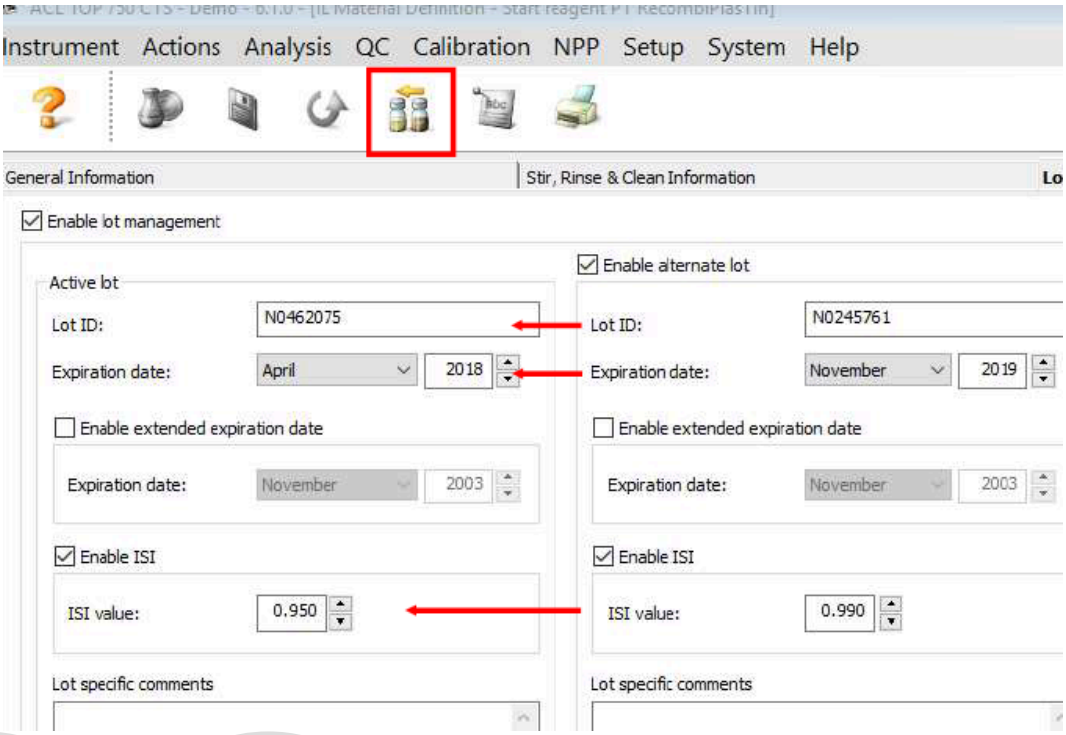
B. **LTD**:
1. Update LTD and procedures.

C. **Bulletin**
1. Prepare a "Laboratory Bulletin" for distribution.

VIII. ROLLOVER DAY:

NOTE: Print all alternate QC files before activating any Alternate Lots as the data will be gone and irretrievable once activation occurs.

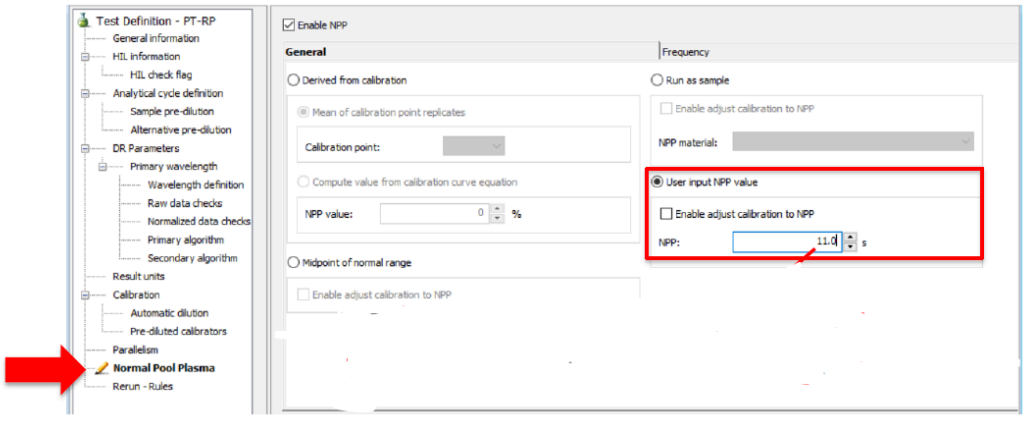
A. **Activate Alternate Lot (All Sites):**
1. Remove all materials (reagents, quality controls, and calibrators) from the analyzer.
2. Choose **Setup> Material List>** double click on each reagent and control material.
3. Choose **Activate** and **Save**



4. **(RYO ONLY)**
    a. **Update reflex list for dRVVT Screen if needed**
    b. Choose **Setup> Test List>** double click on the dRVVT S/C test, and choose **Normal Pool Plasma** value to change the mean for both dRVVT S and dRVVT C.

B. **Enter Geometric Mean (All Sites) :**

1. Choose **Setup> Test List>** double click on PT test, and choose **Normal Pool Plasma** value.

2. 

C. **Start4 Analyzer (RYO Only):**

1. Post the new QC ranges.
2. Program the Start4 with the new fibrinogen reagent lot numbers and calibration. Refer to

the Fibrinogen Start4 procedure for information on how to enter the new reagent lot numbers and calibration.

3. Enter the PT reagent lot numbers, geometric mean, and ISI value. Verify that there is a witness present.
    a. Enter PT reagent lot numbers, geometric mean, and ISI value.
    b. Select calibration by pressing the [2} key and confirm with [ENT].
    c. Next, select others by pressing the [8] key and confirm with [Ent].
    d. Select Mode 1 by pressing the [1] key.
    e. Press any key.
    f. In the next display, enter the reagent lot number confirmed with [ENT].
    g. The Next display asks for Reference times as T1 and T2.
    h. Enter the geometric mean for T1 and T2 and confirm with the [ENT].
4. Enter the ISI value from the Main Menu.
    a. Select Test Parameters by pressing the [3] key and confirm with [ENT].
    b. Select others by pressing the [8] key and confirm with the [ENT].
    c. Select Mode 1 by pressing the [1] key.
    d. Press the enter key until the cursor is under the Select the Unit.
    e. Select the Unit Sec-INR by pressing the [3] key and validate with the [ENT].
    f. Enter the ISI value of the RecombiPlatin 2G reagent lot number.
5. Run test patients and check the PT INR calculations.

D. On the New Lot# of RecombiPlastin 2G Witness Form, document the change of the prothrombin time normal mean and ISI value (see an example in **Attachment A).**

Attachments

Attachment A- New Lot Of RecombiPlastin 2G.pdf

Coagulation New Reagent Lot Number Rollover – Attachment B.pdf

Approval Signatures

Step Description	Approver	Date
	Ann Marie Blenc: System Med Dir, Hematopath	10/30/2024

	Jeremy Powers: Chief, Pathology	10/30/2024
	Masood Siddiqui: Staff Pathologist	10/29/2024
	Hassan Kanaan: OUWB Clinical Faculty	10/29/2024
	Muhammad Arshad: Chief, Pathology	10/29/2024
	Ryan Johnson: OUWB Clinical Faculty	10/29/2024
	John Pui: Chief, Pathology	10/29/2024
Coagulation Medical Director Designee	Marc Smith: System Med Dir, Coagulation	10/29/2024
Policy and Forms Steering Committee Approval (if needed)	Tamara Sabih: Medical Technologist Lead	10/28/2024
	Udayasree Bartley: Medical Technologist Lead	10/24/2024
	Helga Groat: Supv, Laboratory	10/18/2024
	Jennifer Yaker: Mgr, Laboratory	10/10/2024
	Kristen DiCicco: Mgr, Laboratory	10/10/2024
	Katherine Persinger: Mgr, Laboratory	10/10/2024
	Ashley Beesley: Mgr, Laboratory	10/9/2024
	Sharon Cole: Mgr, Laboratory	10/9/2024
	Megan Masakowski: Mgr, Division Laboratory	10/9/2024
	Tamara Sabih: Medical Technologist Lead	10/8/2024

Applicability

Dearborn, Farmington Hills, Grosse Pointe, Royal Oak, Taylor, Trenton, Troy, Wayne