PROCEDURE
Corewell Health East - Coagulation New Reagent Lot Number Rollover

This Procedure is Applicable to the following Corewell Health sites:
Corewell Health Beaumont Grosse Pointe Hospital, Corewell Health Beaumont Troy Hospital, Corewell Health Dearborn Hospital, Corewell Health Farmington Hills Hospital, Corewell Health Taylor Hospital, Corewell Health Trenton Hospital, Corewell Health Wayne Hospital, Corewell Health William Beaumont University Hospital (Royal Oak)

Applicability Limited to: N/A

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Effective Date: 09/04/2025

Functional Area: Clinical Operations, Laboratory

Lab Department Area: Lab - Coagulation

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1. **Principle**
   Currently, all 11 Corewell Health East hospitals are on the same instrument platform (ACL TOP) and have transitioned to the same lot number of Prothrombin Time (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.

2. **Responsibility**
   Personnel who have completed the competency requirements will perform this testing.

3. **Definitions**
   A. Abnormal Control 3 (ABN 3)
   B. Activated Partial Thromboplastin Time (APTT)
   C. Dearborn (DBN)
   D. D-Dimer HS 500 (DDHS 500)
   E. Dilute Russell's viper venom time confirm (dRVVT C)
   F. Dilute Russell's viper venom time screen (dRVVT S)
   G. Disseminated Intravascular Coagulation (DIC)
   H. Farmington Hills (FMH)
   I. Fibrinogen QFA (QFA)
   J. Information Technology (IT)
   K. International Normalized Ratio (INR)
   L. International Sensitivity Index (ISI)
   M. Laboratory Information System (LIS)
   N. Laboratory Test Directory (LTD)
   O. Low Fibrinogen Control (Low Fib)
   P. Normal Control 1 (Normal 1)
   Q. Prothrombin Time (PT)
   R. RecombiPlastin 2G (RP2G)

S. Royal Oak (RYO)
T. Troy (TRY)
U. Wayne (WYN)

4. Reagents:
A. Abnormal Control 3 (ABN 3)
B. Calcium Chloride
C. Clean B
D. D-Dimer HS 500
E. Diluted Clean B
F. Factor Diluent
G. Fibrinogen (QFA)
H. HemosIL Calibrator Plasma
I. Heparin Calibrators
J. Low Fibrinogen Control (Low Fib)
K. Normal Control 1 (Normal 1)
L. RecombiPlastin 2G (RP2G)
M. Synthasil

5. Procedure
A. **ESTABLISH A HEPARIN THERAPEUTIC RANGE**
1. **For RYO Only:**
a. Obtain two lot numbers of APTT reagents from the manufacturer to perform the cumulative summation study (see steps b-d). Once complete, the coagulation medical director will select the preferable lot number to send to each of the five representative hospitals.
b. Obtain 15 -20 patient samples as described in Section 2 below.
c. 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.
d. 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.
e. Determine the mean for the current and new APTT reagent lot.
f. The difference between the means is recorded for future reference.
g. Prepare a cumulative summation of differences.
h. Within one month run the anti-Xa test on the frozen samples (if needed).
2. **For 5 hospitals (RYO, TRY, FMH, WYN, and DBN): Samples will be screened by the pharmacy.**
a. **Please review the criteria for the heparin samples:**
1) INR <1.3.
2) APTT <200 seconds
3) Do not save hemolyzed samples.
b. 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.
c. Double-spin the specimen before saving the aliquot. Save plasma from 15-20 heparin patients after the ordered test is completed and print the patient's results within one hour of collection.
NOTE: The importance of adequate hard spin of the sample is essential to avoid any release of PF4, which is a heparin inhibitor that leads to an under-estimation of the heparin level in tested samples.
d. **Only the approved aliquot tubes should be used to prepare specimen aliquots (Screwcap tube, 5 ml, 75 x 13 mm, round base, polypropylene).**

e. Place samples in the -20 or lower freezer and compile all patient results for transcription into the electronic file.
f. 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.
g. Once all samples have been completed and are frozen, send them to RYO.

3. **For the other locations (Canton, Grosse Pointe, Lenox, Livonia, Taylor, and Trenton)**
   a. Reconstitute each vial of the Heparin calibrator according to the package insert
   b. Prepare the mixtures at the end of 30 minutes of reconstitutions:

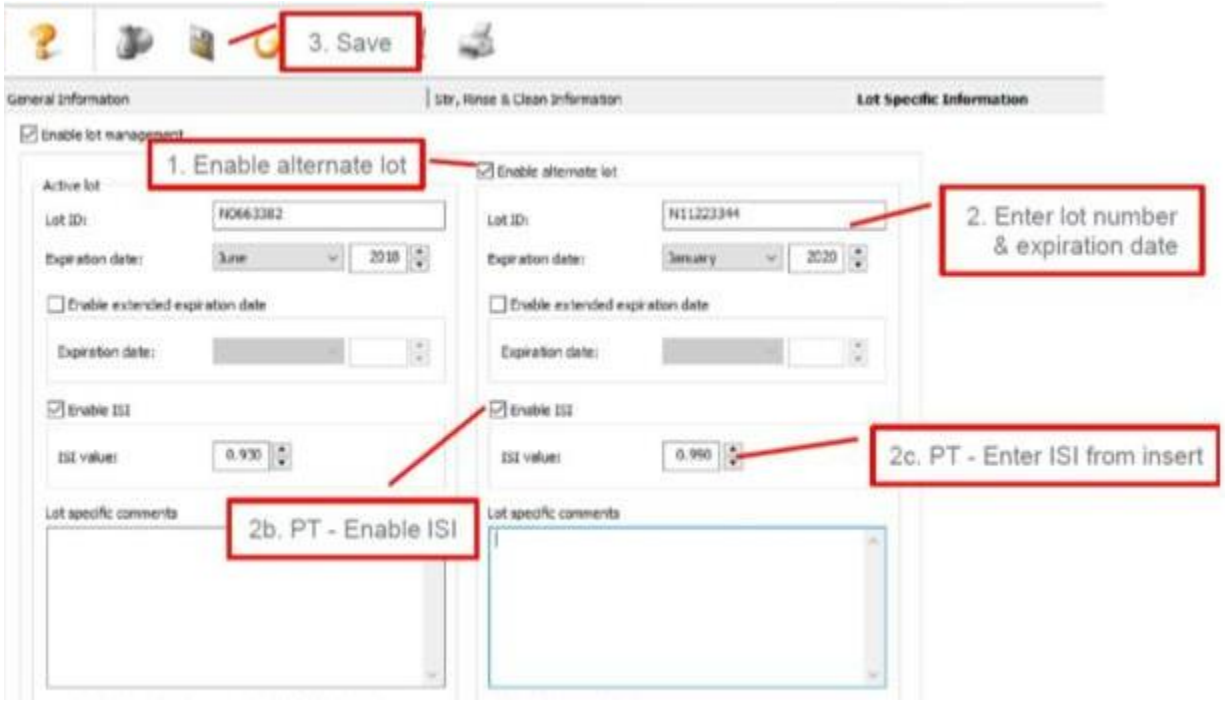
Test	Run Heparin Calibrator per Dilution Below
Heparinized APTT Samples	0.0 Heparin Calibrator
	300 µL 0.0 + 100 µL 0.8 calibrator
	200 µL 0.0 + 200 µL 0.8 calibrator
	0.8 Heparin Calibrator
	200 µL 0.00 + 200 µL 2.0 calibrator

   c. Perform all testing within 30 minutes. Run samples as soon as the dilutions are prepared and in the extended mode to avoid further delay in actual testing times between analyzers.
   NOTE: This step is time sensitive to help prevent heparin degradation.
   d. Run samples on the fresh current lot & new lot on the reference analyzer.
   e. Move the new lot to the other ACL TOP and repeat testing on the same samples.
   f. 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.

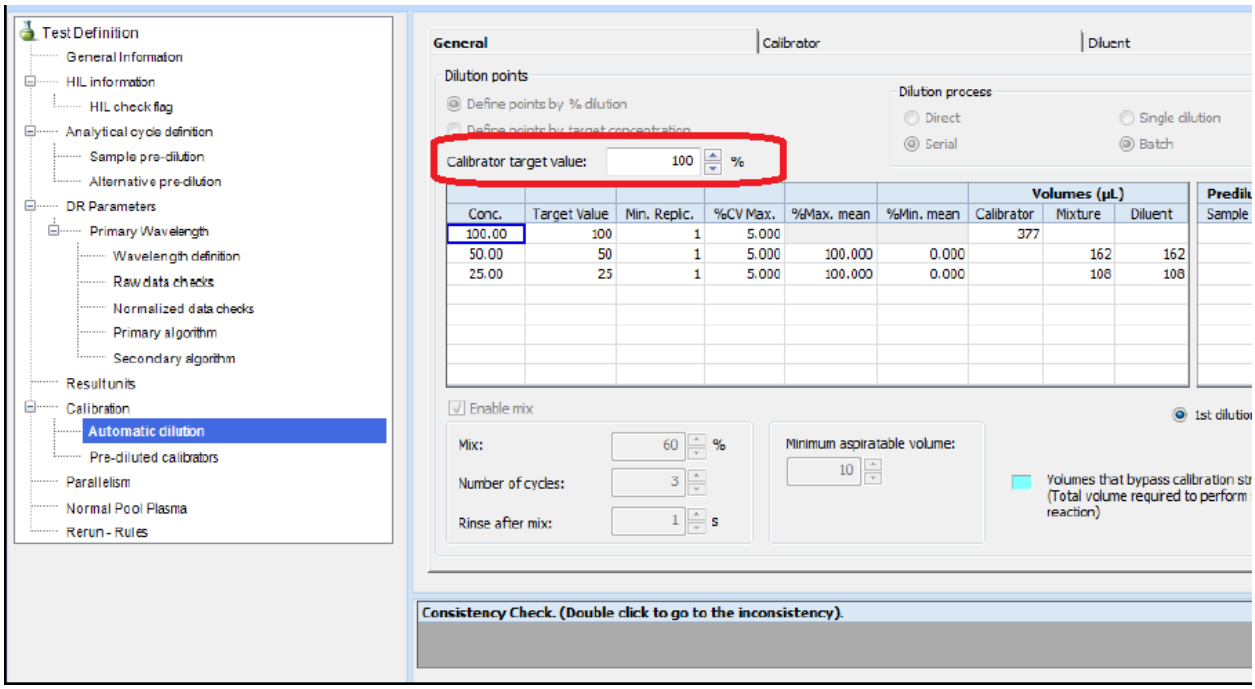
B. **ISI (ALL SITES):**
   1. Enter the ISI value provided on the package insert of the RP2G from the Material List window.
   2. The ISI is specific to each lot number and describes the reagent's sensitivity and the geometric mean used to calculate the INR.
   3. It is imperative to enter the geometric mean, established from the normal patient population studies, when the new lot is activated.

C. **Program for new lots: Program all ACL TOP analyzers for new lots of the following (ALL SITES):**
   1. Reagents: APTT, PT, QFA (if applicable), and D-Dimer HS 500 (may be performed at a different time than the system rollover. Werfen does not allow annual sequestration of DDHS 500).
   2. Controls: Normal 1, ABN 3, Low Fib and D-Dimer HS 500 (if applicable).
   3. Calibrators: HemosIL Calibrator Plasma, and DDHS 500 calibrator (if applicable).
   4. Remove all materials (reagents, quality controls, and calibrators) from the analyzer.
   5. **Choose Setup> Materials List.**
   6. Choose the **Lot Specific Information tab > Enable Lot Management > Alternate** Lot button.
   7. Enter the lot number and expiration date for each reagent and control and select the Save icon to store the information.
   8. Enter the control ranges established by Werfen and reflected on the package insert for each quality control (QC) material while gathering data to determine site-specific QC ranges.
   9. Enter HemosIL Calibrator Plasma and D-Dimer HS 500 calibrator (if applicable) lot numbers and expiration dates.

10. 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.
11. Enter the calibrator value from Calibrator Plasma and D-Dimer HS 500 package insert and Choose OK.
12. Choose the **Previous Screen** icon to exit.



D. **Prepare Standard Curve (For sites that perform QFA and/or D-Dimer Assays):**
   1. Always start with fresh Factor Diluent, verify all maintenance pertaining to probes and syringes is up to date, and perform the Enhance Clean for all Probes with fresh Clean B prior to calibration.
   2. Enter the calibrator value from the calibrator package insert select **Setup**>**Test List**> select the desired assay> **Test Definition**> **Calibration**> **Automatic dilution**.



3. Load required calibrator, diluents, and reagents.
4. Select Calibration, Status, Double click desired test, then click Run icon in toolbar.
5. If Run icon is disabled, hover over the Run icon to display needed materials and their location.
6. Select OK at the “Do you confirm the operation?” prompt.
7. Once the calibration is complete, review the calibration results. The calibration must be validated before usage for calculating results.
8. 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.
9. If the calibration is acceptable, choose the Validate icon to validate the calibration curve. The lettering of the calibration tab will change to blue.
10. All calibration curves with errors must be repeated. Contact Werfen for assistance if needed.

E. **Establish New Control Ranges:**
   1. Using the new lot number of reagents, run the new lot numbers of controls for several days utilizing several operators.
   2. For the PT and APTT: Run 20 points for the new control levels on each ACL TOP analyzer.
   3. For QFA (If applicable): Run 20 points for level 1 and Low Fib.
   4. For DDHS 500 (If applicable): Run 20 points for D-Dimer HS 500 Controls level 1 and level 2.
   5. 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)
   6. 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.
   7. 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.

F. **Perform Patient Correlation Studies: Use the reference (primary) analyzer**:
   1. **PT and APTT (All Sites):**
      a. 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. Use the new lot of reagents to rerun samples for PT and APTT on other ACL TOP analyzers, if applicable.

2. **QFA (For sites that perform QFA Assays):**
   a. 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.
   b. Use the new lot of reagents to rerun samples for QFA on other ACL TOP analyzers, if applicable.
3. **D-Dimer HS 500 (For sites that perform D-Dimer HS 500)**
   a. Run a minimum of 5 patient correlations. Run 2 normal patients and 3 abnormal patients using both the current and new lot of D-Dimer HS 500 reagent.
   b. Use the new lot of reagents to rerun samples for D-Dimer HS 500 on other ACL TOP analyzers, if applicable.
4. **Thrombin Time: (RYO Only):**
   a. Run a minimum of 10 patient correlations. Use 5 normal patients and 5 abnormal patients using the current and new lot of reagents.
   b. Use the new lot of reagents to rerun samples TT on other ACL TOP analyzers, if applicable.

G. **Verify Reference Ranges (All Sites):**
1. 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. Patient samples must not be used for this study.
2. **Confirm that blood donors have not taken any listed anticoagulant medications in the last 7 to 10 days. (See Attachment A)**

NOTE: PATIENTS MUST NOT BE USED FOR THE STUDY ONLY NORMAL DONORS.

3. Run the normal donors on the primary analyzer for the current and the new lot of reagents. Run the normal donors, using the new lot of reagents, on the rest of the analyzers and other alternate testing methods, if available
4. Combine all site data for reference ranges.
5. PT geometric mean is to be calculated for all sites (RYO).

NOTE: The PT geometric mean in combination with the manufacturer provided ISI is used to calculate INR values.

6. It is imperative to enter the geometric mean when the new lot is activated.

H. **(RYO Only):**
1. **Perform Factor Sensitivities Individually for All Factors Tested for in RYO Laboratory:**
   a. Load the new lot APTT and PT reagents.
   b. Load the Precision Biologic reference plasma in a 2 mL cup in the sample rack.
   c. Load the factor-deficient plasma in the diluent rack in lane D1 or D2 and assign it as Factor Sensitivity Diluent.
   d. 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 the test>Calibration>Automatic Dilution)
   e. Select Calibration, Status List.
   f. Double-click on the INFacSen/ ExFacSen test code to open the Calibration details screen.
   g. Choose the Run icon
   h. Select OK at the “Do you confirm the operation?” prompt.
   i. 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.
e. Run 20 samples (10 from normal donors and 10 abnormal patients) for comparison with the ACL TOP.

3. **NEW LOT OF dRVVT SCREEN AND dRVVT CONFIRM:**
   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: 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: The patient sample result in seconds is divided by the Mean of the dRVVT S normal range.

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

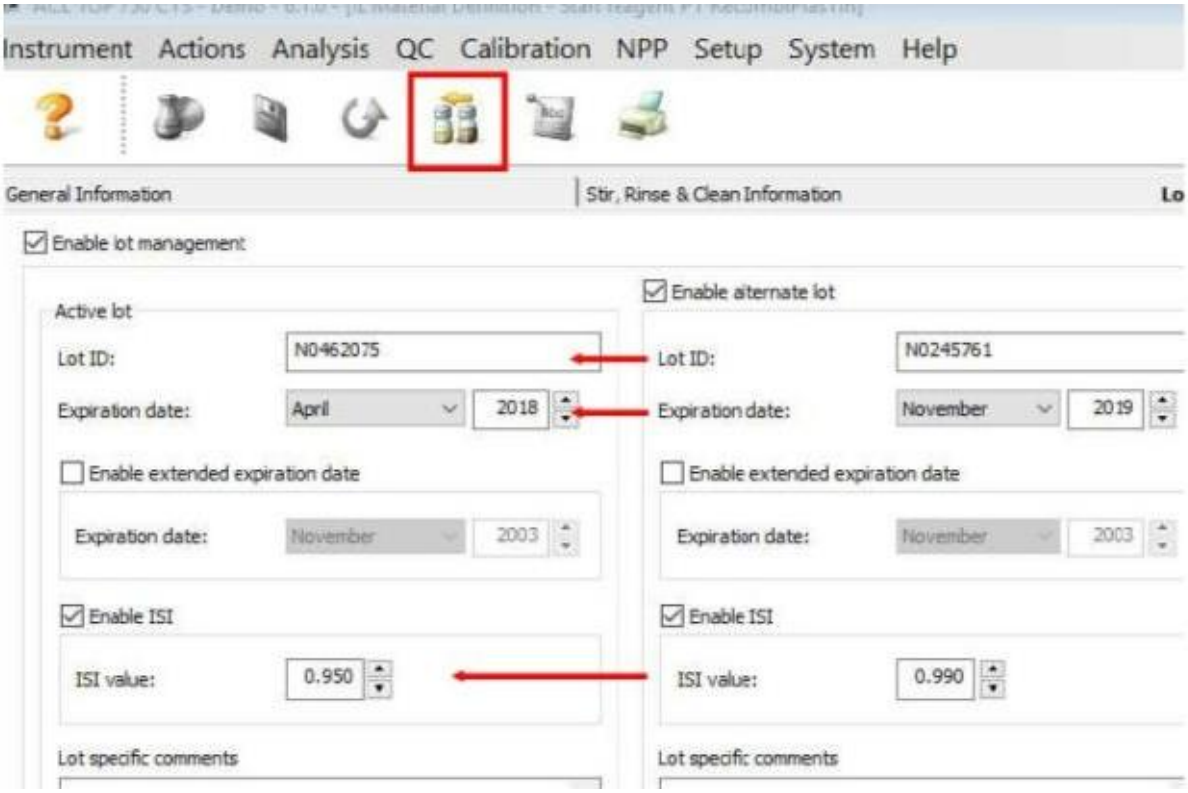
      3) Normalized dRVVT Ratio: The ratio result from the dRVVT S is divided by the ratio result from dRVVT C.

$$\textbf{Normalized dRVVT Ration} = \frac{\textbf{dRVVT Screen Ratio}}{\textbf{dRVVT Confirm Ratio}}$$

I. **BEFORE THE GO-LIVE DATE**:
   1. **LIS**:
      a. Submit an Information Technology (IT) ticket to update reference ranges for the PT, APTT, QFA, and Thrombin time (if needed).
      b. Submit an IT ticket to update the auto-verification run for the INR.
      c. Submit an IT ticket to update the Heparin Therapeutic Range (if needed).
      d. Submit an IT ticket to update the dRVVT reference ranges (if needed).
   2. **LTD:**
      a. Update the LTD and procedures.
   3. **Bulletin:**
      a. prepare a "Laboratory Bulletin" for distribution.

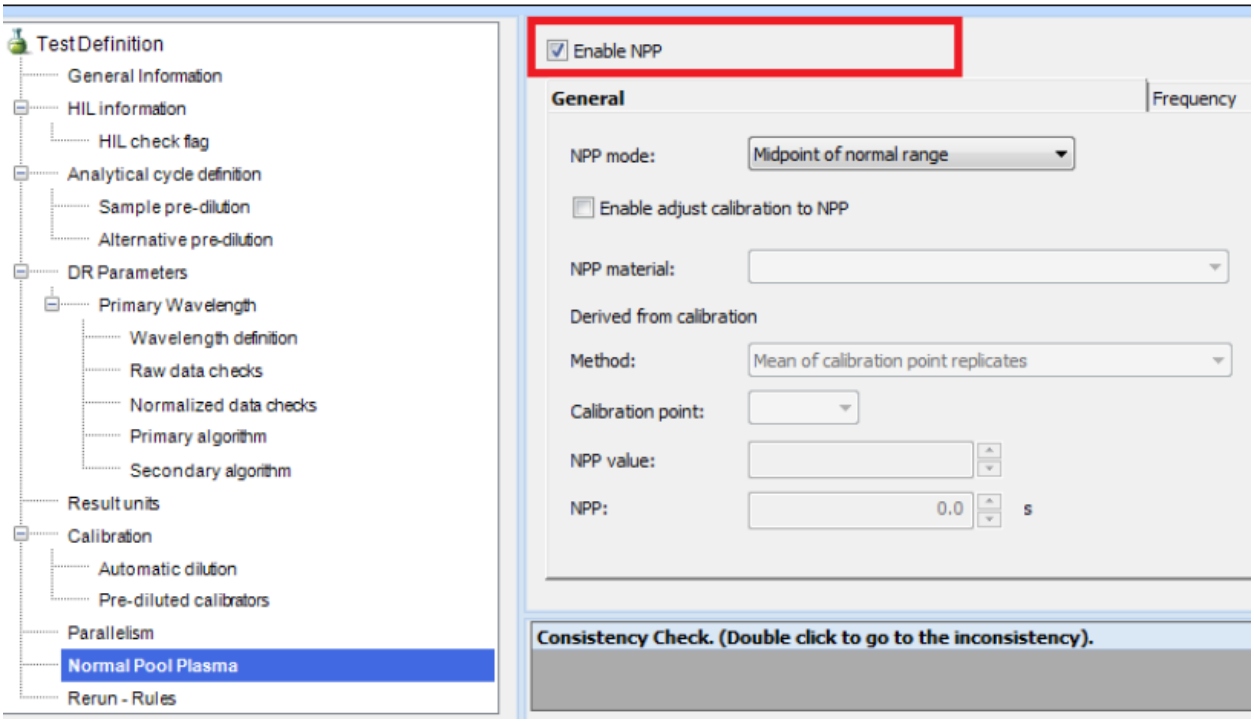
J. **ROLLOVER DAY (All Sites):**

1. **Print all alternate QC files before activating any Alternate Lots as the data will be gone and irretrievable once activation occurs.**
2. **Activate Alternate Lot:**
   a. Remove all materials (reagents, quality controls, and calibrators) from the analyzer.
   b. **Choose Setup> Material List**> double click on each reagent and control material.
   c. Choose **Activate** and **Save**



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

1) On the New Lot# of RecombiPlastin 2G Witness Form, document the change of the prothrombin time normal mean and ISI value for each analyzer (**Attachment B).**



K. **(RYO ONLY):**
   1. Update reflex list for dRVVT Screen if needed
   2. 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.
   3. **Start4 Analyzer**:
      a. Post the new QC ranges.
      b. 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.
      c. Enter the PT reagent lot numbers, geometric mean, and ISI value. Verify that there is a witness present.
         1) Enter PT reagent lot numbers, geometric mean, and ISI value.
         2) Select calibration by pressing the [2} key and confirm with [ENT].
         3) Select others by pressing the [8] key and confirm with [Ent].
         4) Select Mode 1 by pressing the [1] key.
         5) Press any key.
         6) In the next display, enter the reagent lot number confirmed with [ENT].
         7) The Next display asks for Reference times as T1 and T2.
         8) Enter the geometric mean for T1 and T2 and confirm with the [ENT].
      d. **Enter the ISI value from the Main Menu**:
         1) Select Test Parameters by pressing the [3] key and confirm with [ENT].
         2) Select others by pressing the [8] key and confirm with the [ENT].
         3) Select Mode 1 by pressing the [1] key.
         4) Press the enter key until the cursor is under the Select the Unit.
         5) Select the Unit Sec-INR by pressing the [3] key and validate with the [ENT].
         6) Enter the ISI value of the RecombiPlastin 2G reagent lot number.
         7) Run test patients and check the PT INR calculations.

6. Revisions

Corewell Health reserves the right to alter, amend, modify or eliminate this document at any time without prior written notice.

7. Procedure Development and Approval

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8. Keywords

Not Set