Adventist HealthCare

TRAINING UPDATE

Lab Location:	All Laboratory sites	**Date Distributed:**	2/20/24
Department:	Core Lab/ Technical Specialists	**Due Date:**	3/20/24
		Implementation:	**Immediately**

DESCRIPTION OF PROCEDURE REVISION

Name of procedure:
Coagulation Reagent Lot Conversion (AHC.G848)
Description of change(s):
6.6 The INR Calculation must be checked on the day the new lot number is placed into use. This documentation must be uploaded into MediaLab, attached or amended to the new lot correlation. SOP will become effective as soon as approved on ML.

Document your compliance with this training update by taking the quiz in the MTS system.

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Non-Technical SOP

Title	**Coagulation Reagent Lot Conversion**	
Prepared by	Leslie Barrett, Zanetta Morrow	Date: 10/7/2013
Owner	Robert SanLuis	Date: 10/7/2013

Laboratory Approval		
Print Name and Title	**Signature**	**Date**
Refer to the electronic signature page for approval and approval dates.		
Local Issue Date:	Local Effective Date:	

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1. PURPOSE

This procedure describes the process for new reagent lot conversion for coagulation testing.

2. SCOPE

This SOP outlines the process for the lot conversion of a new lot of Coag Normal and Abnormal Control, Neoplastine, and PTT reagent with the support of the Stago TSS, technical supervisor or designee.

3. RESPONSIBILITY

The technical supervisor or designee will ensure this process is followed.
The Stago TSS will assist and provide technical support for new coagulation lot conversions.
The Medical Director or designee (Laboratory Director) is responsible for review and approval of the lot conversion data.

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4. DEFINITIONS

IHN – Integrated Healthcare Network
TSS – Technical Support Specialist
FSE – Field Support Engineer

5. PROCEDURE

1.0 General Comments

1.1 New reagent lots and/or shipments are tested in parallel with old lots before or concurrently with being placed in service to ensure that the calibration of the new lot of reagent has maintained consistent results for patient specimens. Good clinical laboratory science includes patient-based comparisons when possible, since it is patient specimens that are tested. Other reference material may also be used for this purpose. (Approach A)

1.2 If the new lot of reagent exceeds cumulative summary acceptability criteria, reference ranges and/or therapeutic ranges must be verified or re-established as determined by the Laboratory Medical Director. (Approach A and B)

1.3 An alternate method with lot change is the exclusive establishment of new reference and therapeutic ranges for the new reagents. (Approach C)

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2.0 Lot Conversion Processes

2.1 There are several acceptable approaches to these studies. Approach A is the standard process. Approach B may be utilized if there is a change in method. See the following table:

Task	IHN Approach A	IHN Approach B	IHN Approach C
Patient sample correlations between current and new lot of reagent	Performed at Central Facility only	Performed at all sites	Optional
System correlation with commercial samples (George King Samples)	Performed at all sites. Test with the new lot of reagent only	Performed at all sites. Test with the new lot of reagent only	Performed at all sites. Test with the new lot of reagent only
Total Precision (QC) ranges	See 7.0 below	See 7.0 below	See 7.0 below
Backup analyzers	See 8.0 below	See 8.0 below	See 8.0 below
Reference range	A minimum of 20 normal samples must be run at each site.	A minimum of 20 normal samples must be run at each site.	A minimum of 20 normal samples must be run at each site.

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Task	IHN Approach A	IHN Approach B	IHN Approach C
Heparin Therapeutic range	Studies performed ***if indicated***: if current to new lot studies exceed criteria	Studies performed at each lot conversion	Studies performed at each lot conversion
Transfusion and Liver Biopsy Protocols	Evaluated at each lot conversion	Evaluated at each lot conversion	Evaluated at each lot conversion
D-Dimer cutoff value for DVT/PE	Evaluated at each lot conversion	Evaluated at each lot conversion	Evaluated at each lot conversion

3.0 Instrument Specifications

3.1 Weekly and monthly maintenance is to be performed on the analyzer prior to the lot conversion testing. This should include changing filters and syringe tips and cleaning of needles.

3.2 If the Stago Preventive Maintenance (PM) is due, it should be performed by the Stago FSE before proceeding to the lot conversion studies.

3.3 Controls are to be within acceptable limits for all tests before proceeding. The Diagnostica Stago Hotline should be utilized for troubleshooting help if quality control is unacceptable. **Any troubleshooting issues must be resolved before the protocol is attempted.**

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4.0 Test Setup

4.1 At least a week prior to the lot conversion, a George King Set needs to be purchased from George King Bio-Medical, Inc. The George King Set consists of the commercial samples that will be used in the lot conversion. These samples have strict stability requirements and must be handled according to the package inserts.

4.2 Verify that the test setups for New PT and New PTT have been created on the instrument (Operators Manual Chapter 3 Test Setup). Refer to the separate protocol for loading **New** reagents (Operator's Manual Chapter 4 Loading of Products & Samples). **The Key operator must be available to work with the TSS during lot conversion.**
Note: Fibrinogen, D-Dimer and Anti-Xa follow the standard new lot comparison process specified in the SOP *Reagent Parallel Testing.*

4.3 Verify test setups for New PT and New PTT, are correct and reflect the current PT, and PTT settings. For example, if you have changed your reportable limit for PTT within the year, set New PTT to match. All sites in the IHN should have the same routine test setups.

4.4 Program the New PT and PTT tests to run either your current control material or a new lot of control material as described in separate protocol(s).

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5.0 Current Lot vs. New Lot Correlation using Patient Samples

5.1 Performed at the Central facility only or at each site as defined by the IHN.

5.2 **Specimens should represent values across the <u>entire</u> reportable range**. Patient samples should primarily be used for correlation studies. If System Correlation samples are used for correlation they **<u>MUST BE</u>** supplemented with stabilized coumadin and heparin samples.

5.3 Prothrombin Time

5.3.1 On the day of the lot conversion, collect 50 **patient** samples across the reportable range, using the following division of samples: 20 normal samples, 20 therapeutic INR (1.5 - 4.0), and 10 samples to verify the upper limit of the reportable range. Samples can be created by mixing patient samples with saline or over diluting controls. Samples may be collected ahead of time and frozen according to CLSI (formerly NCCLS) guidelines.

5.3.2 Any deviation from the 50 samples across the reportable range will be noted on the final signoff sheet.

5.3.3 Enter the correct ISI for the new lot of Neoplastine reagent and the current geometric mean in the instrument. This will be used for the INR calculation. Alternately, program New PT in raw mode and calculate INR in an Excel template.

5.3.4 Run the samples with the current and new lot of reagent. It is recommended that the samples be tested with current and new lot numbers at the same time to exclude sample stability issues. This is especially important if the samples were frozen.

5.3.5 **The geomean recovered on the current reagent must match the actual geomean in use by 0.3 seconds in order for the new calculated geomean to be valid. If this does not match within 0.3 seconds, the geometric mean should be verified with 20 fresh screened normal samples.**

5.3.6 Perform combined data analysis for correlation statistics.

5.3.7 If the raw data and/or INR correlations do not meet criteria, a new reference range and geometric mean must be determined for the IHN.

5.3.8 Criteria for acceptance: See Table 3 and cumulative summary analysis.

5.4 APTT

5.4.1 Collect 50 patient samples across the reportable range using the following division of samples: 20 normal samples, 20 therapeutic range (PTT equivalent to anti-Xa IU/mL 0.3-0.7), and 10 samples to verify the upper limit of the reportable range. Samples can be created by mixing patient samples with saline, over dilution of controls, or spiking normal pool with

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heparin. Samples may be collected ahead of time and frozen according to the CLSI guidelines. If possible, aliquot the samples containing UF heparin into 2 tubes. The second tube can be used to run the heparin assay if it is deemed necessary to establish a new therapeutic range.

5.4.2 Any deviation from the 50 samples across the reportable range will be noted on the final signoff sheet.

5.4.3 Run the samples with the current and new lot of reagent. It is recommended that the samples be tested with current and new lots at the same time to exclude sample stability issues. This is especially important if the samples were frozen.

5.4.4 Perform combined data analysis for normal and therapeutic range correlation statistics.

5.4.5 If the data does not meet criteria, a new heparin therapeutic range and reference range must be determined for the IHN.

5.4.6 Criteria for acceptance: See Table 3 and cumulative summary analysis.

5.5 Retention of Current Ranges

5.5.1 If all the data meets acceptability criteria, the current ranges may be retained and no further action is necessary.

5.5.2 If the data indicates the need for either new reference ranges or therapeutic ranges, follow the steps listed below in sections 10.0 and 11.0.

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6.0 Verify Geometric Mean – All sites

6.1 **A new site specific Geometric Mean must be verified for each new lot of PT reagent.**

6.2 It is recommended that each site run a **minimum** of 20 **screened** normal samples with the **new PT reagent**. If there are 2 or more analyzers, the same normal samples should be run on each analyzer to account for any variability. Data should be carefully reviewed by comparing individual analyzer ranges for differences. **The individual % difference should be a combination of positive and negative values. The data should not be biased in one direction.** Use troubleshooting measures if any analyzer shows a difference in ranges. Following resolution, more samples should be run and the "suspect" data excluded.

6.3 Each site will collect "normal" donors in 3.2% sodium citrate according to the CLSI collection guidelines (CLSI H21-A4). Reference 10.0

Note: Optional; since each site has normal samples on hand from this study, each site may also choose to run these samples with the new aPTT reagent to verify the new lot reference range.

6.4 Calculation of the geometric mean (GM) is indicated below and is available in many spreadsheet programs such as Excel.

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GM = antilog [(log(X1) + log(X2) + log(X3) + . . . log(Xn))/n]

6.5 The new **site specific** geometric mean must be entered into the calibration page of the analyzer when a new lot number of Neoplastine reagent is put into use to allow correct calculation of the INR.

6.6 The INR Calculation must be checked on the day the new lot number is placed into use. This documentation must be uploaded into MediaLab, attached or amended to the new lot correlation.

7.0 Total Precision (Quality Control)

7.1 Total Precision will be tested on the analytes performed at each site. It is recommended that a minimum of 30 data points be collected to validate a new site specific range before going live with the new lot. However, it is acceptable to use the assigned control range for a short period of time (up to 4 weeks) while control data is being collected.

7.1.1 Perform six replicates for 5 days on two levels of QC material. These replicates should be across the entire working day with reagent and controls that have aged, but not expired. This allows the capture of the variations of the instrument and reagent combination to ensure a more accurate "true working" quality control range.

7.1.2 A minimum of 30 data points for each level for routine assays is recommended to be run and results compiled into a site specific range. All results must be within the Stago bar coded range. This is to verify that the new lot is working within manufacturer's specifications. Deviation from this minimum requirement will be documented on final signoff sheet and acknowledged with customer signature.

7.1.3 Perform data statistics for mean, SD and CV (where applicable).

7.1.4 Criteria for acceptance: see Table 1.

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8.0 Backup Analyzer

8.1 Total Precision studies with the new lot of reagent(s) should be performed to determine Quality Control ranges for the backup analyzer.

8.2 Patient sample correlations - this step may be performed at the time of the lot conversion studies or on a different schedule as defined by the Laboratory.

8.2.1 Correlate only the tests that will be performed on the backup analyzer (the backup analyzer with the new lot of reagents) at each site. Perform 10-20 comparisons for the routine tests Prothrombin Time and aPTT. These samples should span the reportable range.

8.2.2 **Correlation data should be carefully reviewed by comparing individual analyzer ranges for differences in both the normal and therapeutic ranges. <u>The individual % difference should be a</u>**

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combination of positive and negative values. The data should not be biased in one direction.

8.2.3 Perform data analysis for correlation statistics:

8.2.3.1 Criteria for acceptance: see Table 2 for comparison between identical instruments and reagent systems.

8.2.3.2 If the backup instrument is not an identical platform to the primary instrument the criteria for acceptance in Table 2 is still the "target" for acceptability.

9.0 System Correlation

9.1 **Performed with each lot crossover to validate "transference".**

9.2 On the primary instruments at each site, perform PT and APTT on specimens created or provided from a commercial source using the **new reagent only.** The correlation specimens must span the reportable range for the routine tests listed. Acceptance Criteria enables all hospital sites to share reference and therapeutic ranges throughout the health network.

9.3 Commercial vendor sets must be removed from the dry ice for a minimum of 24 hours before use.

9.4 Thaw samples in 37° C waterbath for 5 – 15 minutes, depending on the vial size, to make sure the entire sample is thawed. Mix each sample by inverting the vial several times to insure complete mixing. Remove the cap from each vial, pour sample into an appropriate tube and allow the tubes to equilibrate for 60 minutes.

9.5 Perform data analysis, correlating each site to the reference value for the IHN (average of all the sites).

9.6 Criteria for acceptance: See Table 2.

10.0 Full Validation – Reference Range

10.1 **Reference range data must be collected if current vs. new lots do not meet criteria**. It is also an option to perform only these studies at each lot conversion if desired by the IHN (IHN Approach C).

10.2 The number of samples, as suggested by CLSI, is a minimum of 120 for non-parametric analysis. This may not be practical for small groups. When a valid reference range study already exists and was done properly, it may be preferable to verify a reference interval without having to perform a new, full-scale study. Verification can only be deemed acceptable if the test subject population, and the entire methodology are the same or appropriately comparable. The reference interval verification study may be performed using a minimum of 20 screened normal samples. These studies should be performed over several runs and should represent the laboratory's healthy population.

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10.3 Sample collection must be divided among all sites, with a minimum of 20 samples at each site. 50% of the samples should be processed and assayed fresh. Any deviation from 20 minimum per site sample requirement will be noted on the final signoff sheet.

10.3.1 For example, in a 3 hospital integrated network the distribution could be as follows:

- Hospital A, 20 normal donors
- Hospital B, 20 normal donors
- Hospital C, 20 normal donors

10.4 Each site will collect "normal" donors in 3.2% sodium citrate according to the CLSI collection guidelines (CLSI H21-A4). Each site should draw one 3.2% sodium citrate (blue top) tube.

10.4.1 The data collected will be used to generate shared reference ranges **using the new reagent**. The collection should encompass several days, and the samples tested across the entire working day with reagents that have aged, but not expired. In this way a realistic reference range using the variations of the instrument and reagent can be captured.

10.4.2 Centrifuge the blood for platelet poor plasma. Perform routine tests within 4 hours of collection.

10.5 Criteria for reference range "normal" donors:

- Age — Include ages that span the population reflecting your patient diversity. (Be careful not to use all young lab employees.)
- Sex — Equal numbers of males and females
- Drug History — Patients excluded if taking the following drugs:
  - Birth control or estrogen containing products
  - Coumadin
  - Heparin (UFH, LMWH or heparinoid)
  - Direct Thrombin Inhibitors
  - Antibiotics
- Conditions — Patients excluded if they are pregnant or have any known immunologic diseases.
- Note: — Possible source for normal samples is ambulatory out-patient surgery, i.e. eye surgery.

10.6 The data from each site will be compiled to develop standardized reference ranges to be used throughout the IHN.

10.6.1 Determination of the Geometric Mean for INR calculation

Using Excel software, the Geometric Mean of the individual and shared reference range values for PT are computed. (See Legend for complete definition of the Geometric Mean).

10.6.2 Determination of individual test reference ranges

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Using Excel software, the arithmetic mean of the individual reference range values for each assay are determined.
Standard deviation (SD) from the mean is computed and applied to the mean value to determine the actual reference range. This can be plus or minus 2.0, 2.5, or even 3.0 SD from the mean value. The degree of SD applied to the mean value is determined by the IHN.

11.0 Full Validation – Therapeutic Ranges and Transfusion/Liver Biopsy Cut-off Values

11.1 **Heparin therapeutic range data must be collected if the current vs. new lot do not meet acceptance criteria.** It is also an option to perform only these studies at each lot conversion if desired by the IHN (IHN Approach C).

11.2 Heparin Therapeutic Range Procedure

11.2.1 For an accurate assessment of the APTT heparin therapeutic range, sites are requested to collect data on specimens from patients receiving unfractionated heparin. The total number of samples should be 60 – 100. A minimum of 30 well screened and carefully processed samples *may* be acceptable for a valid range. The total number of samples collected may be divided among the number of hospitals involved in the network to ease the duress of collection. These specimens will be sent to the central facility for heparin level determination and subsequent correlation with the APTT.

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11.2.2 **Collection and processing are critical to the success of this study.**

Sample Collection: Blood is collected from patients receiving **unfractionated** heparin (low molecular weight heparin is unacceptable). Centrifuge the blood for platelet poor plasma (CLSI H21-A4). Perform tests within 2 hours of collection, according to the package insert.

11.2.3 Screening Tests. Perform APTT and PT on each specimen with the current reagent. If the PT is normal (INR is ≤ 1.3) and the APTT is abnormal the specimen is deemed acceptable for the study. Exclusion criteria allow only two different samples from the same patient. This ensures that the therapeutic range is derived from a variety of patients. Record the sample identification and the PT and APTT results on a data collection sheet.

11.2.4 Further Processing. If the sample is "deemed acceptable" carefully remove the plasma, without disturbing the cellular components. Place the plasma in a non-polystyrene tube (suggest **polypropylene**) and spin again. Remove the plasma carefully from the top layer and dispense the plasma as a l mL aliquot in a non-polystyrene plastic vial appropriate for -70° C storage.

11.2.4.1 The residual platelet count on the plasma before storage is recommended to contain <10,000 platelets/*u*L. Platelet counts should be performed to ensure the recommended platelet poor

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plasma. Greater platelet counts allow the innate platelet factor 4 (PF4) to neutralize the heparin in the sample, and thus invalidate the study.

11.2.4.2 Label the vial with the patient ID and freeze at -70° C. If unavailable, freeze at <-20° C. Optimally, the specimens should be kept frozen in a freezer that does not go through defrost cycles.

11.2.5 Frozen samples will be sent to the central facility for Unfractionated Heparin testing (Anti-Xa methodology). Once the UF heparin level is determined on each sample, the data will be compiled to develop a standardized aPTT heparin therapeutic range to be used throughout the IHN.

11.2.6 The heparin therapeutic ranges are developed utilizing a procedure derived from Brill-Edwards, *et.al.*, in which APTT values and heparin levels are obtained from patients actually receiving heparin (*ex vivo* blood samples). Using linear-regression, a graph is prepared that correlates the APTT in seconds to the heparin IU/mL. The ranges established, are the time in seconds equivalent to 0.1 to 0.3 and 0.3 to 0.7 IU/mL of UF heparin, according to the literature.

11.2.7 The following exclusionary criteria are applied to the data obtained during the study:

- Patient baseline APTT (if known) should be within the normal APTT reference range.
- Patient should not be receiving fibrinolytic treatment.
- Patient should not be receiving oral anticoagulation (INR <1.3)
- APTT should be greater than upper limit of the normal reference range and less than150 seconds.
- Heparin value should be greater than 0.1 and less than 1.0 IU/mL.
- No more than two samples from an individual.
- Obvious disparity between UF heparin level and APTT (such as heparin resistance, LMWH therapy or conversely, oversensitive response).
- Minimum number of samples meeting acceptability criteria is 30.

11.2.8 Once the APTT heparin therapeutic range has been established the nomogram can be adjusted using a heparin conversion chart to appropriately reflect the response of the new reagent and instrument combination. This recalculation should be closely coordinated between the Laboratory and the individual site Pharmacies.

11.3 Transfusion, Liver Biopsy and Pharmacy Protocols

11.3.1 Transfusion protocols utilize cutoff values based on either the Prothrombin Time/INR or APTT. Liver biopsy protocols utilize cutoff values based on the Prothrombin Time/INR. These values may change when the new lots of reagents are implemented. If a new PT/INR range

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has been established, the Laboratory needs to adjust these numbers to appropriately reflect the response of the new reagent and instrument combination. This will help provide a smooth transition to the new lot of reagent for physicians who are reliant on this system.

11.3.2 Current cutoff values (often found as part of the Blood Bank or Transfusion Service protocols) may need adjustment if there is a change in reference or therapeutic range. Provide this information to the BB Manager and Medical Director for review.

11.3.3 If reference ranges or cutoff values change, provide this information to Pharmacy for possible adjustment of their protocols.

12.0 Data

12.1 All raw data is provided to the TSS who enters it into the appropriate data template.

12.2 All data will be reviewed by the Technical Service Manager or designee and verified that the data is accurate and acceptable before the site can go live.

12.3 A hard copy of all raw data will accompany the respective template (on CD) and will be sent to the customer. The signature of the customer is required upon receipt of all completed lot conversion data.

12.4 A copy of this data will be placed in the DSI site folder

12.5 Data is filed electronically and approved via the document control system.

13.0 Specificity (Interferences)

13.1 Note each Product Package Insert

13.2 Technical procedure limitations must address the referenced known interferences.

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6. RELATED DOCUMENTS

N/A

7. REFERENCES

Lot Conversion Protocol for IHN, Diagnostic Stago, Inc., APL-02-002, 3/13/12

8. REVISION HISTORY

Version	Date	Reason for Revision	Revised By	Approved By
0	11/17/17	Header: added other sites	L Barrett	R SanLuis

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Version	Date	Reason for Revision	Revised By	Approved By
1	8/4/20	Header: changed WAH to WOMC Section 2 & 3: updated TSS role in process Section 5: specified standard approach (2.0); added note for FIB, D-Dimer & Xa (4.0); deleted other references to FIB & D-Dimer (4,8,9); added geo mean calculation (6.4), added pharmacy protocols (11.3); updated data submission process (12)	A Chini L Barrett	R SanLuis
2	8/2/22	Header: Changed site to All Laboratories Footer: Changed prefix to AHC	D Collier	R SanLuis
3	2/19/24	Section 6.6: Added INR calc. chk on day of go live	R SanLuis	R SanLuis

9. ADDENDA AND APPENDICES

A. Sample Processing – How to double-spin samples prior to freezing.
B. STA System Validation Studies - Legend of Statistical Terms
C. Precision Limits (Table 1)
D. System Correlations: Comparison between Identical Instrument and Reagent Systems (Table 2)
E. Lot Conversion (Table 3)

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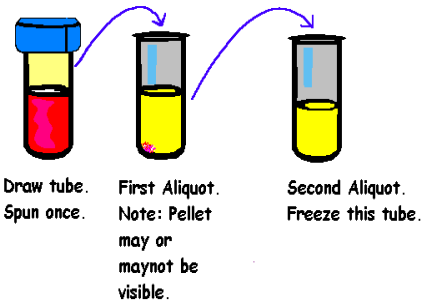
Addenda A

Sample processing: Process samples within 2 hours.

Double Spinning Samples for Coagulation testing

1. Centrifuge the draw tube.
2. Take plasma layer off to an aliquot tube. Be careful not to disturb the platelet layer.
3. Centrifuge the First Aliquot tube.
4. Take off plasma leaving a small amount at the bottom of the tube. Use care not to aspirate the pellet of Platelets/RBC at the bottom of the tube.
5. Transfer this platelet-free plasma to clean polypropylene aliquot tube. This is the Second Aliquot tube. Freeze this tube.



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Addenda B

STA System Validation Studies Legend

Bias: The difference between the test result and a reference value. Bias may be expressed as the raw difference or the % difference.

Coefficient of regression (r): the correlation coefficient between two data sets.

Coefficient of variation (C.V.): the ratio of the standard deviation to the mean multiplied by 100; measures the variability relative to the magnitude of the data and expressed as %.

Geometric Mean: The geometric mean is determined by: 1) transforming each data point to the log value; 2) determining the mean of the log values; and then 3) transforming the result back to the original units. The distribution of the normal Prothrombin Time data is more symmetrical when the logarithm of each value is determined. The geometric mean is usually lower than the arithmetic mean and similar to the median. ***It is the preferred computation in calculation of the INR.*** The equation for the geometric mean can be obtained through computer-based statistical programs.

Intercept (b): the point at which a line will intersect the y-axis by using a best fit regression line plotted through known x-values and y-values: equates to the bias between data sets.

Mean % Difference (Mean Bias):
(Mean of the raw difference between data points/ reference value) X 100 Used as a target value to show correlation between data sets. The reference value is defined for a particular data set and may be a current reference method or mean of sample values.

Mean (arithmetic mean): the average value of a large number of observed data points or values.

Median: the middle point in a series of given values, or the 50th percentile of a sample of data. It is an accurate estimate of the center of a sample of data, since outliers have little effect on it. For this reason, it is often used in calculating the INR. It is very close in value to the geometric mean.

Number (n): the number of observed data points or values.

Reference Interval Verification: performed by collecting and analyzing specimens from 20 screened individuals who represent the reference sample population. If two or fewer test results fall outside the claimed or reported reference limit, the reference interval is considered verified.

Reference Time: a generic term for the Mean, Median or Geometric Mean value used to determine a calculated result such as INR or "ratio" result.

Slope (m): the slope of the linear regression line through the observed paired data points.

Standard deviation (s.d.): the square root of the arithmetic mean of the squares of all the deviations from the mean.

Transference: A term used to describe the assumption of a reference range based on equivalency of, 1) reference population demographics from which the data is derived, 2) instrumentation for determination, and 3) assay methodology.
Actual equivalency may be assessed by 1) comparison of individual site reference range to the pooled [group] reference range, 2) comparison of the individual site reference range to another site reference range, or 3) acceptability of correlation studies between sites across the reportable range.

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Addenda C

Precision Limits (Table 1)

Analyte	Intra-Run Precision				Total Precision (QC)			
	CV		SD		CV		SD	
	NL	ABN	NL	ABN	NL	ABN	NL	ABN
Prothrombin Time	≤ 2.5	≤ 2.5			≤5.0	≤5.0		
aPTT	≤ 2.5	≤ 2.5			≤5.0	≤10.0		
Fibrinogen	≤5.0	≤8.0			≤10.0	≤10.0		
D-Dimer			≤ 0.1	≤ 0.2			≤ 0.2	≤ 0.4
Antithrombin	≤10.0	≤10.0			≤20.0	≤20.0		
Antiplasmin	≤10.0	≤10.0			≤20.0	≤20.0		
Extrinsic Factors	≤10.0	≤10.0			≤20.0	≤20.0		
Intrinsic Factors	≤10.0	≤10.0			≤20.0	≤20.0		
Heparin Assay			≤ 0.1	≤ 0.1			≤ 0.1	≤ 0.1
Plasminogen	≤10.0	≤10.0						
Protein C	≤10.0	≤10.0			≤20.0	≤20.0		
Protein S	≤10.0	≤10.0			≤20.0	≤20.0		
Reptilase Time	≤5.0	≤5.0			≤10.0	≤10.0		
Staclot LA	≤10.0	≤10.0			≤20.0	≤20.0		
Thrombin Time	≤5.0	≤5.0			≤10.0	≤10.0		
vWF	≤10.0	≤10.0			≤20.0	≤20.0		

NOTE: Empty Cells = CV or SD Limit not applicable

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Addenda D

System Correlations:
Comparison between Identical Instrument and Reagent Systems (Table 2)

Analyte	System Correlations		
	R value	Slope	Mean Bias (%) from Average*
Prothrombin Time	≥ 0.95	0.9 – 1.1	+/- 5
INR	≥ 0.95	0.9 – 1.1	+/- 10
aPTT	≥ 0.95	0.9 – 1.1	+/- 8
Fibrinogen	≥ 0.95	0.9 – 1.1	+/- 10
D-Dimer	≥ 0.95	0.9 – 1.1	+/- 20
Antithrombin	≥ 0.95	0.8 – 1.2	+/- 15
Antiplasmin	≥ 0.95	0.8 – 1.2	+/- 15
Extrinsic Factors	≥ 0.95	0.8 – 1.2	+/- 15
Intrinsic Factors	≥ 0.95	0.8 – 1.2	+/- 15
Heparin Assay	≥ 0.95	0.8 – 1.2	+/- 15
Plasminogen	≥ 0.95	0.8 – 1.2	+/- 15
Protein C	≥ 0.95	0.8 – 1.2	+/- 15
Protein S	≥ 0.95	0.8 – 1.2	+/- 15
Reptilase Time	≥ 0.95	0.8 – 1.2	+/- 8
Staclot LA	≥ 0.95	0.8 – 1.2	+/- 15
Thrombin Time	≥ 0.95	0.8 – 1.2	+/- 8
vWF	≥ 0.95	0.8 – 1.2	+/- 15

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* The Mean Bias (Mean Difference) % is calculated using the following formula:
(Mean of Raw Differences/Mean of Averages) x 100

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Addenda E

Lot Conversion (Table 3)

Analyte	Correlations			
	R value	Slope	Mean Bias (%) from Reference Value*	Mean Bias (Raw) from Reference Value^
Prothrombin Time	≥ 0.95	0.9 – 1.1	+/- 5	
INR	≥ 0.95	0.9 – 1.1	+/- 10	
aPTT Normal	≥ 0.95	0.9 – 1.1	+/- 5	
aPTT Overall	≥ 0.95	0.9 – 1.1	+/- 8	
Fibrinogen	≥ 0.95	0.9 – 1.1	+/- 10	
D-Dimer < 1.0	≥ 0.95	0.9 – 1.1	+/- 20	+/- 0.15 ug/mL FEU
D-Dimer ≥1.0 – 4.0	≥ 0.95	0.9 – 1.1	+/- 20	+/- 0.5 ug/mL FEU
Antithrombin	≥ 0.95	0.8 – 1.2	+/- 15	
Antiplasmin	≥ 0.95	0.8 – 1.2	+/- 15	
Extrinsic Factors	≥ 0.95	0.8 – 1.2	+/- 15	
Intrinsic Factors	≥ 0.95	0.8 – 1.2	+/- 15	
Heparin Assay	≥ 0.95	0.8 – 1.2	+/- 15	+/- 0.2 IU
Plasminogen	≥ 0.95	0.8 – 1.2	+/- 15	
Protein C	≥ 0.95	0.8 – 1.2	+/- 15	
Protein S	≥ 0.95	0.8 – 1.2	+/- 15	
Reptilase Time	≥ 0.95	0.8 – 1.2	+/- 8	
Staclot LA	≥ 0.95	0.8 – 1.2	+/- 15	
Thrombin Time	≥ 0.95	0.8 – 1.2	+/- 8	
vWF	≥ 0.95	0.8 – 1.2	+/- 15	

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* The Mean Bias (Mean Difference) % is calculated using the following formula:
(Mean of Raw Differences/Mean of Reference Values) x 100

^ The Mean Bias (Raw Difference) is the average of the individual differences between the "new" and the reference values in the reported unit of the assay

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