Procedure for Evaluating the Unfractionated Heparin Sensitivity of New aPTT Reagents

Purpose

This procedure provides instructions for evaluating the Unfractionated Heparin Sensitivity of new aPTT reagents. A regional heparin therapeutic range has been established based on the heparin sensitivity of a specific lot of aPTT reagents. This procedure provides guidance for the laboratory to select a new aPTT reagent lot that has the same (or nearly the same) heparin responsiveness as the lot used to establish the range. By doing so, clinician behavior need not change. It is important to control for (and prevent) drift with multiple changes over time.

Scope

The intended users of this document include Clinical Laboratory Scientist (CLS) and Laboratory Technical Supervisors performing/reporting heparin assay results.

Policy

Each time there is a change in reagents or instrument, comparison testing should be performed. In addition to recording the differences in the mean, the laboratory should prepare a cumulative summation of the differences that have occurred in the past. In doing so, the cumulative shift in the reagent performance in the presence of heparin can be determined. A difference between reagent means or a cumulative change of more than **seven seconds** is reason for concern and requires action.

Selecting a new PTT reagent

Contact vendor to obtain new aPTT reagents with responsiveness to heparin that would be predicted to be similar to the lot that is currently being used in the laboratory.

Specimen collection

- Collect at least 30 (20 minimum) samples from patients already in the lab for heparin measurements.
- No more than two specimens from a single patient should be included in this study.
- Note: The specimens can be collected prior to the time that the new reagent will be evaluated in the laboratory. They must be carefully centrifuged to remove all platelets (<10 x $10^3/\mu L$), and frozen (-20°C to -70°C) in aliquots for future aPTT reagent comparisons.

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DOCUMENT NUMBER:
DOCUMENT TITLE:
DOCUMENT NOTES:

LOCATION:	**VERSION:**
DOC TYPE:	**STATUS:**

EFFECTIVE DATE:	**NEXT REVIEW DATE:**
RELEASE DATE:	**EXPIRATION DATE:**

AUTHOR:	**PREVIOUS NUMBER:**
OWNER:	**CHANGE NUMBER:**

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Comparison Testing

- Perform aPTT split testing on 25 to 30 heparinized patient samples using each of the two reagents (old aPTT reagent and new aPTT reagent) on the instrument(s) used for production.
- Plot the comparison data with the old reagent on the x-axis and the new one on the y-axis.
- Use visual or regression analysis to determine the acceptability of the comparison data and to ID/reject outliers. (e.g. $r \geq 0.95$; slope = 1.0 ± 0.1)
- Calculate the sum, mean and standard deviations of each reagent.
- Record the difference between the means of the new and old aPTT reagent

Reagent Lot rejection

A difference in reagent means or a cumulative change of more than **seven seconds** is reason for concern and requires action. Suitable actions include:

a. Rejecting the new aPTT reagent and evaluating a different lot with an acceptable variation or
b. Informing all physicians using heparin of a change in the therapeutic range and recommend that they adjust their thresholds or
c. Conducting a new heparin therapeutic range study to establish new ranges with this new lot.

Note: Bullet points b and c are very undesirable options. It would be far easier and less disruptive to evaluate a different lot with acceptable variation.

Cumulative Summation Table example

Cumulative summation of Reagent Mean Differences

Patient Data Set (New Reagent Evaluations in Sequence)					
aPTT Reagent Lots	Mean Old Lot (sec)	Mean New Lot (sec)	Difference [New - Old] (sec)	Cumulative summation (sec)	ACTION
Lot 12354	78.6	73.9	-4.7	-4.7	Accept
Lot 45135	**48.3**	**41.7**	**-6.6**	**-11.3**	**Reject**
Lot 12468	47.6	53.6	6.0	1.3	Accept
Lot 06478	71.9	72.3	0.4	1.7	Accept
Lot 79246	**62.0**	**71.2**	**9.2**	**10.9**	**Reject**
Lot 58123	62.8	60.3	-2.5	0.8	Accept

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References

- CAP CGL-A 2017 Coagulation, Limited Participant Summary p.8-10
- CAP CGS4-A 2017 Heparin Participation Summary
- CAP Hematology and Coagulation Checklist HEM.23453 Heparin Therapeutic Range 07/28/2015
- Stago USA IHN Merged LC (16-USOP-010) p. 15-17
- Stago System Correlation Instructions (15-SOP-018) 01/01/2015
- CLSI H21-A5 Collection, Transport, and Processing of Blood specimens for Testing Plasma-Based Coagulation Assays and Molecular Hemostasis Assays; Approved Guideline – Fifth Edition

Signature Manifest

Document Number: RRL-PPP-0935 **Revision:** 01

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All dates and times are in Pacific Standard Time.

Evaluating new aPTT reagents

New Document or Change Request

Name/Signature	Title	Date	Meaning/Reason
Mary Anne Umekubo (K076412) for Mary Anne Umekubo (K076412)	ASST DIR		
Gene Usher (E517068)	SECTION MANAGER	20 Oct 2017, 11:16:21 AM	Approved

Collaboration

Name/Signature	Title	Date	Meaning/Reason
Mary Anne Umekubo (K076412)	ASST DIR		
Vincent Dizon (I713793)	Director of Lab Services, Chem	20 Oct 2017, 11:49:38 AM	Complete
Gene Usher (E517068)	SECTION MANAGER	31 Oct 2017, 11:06:02 AM	Complete

Initial Approval

	Title	Date	Meaning/Reason
Ji Yeon Kim (B727360)	Physician Director, Chem Svcs	31 Oct 2017, 09:37:06 PM	Approved

Final Approval

	Title	Date	Meaning/Reason
David Quam (P092597)	Rgnl Mg Admn-Pmg Executive	09 Nov 2017, 10:06:18 AM	Approved

Set Effective Date

	Title	Date	Meaning/Reason
Vincent Dizon (I713793)	Director of Lab Services, Chem		
Mary Anne Umekubo (K076412) for Mary Anne Umekubo (K076412)	ASST DIR		
Gene Usher (E517068)	SECTION MANAGER	09 Nov 2017, 02:34:42 PM	Approved

Notify Trainers

			Meaning/Reason
Gene Usher (E517068)	SECTION MANAGER	09 Nov 2017, 02:34:43 PM	Email Sent
Vincent Dizon (I713793)	Director of Lab Services, Chem	09 Nov 2017, 02:34:43 PM	Email Sent
Mary Anne Umekubo (K076412) for Mary Anne Umekubo (K076412)	ASST DIR	09 Nov 2017, 02:34:43 PM	Email Sent

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