Heparin Calibration Verification / Linearity Test Kit

INTENDED USE
VALIDATE Heparin Calibration Verification / Linearity Test Kit solutions are assayed quality control materials intended for *in vitro* diagnostic use in the quantitative determination of linearity, calibration verification and verification of reportable range for Heparin Anti-Xa activity on automated instruments in a clinical laboratory setting by laboratory personnel. The product is intended for use on the Siemens Sysmex analyzers.

SUMMARY
Each **VALIDATE** Heparin Calibration Verification / Linearity Test Kit contains purified chemicals in a human plasma matrix. Multiple levels are provided to establish the relationship between theoretical and actual performance of the Heparin Anti-Xa analyte. The **VALIDATE** Heparin Calibration Verification / Linearity Test Kit will assist in the documentation of linearity, calibration verification and verification of linear range required by many inspection agencies. The solutions will also provide assistance when troubleshooting instrument systems, reagent problems and calibration anomalies.

Each test kit contains one bottle each of Levels 1 through 5. Each bottle contains 3.0 milliliters. There exists a linear relationship among Levels 1 through 5.

REAGENTS
Reactive Ingredients:
Purified chemicals for Heparin in a human plasma matrix.

Nonreactive Ingredients:
Preservatives and stabilizers.

Precautions and Warnings:
For In Vitro Diagnostic Use
Disposal of all waste materials should be in accordance with local guidelines.

WARNING: Potentially Biohazardous
Human source material is considered potentially biohazardous. Material of human origin used in the manufacture of this test kit was tested at the donor level using FDA or CE approved methods and found to be non-reactive for HBV, HCV and HIV. Because no test method can offer complete assurance that infectious agents are absent, these specimens should be handled and treated as potentially infectious.

STORAGE AND STABILITY
VALIDATE Heparin Calibration Verification / Linearity Test Kits are stored at -10° to -25°C.
Do NOT store in a frost-free freezer.

Test kits are stable until the expiration date printed on the bottle and storage container when handled according to instructions.

A maximum of two (2) freeze-thaw cycles is recommended when stored at -10° to -25°C.

PREPARATION
Prior to use, remove the **VALIDATE** Heparin Calibration Verification / Linearity Test Kit from storage. Do NOT thaw at room temperature, thaw for 5 minutes in 37°C water bath. Invert gently several times before dispensing.

To maximize stability, it is recommended that exposure to room temperature be minimized. Tightly cap opened bottles and return to -10° to -25ºC after dispensing.

Discard any solutions that appear to have gross bacterial contamination.

The **VALIDATE** Heparin Calibration Verification / Linearity Test Kit should be treated in the same manner as patient samples. If dilutions or pre-treatment are required as part of the testing procedure, follow the manufacturer's instructions.

MATERIALS REQUIRED BUT NOT PROVIDED
Siemens Sysmex analyzer

ASSAY
Analyze each level in replicates of 2 or 3. If following the CLSI EP6 guidelines for linearity, use a random analytical sequence to assay each level.

CALCULATION OF RESULTS
VALIDATE Calibration Verification / Linearity material is prepared in a manner such that an equal distance (delta) exists between each consecutive level. This dilution scheme is consistent with the CLSI EP6 recommendation for preparing linearity sets.

Two examples for calculating the theoretical values of Levels 1 through 5 are provided below.

Example 1:
Choose two consecutive levels and calculate the delta between the recovered values. The following example demonstrates the use of the delta between Levels 2 and 3 to calculate the theoretical value for Levels 1, 4 and 5:

Mean Recovered Values	
Level 1	1
Level 2	496
Level 3	990
Level 4	1483
Level 5	1990

Using Level 2 and Level 3 recovered values to calculate the Delta, the above data produces the following:

Level 3 - Level 2 = Delta, or (990 - 496 = 494)

Level 1 Theoretical = Level 2 Recovered - Delta, or (496 - 494 = 2)
Level 4 Theoretical = Level 3 Recovered + Delta, or (990 + 494 = 1484)
Level 5 Theoretical = Level 4 Theoretical + Delta, or (1484 + 494 = 1978)
Using the delta between Level 2 and Level 3, the theoretical value for each level would be:

Level	Theoretical (x-axis)	Recovered (y-axis)
1	2	1
2	496	496
3	990	990
4	1484	1483
5	1978	1990

NOTE: The user can select the calculated delta between any two consecutive levels to calculate the theoretical values. Typically, the user should choose an area of recovery known to be linear for the method being studied.

Example 2:
Theoretical values can be determined using the recovered values for Levels 1 and 5. Using this method, the following formulas apply:

Level 2 Theoretical = 0.75 * (Level 1) + 0.25 * (Level 5)
Level 3 Theoretical = 0.5 * (Level 1) + 0.5 * (Level 5)
Level 4 Theoretical = 0.25 * (Level 1) + 0.75 * (Level 5)

Using the recovered values for Level 1 (1) and Level 5 (1990), the following applies:

Level 2 Theoretical = 0.75 * (1) + 0.25 * (1990) = 498
Level 3 Theoretical = 0.5 * (1) + 0.5 * (1990) = 996
Level 4 Theoretical = 0.25 * (1) + 0.75 * (1990) = 1493

Level	Theoretical (x-axis)	Recovered (y-axis)
1	1	1
2	498	496
3	996	990
4	1493	1483
5	1990	1990

After theoretical values are calculated, for each analyte plot the expected (Theoretical) value on the x-axis versus the Recovered value on the y-axis using standard linear graph paper. If the system is linear, the plot should approximate a straight line. The point at which the line is no longer straight can be used to determine the limit of linearity or the reportable range.

Data reduction is available from LGC Maine Standards. Commercially available linear regression software may also be used. The software should provide data point display and x-y graphical presentation. Linear regression should be interpreted using standard statistical analysis and the results should be compared with the instrument manufacturer's claims for linearity or with individual laboratory performance requirements. The degree of acceptable nonlinearity is an individual judgment based on methodology, clinical significance and medical decision levels of the test analyte.

LIMITATIONS
VALIDATE Heparin Calibration Verification / Linearity Test Kit solutions are not intended for use as calibration materials. They are limited for use with: Siemens Sysmex analyzers.

EXPECTED VALUES
VALIDATE Heparin Calibration Verification / Linearity Test Kits are manufactured such that a linear relationship exists among Levels 1 through 5.

TYPICAL VALUES
Actual results obtained may vary depending on instrumentation and methodology. Results may also be dependent on the accuracy of the instrument / reagent system calibration. The degree of acceptable nonlinearity is an individual judgment based on methodology, clinical significance and medical decision levels of the test analyte.

VALIDATE Heparin Calibration Verification / Linearity Test Kit solutions are manufactured such that an equal distance (delta) exists between levels as recommended by CLSI EP6 for accessing linearity. Typical, not lot specific, recovered values for the Siemens Sysmex Low Level 1 and High Level 5 are presented in the table below. Actual expected values will be included in the kit lot Certificate of Analysis sheet for each Level 1 and Level 5. You can find the **VALIDATE** Heparin Certificate of Analysis at: http://www.mainestandards.com/products/doc-search. Typical values for Mid-Levels are calculated based on an equal distance (delta) between levels.

Typical Values by Level

VALIDATE Heparin 903se							
Instrument	Analyte	Units	Level 1	Level 2	Level 3	Level 4	Level 5
Siemens Sysmex CS-2500	Heparin Anti-Xa	IU/mL	0.13	0.46	0.78	1.11	1.43

PRECISION AND REPRODUCIBILITY

Product precision and reproducibility were established following the CLSI EP05-A3 standard requirements. Three lots of **VALIDATE** Heparin Anti-Xa were tested with one lot of Siemens Sysmex reagent and quality controls on the Siemens Sysmex instrument system over 20 days, 2 runs per day, 2 replicates per run for Level 1 through Level 5 to obtain a total of eighty (80) replicates per kit Level per individual lot (total of 240 replicates per kit Level over 3 lots).

VALIDATE Heparin Anti-Xa Precision Study Summary Three Individual Lots – Siemens Sysmex

VALIDATE Heparin Precision Study Summary Across All Lots (AC08918RD, AH08918RD, AM08918RD IU/mL) - Siemens CS 2500												
Sample	N	mean	Within-Run		Between-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Level 1	240	0.13	0.007	5.6%	0.006	4.4%	0.000	0.0%	0.000	0.0%	0.009	7.1%
Level 2	240	0.41	0.010	2.4%	0.013	3.1%	0.007	4.3%	0.005	1.2%	0.018	4.5%
Level 3	240	0.69	0.015	2.1%	0.019	2.7%	0.011	1.6%	0.000	0.0%	0.026	3.8%
Level 4	240	0.99	0.014	1.4%	0.026	2.7%	0.019	2.0%	0.009	0.9%	0.037	3.7%
Level 5	240	1.31	0.024	1.8%	0.031	2.4%	0.029	2.2%	0.008	0.6%	0.050	3.8%

Reproducibility was evaluated with the **VALIDATE** Heparin Anti-Xa kit containing 5 levels following the product package insert instructions. One lot of **VALIDATE** Heparin Anti-Xa Calibration Verification / Linearity Test Kit was tested with one lot of Siemens Sysmex reagent and quality controls on three instruments, multi-site, over 5 days, with 1 run per day of Level 1 through Level 5, with 5 replicates per run to obtain seventy-five (75) replicates per kit level.

VALIDATE Heparin Reproducibility Study - Siemens CS 2500 Lot AC08918RD IU/mL								
Sample	N	mean	Repeatability		Within Laboratory		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV
Level 1	75	0.13	0.006	4.4%	0.010	7.6%	0.011	8.9%
Level 2	75	0.38	0.008	2.2%	0.012	3.1%	0.026	6.8%
Level 3	75	0.67	0.011	1.6%	0.013	2.0%	0.032	4.8%
Level 4	75	0.95	0.013	1.3%	0.019	2.0%	0.050	5.2%
Level 5	75	1.22	0.017	1.4%	0.027	2.2%	0.099	8.1%

ORDERING INFORMATION

ORDER NO.: 903se

VALIDATE Heparin
Calibration Verification / Linearity Test Kit: 5 x 3 mL

Contact Information:
1-800-377-9684 (United States and Canada)
+1-207-892-1300 (Outside the United States and Canada)
+1-207-892-2266 Fax
msc.sales@LGCGroup.com
msc.techsupport@LGCGroup.com
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Please allow 5 to 7 days for delivery.

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Symbols – The following symbols may be used where applicable in labeling for Maine Standards Company products:

LOT **Lot Number**

Expiration Date

Manufacturer

Storage Temperature

IVD ***In Vitro* Diagnostic Medical Device**

REF **Catalog Number**

Insert

Biological Risk

CE EC REP Wellkang Ltd (www.CE-marking.eu) 29 Harley St., London W1G 9QR, UK

For a list of countries in which VALIDATE® is registered see:
http://www.mainestandards.com/Products/ce_reg.php

A worksheet to assist with manually calculating theoretical values can be found at www.mainestandards.com/Products or by calling Customer Support at 1-800-377-9684

Rx Only