**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION**
**DECISION SUMMARY**

**A. 510(k) Number:**
k092937

**B. Purpose for Submission:**
New device - combining two previously cleared devices into a single test kit.

**C. Measurand:**
Calibrator for heparin (unfractionated heparin and Low Molecular Weight Heparin) activity

**D. Type of Test:**
Quantitative

**E. Applicant:**
Diagnostica Stago, Inc.

**F. Proprietary and Established Names:**
STA® - Hybrid Hep Calibrator

**G. Regulatory Information:**

1. Regulation section:
   21 CFR 864.7525 Heparin assay
   21 CFR 862.1150, Calibrator
2. Classification:
   Class II
3. Product code:
   KFF, Assay, heparin
   JIT, Calibrator, secondary
4. Panel:
   81 Hematology

**H. Intended Use:**

1. Intended use(s):
   The STA® - Hybrid Hep Calibrator is a set of calibrator plasmas intended for use with analyzers of the STA® line suitable to these reagents, for the calibration of heparin (UFH and LMWH) activity assay by measuring the anti-Xa activity using the chromogenic method, STA® - Rotachrom® Heparin.
2. Indication(s) for use:
   Same as intended use
3. Special conditions for use statement(s):
   Not applicable
4. Special instrument requirements:
   Not applicable

**I. Device Description:**
STA® - Hybrid Hep Calibrator is a new device that bundles two of the company's previously FDA cleared devices, STA® - Hepanorm® H and STA®- Calibrator HBPM/LMWH into a single kit. The primary difference between the subject product and predicate devices is that it contains a set of calibration plasmas for calibration of assays of unfractionated heparin (UFH) and Low Molecular Weight Heparin

(LMWH) bundled together in a single kit.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):
   STA® - Calibrator HBPM/LMWH Kit
   STA® - Hepanorm® H {formerly cleared as Hepanorm® Calibration Plasma Set}
2. Predicate 510(k) number(s):
   k010350
   k854762
3. Comparison with predicate:

| Similarities | | | |
|---|---|---|---|
| Item | Device | Predicate | Predicate |
| Device Name | **STA® - Hybrid Hep Calibrator** | **STA® - Calibrator HBPM/LMWH** | **STA® - Hepanorm® H** |
| Intended Use | The STA® - Hybrid Hep Calibrator is a set of calibrator plasmas intended for use with analyzers of the STA® line suitable with these reagents, for the calibration of heparin (UFH and LMWH) activity assay by measuring the anti-Xa activity using the chromogenic method, STA® - Rotachrom® Heparin. | The STA® - HBPM/LMWH Calibrator kit provides a set of calibrator plasmas intended for use by analyzers of the STA® brand name, for the calibration of low molecular weight heparin (LMWH) assays based on the anti-Xa principle. (STA® - Rotachrom® Heparin) | The STA® - Hepanorm® H kit provides a set of calibrator plasmas intended for use by analyzers of the STA® brand name, for the calibration of unfractionated heparins (UFH) assays based on the anti-Xa principle. (STA® - Rotachrom® Heparin, STA® - Staclot® Heparin). |
| Matrix | Lyophilized human plasmas reconstituted with distilled water, used in IVD analyzers. | Same | Same |
| Traceability of calibrator plasma | The LMWH levels are determined against the 01/608 International Standard for LMWH established in 2003. The UFH levels are determined against the 97/578 International Standard for UFH established in 1998. | Same | Same |
| Analytes | LMWH/ UFH | LMWH | UFH |
| Storage | 2-8 °C until Expiration date (24 months) | Same | Same |
| Format | Lyophilized | Same | Same |
| Open vial stability | 4 hours on board the analyzers of the STA® line | Same | Same |

There is no difference between the predicates and the new device.

**K. Standard/Guidance Document Referenced (if applicable):**

EP5-A2 Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition.

**L. Test Principle:**

The STA® - Hybrid Hep Calibrator is designed to operate utilizing the STA® product line of IVD coagulation analyzers for the purpose of creating calibration curves for assays of heparin by measuring the anti-Xa activity based on a chromogenic method.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

*a. Precision/Reproducibility:*

Two samples containing different levels of heparin were tested using two different lots of STA® - Hybrid Hep Calibrator for the calibration. Each sample was tested for 22 operating days in two different laboratories. During each of the testing days, two separate runs were performed with alternatively two lots of STA® - Rotachrom® Heparin kit, on two analyzers, by a minimum of two operators.

Precision was estimated separately for each sample using the five components of precision described by the CLSI guidance: repeatability, between-run precision, within-day precision, between-day precision and within-laboratory precision (see results in tables 1-3 provided below).

Table 1 - Precision data for STA® - Hybrid Hep Calibrator in the Laboratory 1:

| **Laboratory 1** | | | Sample 1 (UFH) | Sample 2 (LMWH) |
|---|---|---|---|---|
| Theoretical concentration at which claim is made (spiked samples) | | IU/mL | 0.30 | 0.89 |
| Actual mean | | IU/mL | 0.27 | 0.89 |
| Point estimate of repeatability | SD | IU/mL | 0.01638 | 0.02459 |
| | CV | % | 6.1 | 2.8 |
| Point estimate of between-run | SD | IU/mL | 0.01264 | 0.03117 |
| | CV | % | 4.7 | 3.5 |
| Point estimate of within-day | SD | IU/mL | 0.01658 | 0.02174 |
| | CV | % | 6.1 | 2.4 |
| Point estimate of between-day | SD | IU/mL | 0.00013 | 0.00000 |
| | CV | % | 0.0 | 0.0 |
| Point estimate of within-laboratory precision | SD | IU/mL | 0.02358 | 0.03970 |
| | CV | % | 8.7 | 4.5 |
| Actual number of days involved in the experiment | | | 44 | 44 |
| Actual total number of runs | | | 88 | 88 |
| Total number of observations | | | 176 | 176 |
| Number of instruments used in evaluation | | | 2 | 2 |

Table 2 – Precision performance claims in Laboratory 2

| **Laboratory 2** | | | Sample 1 (UFH) | Sample 2 (LMWH) |
|---|---|---|---|---|
| Theoretical concentration at which claim is made (spiked samples) | | IU/mL | 0.30 | 0.89 |
| Actual mean | | IU/mL | 0.28 | 0.91 |
| Point estimate of repeatability | SD | IU/mL | 0.01344 | 0.02800 |
| | CV | % | 4.8 | 3.1 |
| Point estimate of between-run | SD | IU/mL | 0.01679 | 0.03322 |
| | CV | % | 6.0 | 3.7 |
| Point estimate of within-day | SD | IU/mL | 0.01525 | 0.02092 |
| | CV | % | 5.5 | 2.3 |
| Point estimate of between-day | SD | IU/mL | 0.00005 | 0.00000 |
| | CV | % | 0.0 | 0.0 |
| Point estimate of within-laboratory precision | SD | IU/mL | 0.02256 | 0.04345 |
| | CV | % | 8.1 | 4.8 |
| Actual number of days involved in the experiment | | | 44 | 44 |
| Actual total number of runs | | | 88 | 88 |
| Total number of observations | | | 176 | 176 |
| Number of instruments used in evaluation | | | 2 | 2 |

Table 3 – Site-to-site precision performance of STA – Hybrid Hep Calibrator

| **Laboratory 1 + Laboratory 2** | | | Sample 1 (UFH) | Sample 2 (LMWH) |
|---|---|---|---|---|
| Theoretical concentration at which claim is made (spiked samples) | | IU/mL | 0.30 | 0.89 |
| Actual mean | | IU/mL | 0.27 | 0.90 |
| Estimate of repeatability | SD | IU/mL | 0.01513 | 0.02638 |
| | CV | % | 5.5 | 2.9 |
| Estimate of between-run | SD | IU/mL | 0.01481 | 0.03223 |
| | CV | % | 5.4 | 3.6 |
| Estimate of within-day | SD | IU/mL | 0.01641 | 0.02305 |
| | CV | % | 6.0 | 2.6 |
| Estimate of between-day | SD | IU/mL | 0.00010 | 0.00000 |
| | CV | % | 0.0 | 0.0 |
| Inter-Laboratory variability | SD | IU/mL | 0.02347 | 0.04165 |
| | CV | % | 8.5 | 4.6 |
| Actual number of days involved in the experiment | | | 88 | 88 |
| Actual total number of runs | | | 176 | 176 |
| Total number of observations | | | 352 | 352 |
| Number of instruments used in evaluation | | | 4 | 4 |

b. *Linearity/assay reportable range:*
The entire range claimed for the assay kit is 0.1 to 2.0 IU/mL.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Traceability: The UFH levels are determined against the 97/578 International Standard for UFH established in 1998. The LMWH levels are determined against the 01/608 International Standard for LMWH established in 2003.

Stability: Closed vial: In the lyophilized state the STA® - Hybrid Hep Calibrator plasmas remain stable until the expiration date printed on the box when stored at 2-8°C. This corresponds to 24 months after the date of manufacture.
Open vial: After reconstitution with distilled water, STA® - Hybrid Hep Calibrator reagents are stable for 4 hours on board the STA Satellite® (k082248), STA Compact® (k961579) and STA-R® (k983460) analyzers.
The acceptance criteria for the 5 calibrator reagents are as follows:
Reagent 1: ≤0.10 IU/mL
Reagent 2: 0.20 – 0.35 IU/mL
Reagent 1: 0.40 – 0.60 IU/mL
Reagent 1: 0.70 - 1.10 anti-Xa IU/mL
Reagent 1: 1.60 – 2.00 anti-Xa IU/mL

**Calibrator Value Assignment:**
For each level of calibrator the heparin (UFH or LMWH) value corresponds to the mean of a minimum of four determinations performed with four instruments, using at least two (2) different lots of STA®-Rotachrom® Heparin (K010455). The determinations are carried out by a minimum of two (2) laboratory technicians. The assay calibration is carried out with a pool of plasmas supplemented with the International standard for UFH or LMWH and/or other lots of STA® - Hybrid Hep Calibrator.

Table 4 - Determination of heparin level for a given lot of STA® - Hybrid Hep Calibrator.

| Laboratory technicians | Analyzer | STA® - Rotachrom® Heparin Lot | Heparin level (IU/ml) | | | | |
|---|---|---|---|---|---|---|---|
| | | | Reagent 1 | Reagent 2 | Reagent 3 | Reagent 4 | Reagent 5 |
| 1 | 1 | 061772 | 0.01 | 0.28 | 0.54 | 1.01 | 1.95 |
| 2 | 2 | 060871 | 0.01 | 0.27 | 0.49 | 0.97 | 1.96 |
| 1 | 1 | 061772 | 0.00 | 0.34 | 0.58 | 0.98 | 1.91 |
| 2 | 2 | 060871 | 0.00 | 0.30 | 0.56 | 0.93 | 1.88 |
| 3 | 3 | 062553 | / | / | / | 0.97 | 2.13 |
| 4 | 4 | 100973 | / | / | / | 0.98 | 2.00 |
| 3 | 3 | 062553 | / | / | / | 1.01 | 2.07 |
| 4 | 4 | 100973 | / | / | / | 0.95 | 1.97 |
| 4 | 5 | 100973 | / | 0.30 | 0.48 | / | / |
| 1 | 6 | 061772 | / | 0.29 | 0.48 | / | / |
| 4 | 5 | 100973 | - 0.02 | 0.34 | 0.54 | / | / |
| 1 | 6 | 061172 | 0.00 | 0.33 | 0.57 | / | / |
| $\bar{\bar{X}}$ | | | 0.00 | 0.31 | 0.53 | 0.97 | 1.98 |

Table 5 - After verification of the consistency of the results obtained, the heparin values assigned to the STA® -Hybrid Hep Calibrator are as follows:

| | |
|---|---|
| Reagent 1 - lyophilized human plasma free of heparin | Reagent 1: 0.00 IU/ml |
| Reagent 2 - lyophilized human plasma containing a well defined quantity of UFH | Reagent 2: 0.31 IU/ml |
| Reagent 3 - lyophilized human plasma containing a well defined quantity of UFH that is greater than that of reagent 2 | Reagent 3: 0.53 IU/ml |
| Reagent 4 - lyophilized human plasma containing a well defined quantity of LMWH | Reagent 4: 0.97 anti-Xa IU/ml |
| Reagent 5 - lyophilized human plasma containing a well defined quantity of LMWH that is greater than that of reagent 4 | Reagent 5: 1.98 anti-Xa IU/ml |

STA® - Hybrid Hep Calibrator lot used as an example is 100773

*d. Detection limit:*
Not applicable

*e. Analytical specificity:*
Not applicable

*f. Assay cut-off:*
Not applicable

2. Comparison studies:
   *a. Method comparison with predicate device:*
   Not applicable
   *b. Matrix comparison:*
   Not applicable
3. Clinical studies:
   *a. Clinical Sensitivity:*
   Not applicable
   *b. Clinical specificity:*
   Not applicable
   c. Other clinical supportive data (when a. and b. are not applicable):
   Not applicable
4. Clinical cut-off:
   Not applicable
5. Expected values/Reference range:
   The Expected Values are designated in the Assay Value Insert provided for each respective lot.

**N. Proposed Labeling:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

**O. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.