

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY  
ASSAY ONLY TEMPLATE**

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

K053111

**B. Purpose for Submission:**

To obtain clearance for the STA<sup>®</sup> - Cephascreen<sup>®</sup> kit.

**C. Measurand:**

Activated partial thromboplastin time (APTT)

**D. Type of Test:**

Clotting assay

**E. Applicant:**

Diagnostica Stago, Inc.

**F. Proprietary and Established Names:**

STA<sup>®</sup> - Cephascreen<sup>®</sup> kit

**G. Regulatory Information:**

1. Regulation section:

21 CFR 864.7925

2. Classification:

Class II

3. Product code:

GFO

4. Panel:

81 Hematology

**H. Intended Use:**

1. Intended use(s):

The STA<sup>®</sup> - Cephascreen<sup>®</sup> kits provide reagents for the determination of the activated partial thromboplastin time (APTT) in citrated plasma on the STA<sup>®</sup> line of analyzers suitable to these reagents.

2. Indication(s) for use:

The STA<sup>®</sup> - Cephascreen<sup>®</sup> kits provide reagents for the determination of the activated partial thromboplastin time (APTT) in citrated plasma on the STA<sup>®</sup> line of analyzers suitable to these reagents.

3. Special conditions for use statement(s):

Not applicable

4. Special instrument requirements:

STA<sup>®</sup> line of analyzers suitable to these reagents

**I. Device Description:**

The STA<sup>®</sup> - Cephascreen<sup>®</sup> kits provide reagents for the determination of the activated partial thromboplastin time (APTT) by the STA<sup>®</sup> line of analyzers. The reagent is packaged in two ways 4-ml vials (REF 00308) and 10-ml vials (REF 00310). The reagent contains cephalin (platelet substitute) prepared from rabbit cerebral tissues and a polyphenolic activator in a buffered medium.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

STA<sup>®</sup> - C.K. Prest<sup>®</sup> kit

2. Predicate 510(k) number(s):

K792048

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Reagent for the	Same

<b>Similarities</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
	determination of the APTT	
Reagent Composition: Platelet Substitute	Cephalin	Same
Sample Type	Citrated human plasma	Same
Stability	In vials at 2-8 C until expiration	Same

<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Reagent Composition: Platelet Activator	Polyphenolic activator	Kaolin
Stability	7 or 10 days on analyzer	24 or 48 hours on analyzer
Shelf life	15 months	24 months
Reagent format	Liquid	Freeze-dried

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

Not applicable

**L. Test Principle:**

The APTT involves recalcification of plasma in the presence of a standardized amount of cephalin (platelet substitute) and a factor XII activator (polyphenolic component).

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

1. Analytical performance:

*a. Precision/Reproducibility:*

Intra-assay precision was assessed by testing 21 lyophilized normal and abnormal control plasmas with three different lots of STA<sup>®</sup> - Cephascreen<sup>®</sup> on the STA<sup>®</sup> analyzer. The CVs obtained for both samples using all three lots were  $\leq 1\%$ .

Inter-assay precision was assessed by testing lyophilized normal and abnormal control plasmas over 10 different test runs using STA<sup>®</sup> - Cephascreen<sup>®</sup> on the STA<sup>®</sup> analyzer. The CVs obtained for both were  $\leq 1.5\%$ .

b. *Linearity/assay reportable range:*

Not applicable

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

Unopened vials remain stable for 15 months after the date of manufacture when stored at 2-8 °C as verified by real time stability studies utilizing three samples (normal and abnormal) and three different lots of Cephascreen<sup>®</sup> reagent. No clinically significant differences in clotting times were obtained between newly manufactured reagent and reagent stored for 9, 12, and 15 months post-manufacture.

Opened vials of STA<sup>®</sup> - Cephascreen<sup>®</sup> (with STA<sup>®</sup> - Reducer and perforated cap) is stable for 7 days (STA<sup>®</sup> - Cephascreen<sup>®</sup> 4) or 10 days (STA<sup>®</sup> - Cephascreen<sup>®</sup> 10) on board STA<sup>®</sup> Analyzers. Normal and abnormal lyophilized plasmas were tested with three vials from three different lots of STA<sup>®</sup> - Cephascreen<sup>®</sup> 4 and STA<sup>®</sup> - Cephascreen<sup>®</sup> 10 when the reagent was immediately opened and then following 7 and 10 days respectively on board the STA analyzer.

d. *Detection limit:*

Not applicable

e. *Analytical specificity:*

Interference

Thirty four patient plasmas containing varying levels of FVIII as determined by STA<sup>®</sup> –Deficient VIII were tested with STA<sup>®</sup> - Cephascreen<sup>®</sup> on the STA<sup>®</sup>-R analyzer. For all samples tested with low FVIII levels, the APTT result was above the upper limit (34.9 seconds) of the expected reference range.

Twenty six patient plasmas containing varying levels of FIX as determined with STA<sup>®</sup> –Deficient IX were tested with STA<sup>®</sup> - Cephascreen<sup>®</sup> on the STA<sup>®</sup>-R analyzer. Twenty four of the 26 samples tested with low FVIII levels had an APTT result above the upper limit (34.9 seconds) of the expected reference range.

To assess the responsiveness of STA<sup>®</sup> - Cephascreen<sup>®</sup> to unfractionated heparin (UFH), 60 patient plasmas containing UFH were tested on the STA<sup>®</sup> analyzer. Heparin levels were determined using STA<sup>®</sup> – Rotachrom Heparin. Study results indicated that the majority of samples with heparin levels in the therapeutic range (0.3-0.7 IU/ml) had prolonged APTT values. Of the patients

tested, only one sample with therapeutic levels of heparin had a normal APTT.

To assess the effect of Low Molecular Weight Heparins (LMWH) on STA<sup>®</sup> - Cephascreen<sup>®</sup>, 60 patient plasmas containing varying levels of LMWH, as determined by STA<sup>®</sup> – Rotachrom Heparin, were evaluated on the STA<sup>®</sup> analyzer. The effect on the APTT was minimal.

To assess the sensitivity of STA<sup>®</sup> - Cephascreen<sup>®</sup> 10 LA positive plasmas (as determined by Rosner Index) of varying strength were tested on the STA<sup>®</sup>-R analyzer. LA positivity was determined by the Platelin LS reagent. Four of the 10 samples were within normal range. The STA<sup>®</sup> - Cephascreen<sup>®</sup> was developed to demonstrate relative insensitivity to LA.

*f. Assay cut-off:*

User defined

## 2. Comparison studies:

### *a. Method comparison with predicate device:*

The STA<sup>®</sup> - Cephascreen<sup>®</sup> kits were compared with the predicate device STA<sup>®</sup> - C.K. Prest<sup>®</sup> (K792048). The two kits were run in parallel as described in their respective package inserts to determine the APTT in 125 plasmas comprised of the following: normal plasma, plasma from patients receiving UFH and LMWH, plasma from patient receiving oral anticoagulant therapy, LA positive plasma, and plasma from patients with factor VIII and IX deficiency. Studies resulted in a correlation coefficient (r) of 0.943 and regression equation of  $y_{(STA^{\circledR} - Cephascreen^{\circledR})} = 0.78 \times (STA^{\circledR} - Cephascreen^{\circledR}) + 8.2$ .

Additional correlation studies were performed at three locations in France between the predicate device and the proposed device on the STA or the STA-R instruments. At each site 130-135 plasmas were collected from presumed normal individuals as well as individuals with a variety of pathologies including patients with known Factor VIII or IX deficiencies, Lupus Anticoagulants or patients receiving UFH, LMWH, or vitamin K antagonists. A total of 395 samples tested yielded the following correlation data:  $Y = 0.81x + 6.42, r = 0.94$ .

### *b. Matrix comparison:*

Not applicable

## 3. Clinical studies:

### *a. Clinical Sensitivity:*

Not assessed

*b. Clinical specificity:*

Not assessed

*c. Other clinical supportive data (when a. and b. are not applicable):*

4. Clinical cut-off:

User defined

5. Expected values/Reference range:

The STA<sup>®</sup> - Cephascreen<sup>®</sup> reference range was determined by testing citrated plasmas obtained from 360 presumed healthy individuals (obtained from hospitals in France). Testing was performed on multiple days using three STA<sup>®</sup> analyzers and one STA-R<sup>®</sup> analyzer. The analyzers yielded a reference range of 23.7 – 34.9 seconds ( $\pm$  2SD).

Each laboratory should establish its own normal ranges and acceptable controls values for their particular local patient population. In general, values are considered normal if they fall within the range of mean  $\pm$  2 standard deviations.

**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.

