K082631

DEC 17 2008

Section 7: 510(k) Summary

510(k) Substantial Equivalence Determination Decision Summary
Assay Only Template

This summary of 510(k) safety and effectiveness is being submitted in accordance with the requirements of the Safe Medical Device Act of 1990 and 21 CFR 807.92.

A. 510(k) Number

B. Date and Purpose for Submission
September 9, 2008

To obtain clearance for the ThromboTek PS*e* assay, a functional (clotting) assay for the determination of Protein S activity in human plasma.

C. Measurand
Protein S

D. Type of Test
Quantitative factor determination, clotting assay.

E. Applicant
r^2 Diagnostics, Inc
1801 Commerce Drive
South Bend, IN 46628

F. Proprietary and Established Name
ThromboTek PS*e*

G. Regulatory Information
1. Regulation Section
864.7290, Factor Deficiency Test

2. Classification
II

3. Product Code
GGP

4. Panel
Hematology

H. Intended Use

1. Intended Use

ThromboTek PS*e* is intended for the quantitative determination of functional Protein S activity in human plasma.

2. Indication(s) for Use

ThromboTek PS*e* is intended for the quantitative determination of functional Protein S activity, such as when identifying inherited or acquired Protein S deficiency.

3. Special conditions for use statement(s)

Not applicable

4. Special instrument requirements

Not applicable

I. Device Description

ThromboTek PS*e* is a tissue factor pathway based clotting assay. The assay activator is a lyophilized preparation incorporating rabbit thromboplastin, calcium, buffer, and stabilizers. The remaining components of the assay are lyophilized activated Protein C, lyophilized human plasma depleted of Protein S, Imidazole buffered saline for use as a plasma diluent, and deionized water containing a preservative for reconstitution of the lyophilized components.

J. Substantial Equivalence Information

1. Predicate device name(s)

StaClot® Protein S

1. Predicate device 510(k) number

K913424

2. Comparison with predicate

Table 7-1: Comparison of submitted device (ThromboTek PSe) to predicate device (StaClot Protein S)		
Similarities		
Item	Submitted Device	Predicate Device
Intended use	Quantitative determination of function Protein S activity.	Quantitative determination of function Protein S activity.
Patient sample	Citrated human plasma	Citrated human plasma
Measurement principle	Protein S is rate limiting in a clotting reaction.	Protein S is rate limiting in a clotting reaction.
Format of assay components	Lyophilized activator, lyophilized aPC, lyophilized Protein S deficient plasma	Lyophilized activator, lyophilized aPC, lyophilized Protein S deficient plasma
Analyte	Protein S activity	Protein S activity
Differences		
Item	Submitted Device	Predicate Device
Assay linearity	10%-156% (max tested)	10%-105% (per Directional Insert)
Reconstituted Stability	RT: 8 hrs 2-8C: 24 hrs	RT: 4 hrs 2-8C: 4 hrs (per Directional Insert)
Analytical Sensitivity	1%	8% (per Directional Insert)
Remaining components necessary to run the assay	Imidazole buffered saline and reconstitution solution (water) are provided in kit.	Owen-Koller buffer and calcium chloride are purchased separately, and reconstitution grade water is provided by user

K. Standard/Guidance Documents Referenced (if applicable)
Not applicable

L. Test Principle
Thromboplastin is a tissue-derived complex incorporating the protein Tissue Factor (TF) associated with lipid vesicles. When Thromboplastins are added to plasmas the endogenous Factor VII (FVII) or activated Factor VII (FVIIa) in the plasma complex with the Tissue Factor and lipid vesicle in the presence of calcium, which then activates the Tissue Factor pathway of blood coagulation. This TF/FVIIa complex activates Factor X (FX) to activated FX (FXa). Factor Xa complexes with activated Factor V (FVa) on a lipid surface in the presence of calcium to form the prothrombinase complex. The prothrombinase complex activates Prothrombin to Thrombin. Thrombin, without any cofactors or ion dependency, will cleave Fibrinogen to Fibrin, leading to formation of a solid clot.

Activated Protein C (aPC) in the presence of its cofactor Protein S (PS) degrades activated Factor Va (and VIIIa), reducing the catalytic efficiency of the prothrombinase complex. When the assay conditions are chosen such that an excess of aPC is present and the concentration of Protein S in the patient sample is rate limiting, the time to clot of the patient plasma becomes proportional to the

concentration of the patient PS and can be used to quantify the PS activity in the sample.

M. Performance Characteristics (if/when applicable)

Performance evaluation of the ThromboTek PS*e* kit included studies of precision, linearity, analytical sensitivity, common interferants, normal range, correlation with the StaClot® kit, and reconstituted and accelerated stability. The method, samples, reagents, and results of each study are described in detail in section 23, Performance Data. No bench (section 20), animal (section 21), or clinical (section 22) testing was required. Summaries of the studies are:

Precision: Precision estimates of three lots of ThromboTek PS*e* were determined in a two run per day, twenty day exercise using a normal plasma and an abnormal plasma as described in the CLSI guideline EP5-A2 (7). The average precision results as %CV were:

Plasma	Repeatability	Total
Normal	4.9%	5.7%
Abnormal	7.8%	9.2%

Linearity: Linearity studies of three lots of ThromboTek PS*e* were determined on a Stago ST4 analyzer. The ThromboTek PS*e* assay was linear from 10% Protein S to the maximum tested concentration of 156% Protein S.

Analytical Sensitivity: The lower limit of detection for three lots of ThromboTek PS*e* were determined by replicate measurement of IBS alone as the sample on an AMAX 200 analyzer in mechanical mode, and the % PS activity was calculated from the sum of the mean and 3 standard deviations. The lower limit of detection of the assay was 1% PS.

Interferences: Interference studies of multiple lots of ThromboTek PS*e* were determined on an AMAX 200 analyzer in mechanical mode. Interferant was spiked into pooled normal plasma and a dilution series prepared. The maximum concentration tolerated in the assay was defined as the highest concentration of interferant wherein any consistent shift relative to the recovered value of the base PNP was less than 10%. The maximum concentrations were:

Interferant class	Added interferant	Maximum concentration tested	Maximum tolerated concentration
Hemolysis	Hemoglobin	500 mg/dL	500 mg/dL
Icterus	Unconjugated bilirubin	20 mg/dL	20 mg/dL
Lipemia	IntraLipid®	2,000 mg triglyceride/dL	2,000 mg triglyceride/dL
Heparin	Heparin	2.0 Unit/mL	1.0 U/mL

Normal Reference Range:
In a representative study one hundred twenty healthy donors were analyzed for Protein S activity with each of three lots of ThromboTek PS*e* on an AMAX 200 analyzer in mechanical mode. Assay calibration was performed using the SSC/ISTH Secondary Coagulation Standard Lot #3 available from NIBSC. The geometric means and standard deviations were calculated, and the ranges were calculated as the mean +/- 2 standard deviations. The results were:

Donors	Number	Mean % PS	Range %PS
All	120	120%	47% - 193%
Males only	35	135%	62% - 209%
Females only	85	114%	45% - 183%

Method Comparison:
A total of one hundred seventy-four patient samples were assayed for Protein S activity with multiple lots of ThromboTek PSe and two lots of another commercially available Protein S activity assay. The data was collected in two sites, one using an AMAX 200 analyzer and the other a STart4 analyzer. As determined by Kruskal-Wallis analysis the data was pooled and then further analyzed by linear regression. The correlation coefficient was 0.895 (95% CI, 0.875-0.912) and the coefficient of determination was 0.801, with a slope and intercept of 1.71 and -8.59 respectively.

Reconstituted Stability
The reconstituted stability of the ThromboTek PSe kit was assessed by longitudinal studies of three lots. The recoveries of two control plasmas were assessed at the initial reconstitution of each kit, and thereafter at periodic time points. The kit components were stored capped when not in use and freshly reconstituted control plasmas were prepared at each time point. With criteria of an age-related trend and a maximum shift of twice the precision CV, the predicted reconstituted stability of the ThromboTek PSe kit is 24 hours when stored at 2-8°C and 8 hours when stored at room temperature (23-25°C).

Accelerated Stability:
Expiry dating was predicted by a heat stress accelerated stability study of one lot of ThromboTek PSe. The study used two different sets of the kit lyophilized components, with one set stressed at 37°C for up to 25 days and the second set at

45°C for up to 7 days. Thereafter three lots of control plasmas were assayed with the unstressed and stressed components, and assessed for any age-related shift in recoveries. With criteria of an age-related trend and a maximum shift of 10%, the predicted expiry dating of the ThromboTek PSe kit is 2 years when stored at 2-8°C.

N. Proposed labeling

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

The label text for the directional insert and for the vial and box labels is included in section 15.

O. Conclusion

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

P. Other Supportive Information

Q. Administrative Information

1. Applicant contact information

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

R2 Diagnostics, Inc.
C/o Marc D. Goldford
1801 Commerce Drive
South Bend, Indiana 46628

Re: k082631
Trade/Device Name: Thrombo Tek PSe
Regulation Number: 21 CFR 864.7290
Regulation Name: Factor Deficiency Test
Regulatory Class: Class II
Product Code: GGP
Dated: November 19, 2008
Received: November 20, 2008

DEC 1 7 2008

Dear Mr. Goldford:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed

predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

for Marian Chan, PhD
Acting Division Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Section 6: Indication for Use Statement

Indication for Use

510(k) Number (if known): K082631

Device Name: ThromboTek PS*e*

Indication For Use: r^2 Diagnostics' ThromboTek PS*e* Protein S assay is used for the quantitative determination of functional Protein S activity in human plasma.

Prescription Use X And/Or Over the Counter Use_____
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K082631