

K964934

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9.0 510(k) Summary

510(k) SUMMARY

THROMBONOSTIKA F1.2

This summary of safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and the final rule under 21 CFR 807.92 published December 14, 1994.

(a) (1) The submitter's name, address, telephone number, a contact person, and the date the summary was prepared:

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Date 510(k) Summary Prepared:	December 6, 1996

(a) (2) The name of the device, including the trade or proprietary name if applicable, the common or usual name, and the classification name, if known:

Trade/Proprietary Name:	Thrombonostika F1.2
Common/ Usual Name:	ELISA for Prothrombin Fragment 1.2
Classification Name:	Prothrombin Activation Fragment 1.2 (F1.2)

(a) (3) An identification of the legally marketed device to which the submitter claims substantial equivalence.

Device Equivalent to: Thrombonostika F1.2 (K911434)

(a) (4) A description of the device(System)

Thrombonostika F1.2 is a two-stage enzymed-linked immunosorbent assay for the prothrombin activation peptide F.12. The high specificity of the solid-phase anti-F1.2 monoclonal antibody allows quantitation of nanomolar F1.2 in the presence of micromolar prothrombin that is typically found in plasma. Rabbit polyclonal antibodies to the calcium-dependent conformer of prothrombin (i.e., the amino terminal region present on both prothrombin and F1.2) coupled to horseradish peroxidase (HRP) serves as the conjugate with tetramethylbenzidine (TMB) used as the substrate.

In the first stage, test sample or calibrator is incubated with a monoclonal F1.2-specific antibody (murine) coated on a microelisa well. F1.2 binds to the solid-phase antibody. Following an incubation, unbound proteins (including prothrombin) are aspirated and the well washed with buffer. In the second stage, conjugate (rabbit) labeled with HRP is added. The enzyme-labeled antibody is bound to the solid-phase F1.2 complex. Following a wash and incubation with TMB substrate, blue color is produced that turns yellow when the reaction is stopped with stop solution. Within limits, the amount of prothrombin fragment 1.2 is proportional to the color development.

Prothrombin fragment1.2 (F1.2) is a polypeptide released from prothrombin during its activation to thrombin. When formed, thrombin can convert fibrinogen to fibrin which in turn can incorporate into thrombus. Because thrombin has many natural inhibitors and substrates, thrombin formation need not be coincident with fibrin formation. However, as more prothrombin activation occurs, the amount of thrombin available to form fibrin and potentially thrombi also increases. Conversely, when less prothrombin activation occurs (as may happen during anticoagulation), less thrombin is available to form fibrin and possible thrombi.

F1.2 levels reflect the extent of prothrombin activation in plasma and have been demonstrated to correlate with the thrombotic risk associated with certain patient populations. Mean F1.2 levels are elevated in those that are elderly, have inherited thrombophilia, or have deep vein thrombosis (DVT); these are all conditions with an increased risk of thrombosis. Mean F1.2 levels are depressed in those receiving oral anticoagulant therapy, or

heparin infusion; these are conditions with decreased thrombotic risk. Monitoring of F1.2 levels will provide additional information for assessing thrombotic risk and monitoring efficacy of anticoagulant therapy.

(a) (5) A statement of the intended use of the device.

Device Intended Use: Thrombonostika F1.2 is an enzymed-linked immunosorbent assay for the quantitative determination of prothrombin activation fragment 1.2 (F1.2) in human plasma. It is indicated as an aid to both assess the risk of thrombosis and monitor the efficacy of anticoagulant therapy.

- (a) (6) A summary of the technological characteristics of the new device in comparison to those of the predicate device.

The technological characteristics of the new device in comparison to those of the device [Thrombonostika F1.2 (K911434)] are given in the table 1 below.

TABLE 1

PARAMETERS	ORGNON TEKNIKA THROMBONOSTIKA F1.2 (ORIGINAL)	ORGANON TEKNIKA THROMBONOSTIKA F1.2 (MODIFIED)
CATEGORY	Enzyme-linked Immunosorbent Assay (ELISA)	Enzyme-linked Immunosorbent Assay (ELISA)
INTENDED USE	Thrombonostika F1.2 is an enzymed-linked immunosorbent assay for the quantitative determination of prothrombin activation fragment 1.2 (F1.2) in human plasma. It is indicated as an aid to both assess the risk of thrombosis and monitor the efficacy of anticoagulant therapy.	Thrombonostika F1.2 is an enzymed-linked immunosorbent assay for the quantitative determination of prothrombin activation fragment 1.2 (F1.2) in human plasma. It is indicated as an aid to both assess the risk of thrombosis and monitor the efficacy of anticoagulant therapy.
SAMPLE	Human Plasma	Human Plasma
SENSITIVITY	0.1 nM	0.1 nM
CONTROLS	Level I Control-Lyophilized human plasma containing a low F1.2 level	Level I Control-Lyophilized human plasma containing a low F1.2 level
	Level II Control-Lyophilized human plasma containing a high F1.2 level	Level II Control-Lyophilized human plasma containing a high F1.2 level
MONOCLONAL ANTIBODY	Murine	Murine
CONJUGATE	Rabbit polyclonal antibodies to the calcium-dependent conformer of prothrombin (i.e., the amino terminal region present on both prothrombin and F1.2) coupled to horseradish peroxidase (HRP) serves as the conjugate	Rabbit polyclonal antibodies to the calcium-dependent conformer of prothrombin (i.e., the amino terminal region present on both prothrombin and F1.2) coupled to horseradish peroxidase (HRP) serves as the conjugate
CALIBRATORS	0, 0.25, 1.0, 3.0, 6.0, 10 nM Labeled with target values	0, 1.0, 3.0, 6.0, 10.0 nM Labeled with assayed values
SUBSTRATE	TMB (Tetramethylbenzidine)	TMB (Tetramethylbenzidine)

- (b) (1) A brief discussion of the nonclinical tests submitted, reference, or relied on in the premarket notification submission for a determination of substantial equivalency.

Not Applicable

- (b) (2) A brief discussion of the clinical tests submitted, reference, or relied on in the premarket notification submission for a determination of substantial equivalency.

Comparison Data:

The coefficient of determination (R^2) from regressing F1.2 values obtained without the 0.25 nM calibrator on the corresponding values obtained originally with the 0.25 nM calibrator is 0.998, with an estimated slope and intercept of 1.001 and 0.001, respectively. These data and the estimated regression line are shown in Figure 1.0. Two hundred forty (240) of the 268 test results fall in the 0.0-1.0 nM range.

An additional 51 samples fresh patient samples were analyzed by the current version of the test and compared to results from modified version. The coefficient of determination obtained from regressing F1.2 values without the 0.25 nM calibrator on values obtained with the calibrator is 0.9999. The slope and the intercept of the regression line 0.987 and 0.036, respectively. These data and the estimated regression line are shown in Figure 2.0.

Sensitivity

The minimum F1.2 level distinguishable from Calibrator A is 0.1 nM. This minimum detection limit is the F1.2 value corresponding to the mean absorbance plus two standard deviations for at least 16 replicates of Calibrator A.

Accuracy

A mean recovery of 113.5% (SD=13%) was obtained when purified F1.2, at levels between 0.5-20 nM, was added to 16 plasma samples from 5 different donors

Precision

Estimates of total and intra-assay precision were calculated for each of three kit lots by assaying multiple replicates of the Level I and Level II Controls on multiple plates and occasions. Intra-assay precision was estimated using analysis of variance. Total precision includes both interassay and intra-assay precision. Shown for each control and kit lot are the total number of tests (N), the mean F1.2 level (MEAN) in nM units, the total standard deviation (SD TOTAL) of all tests, the overall coefficient of variation (CV TOTAL), the intra-assay standard deviation (SD INTRA), and the intra-assay coefficient of variation (CV INTRA)

- (b) (3) The conclusion drawn from the nonclinical and clinical tests that demonstrate that the device is as safe, as effective, and performed as well or better than the legally marketed device identified in (a) (3).

In conclusion, the Thrombonostika F 1.2 (Modified) has successfully met all aspects of non clinical and clinical testing and have demonstrated that the device is safe and effective and has performed well and is substantially equivalent to the legally marketed device [Thrombonostika F1.2 (K911434)].