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K020355

i-STAT
CORPORATION

510(k) Summary

This summary of the 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1900 and CFR 807.92.

The assigned 510(k) number is:

Summary prepared on: January 30, 2002

Submitted by:
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Contact:
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Establishment Registration Number: 2245578

Identification of Device:
Device Name: Prothrombin Time (PT) Test
Proprietary/Trade Name: i-STAT® PT Test
Common Name: PT
Device Classification: II
Regulation Number: CFR § 864.7750
Panel: Hematology Kits and Packages
Product Code: GJS

Identification of the Predicate Device:
Device Name: Coaguchek™ S System

Intended Use of the Device:
The i-STAT PT is a prothrombin time test cartridge and is an *in vitro* diagnostic test intended for quantitative prothrombin time testing for the monitoring of oral anticoagulation therapy using fresh venous or capillary whole blood samples. The i-STAT PT test is not intended for evaluating individual factor deficiencies. The cartridge is to be used with the i-STAT Portable Clinical Analyzer with thermal control (Models 200 and 300), but will not run on the Philips Medical Systems (formerly Agilent Technologies) Blood Analysis Module (BAM). As part of the i-STAT System, the PT test is to be used by trained and certified health care professionals in accordance with a facility's policies and procedures.

Description of the Device:
The i-STAT PT test is contained in a single test cartridge. In use, approximately 40 microliters of fresh whole blood are placed in the cartridge as described below. The cartridge is inserted into the thermally controlled i-STAT Portable Clinical Analyzer, and all analytical steps are performed automatically. Patient and user information may be entered into the analyzer via a keypad during the automated analysis cycle.

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In the i-STAT PT test the endpoint is indicated by the appearance of an electroactive marker generated by the thrombin-mediated conversion of a synthetic substrate included in the reagent. Detection of the marker indicates generation of thrombin and therefore complete activation of the coagulation cascade. The result is reported as an International Normalized Ratio (INR) and, optionally, in seconds. The optionally displayed seconds is intended to reflect a typical plasma prothrombin time.

The PT test cartridge is assembled from plastic components that provide the conduits for fluid handling and house the sensor chips. The coagulation test is identified to the user through the name and color code on the cartridge label and by the analyzer through features integral to the cartridge.

During the test the blood sample is mixed with reagents which are coated on the cartridge cover in a segment of the sensor channel. The reagent layer includes tissue thromboplastin as an activating agent, the thrombin substrate, a heparin-neutralizing enzyme, and inert matrix components. These reagents allow activation of the coagulation cascade and detection of clot formation.

Whole blood is introduced into the sample well of the cartridge at the sample port and the cartridge is closed and inserted into the analyzer. Insertion of the cartridge initiates a controlled and monitored sequence of steps in the instrument. These are:

- Electrical contact is made between the analyzer electronic input circuits and the cartridge. The analyzer identifies the type of cartridge being used and the tests contained in the cartridge.
- The dry chips and sensor channel are heated to 37°C.
- The blood is then moved forward. Feedback from the fluid position sensor is used to allow controlled oscillation of the blood segment resulting in dissolution of the reagent layer.
- During the course of testing, the position of the blood segment is actively controlled to maintain the length of the blood containing the reagent coincident with the endpoint detector.
- Calculation of the sample clot time is performed and displayed.

Comparison to Technological Features of the Predicate Device:
The following technological difference between the i-STAT and CoaguChek S Systems is noteworthy:

Endpoint detection in both the CoaguChek S and i-STAT Systems relies upon detecting the action of thrombin, the final enzyme activated in the coagulation cascade, on a substrate within the sample. In the case of the CoaguChek S test, thrombin converts its natural substrate, fibrinogen, to fibrin which then crosslinks and causes localized or extended clotting throughout the sample. The instrument detects clot formation as the resulting restriction of the iron particles motion through the sample. In the i-STAT test, the generated thrombin converts an added substrate to a species that can be detected electrochemically. The signal for the appearance of this marker is used to assign the endpoint time. This is described in detail in section 5.3.2. Since fibrinogen is not a factor affected by warfarin, sensitivity to depleted levels is not a practical limitation for the intended use of monitoring of oral anticoagulant therapy. See section 10.4 for data characterizing the effect of fibrinogen concentration on the i-STAT PT test.

Summary of Non-Clinical Performance in Support of Substantial Equivalence:

- Studies using whole blood heparin-spiked samples established that the i-STAT PT test is insensitive to heparin up to 1.0 U/mL. The package insert for the Coaguchek S System states that it is sensitive to levels of heparin over 0.15 U/mL.
- Studies using manipulated samples of various fibrinogen levels established that the i-STAT PT test is insensitive to fibrinogen levels as low as 70 mg/dL.
- Clinical patient studies demonstrated that the i-STAT PT test is insensitive to fibrinogen levels between 142 and 528 mg/dL.
- Clinical studies established that hematocrits in the range of 24 – 52% do not significantly affect the results of the i-STAT PT test.
- Studies using manipulated samples established that the i-STAT PT test is sensitive to all factors impacted by warfarin therapy.

- From duplicate sample testing in the method comparison study, it can be seen that the within-sample reproducibility of the i-STAT PT test is 5.4%. The Coaguchek S System package insert indicates imprecision of 5.9.8% in whole blood samples in the therapeutic range.
- The imprecision of the i-STAT PT test in plasma controls was established using in-house and user studies. The Level 1 Control %CV was 4.5 at INR of 1.1, and the Level 2 Control %CV was 6.9% at INR of 2.5. This includes within-lot, lot-to-lot, vial-to-vial, analyzer-to-analyzer, and operator-to-operator components of the imprecision. The total imprecision in whole blood controls reported for the Coaguchek S System 10.2% at INR of 1.5 and 15.1% at INR of 3.7.

Summary of Clinical Test Performance is Support of Substantial Equivalence Claims:
Studies conducted at three external sites compared the results of the i-STAT PT test (y) to those of laboratory plasma instruments using Dade Innovin reagent (x) for samples from patients undergoing routine monitoring of oral anticoagulation therapy. Samples collected in plain plastic tubes were analyzed on the i-STAT System while plasma from citrated samples collected during the same venipuncture were analyzed on the laboratory methods. The methods were compared using Deming regression analysis. The results are summarized in the table below:

Statistic	Definition	Site 1	Site 2	Site 3
N	The number of patient samples used in the comparison	183	180	177
Mean, INR	The average of the comparative method result over the sample population	2.3	2.3	2.5
Range, INR	The range of comparative method results obtained over the sample population	1.0 - 3.9	1.0 – 4.3	1.0 – 4.6
S_x, INR	The standard deviation of the comparative method results across the sample population	0.729	0.777	0.779
Slope	The Deming regression estimate of the slope	0.922	1.013	0.914
Intercept, INR	The least squares linear regression estimate of the intercept	0.402	0..012	0.054
Correlation	The correlation coefficient calculated from linear regression	0.898	0.943	0.948
$S_{y.x}$, INR	The standard error of the estimate of the regression of y on x	0.322	0.272	0.191

A comparison of the i-STAT capillary samples and i-STAT venous samples was performed on patients undergoing routine monitoring of oral anticoagulation therapy. The results are presented in the table below:

Statistic	Capillary study site
N samples	59
Mean, INR	2.5
Range, INR	1.3 – 6.4
S_x, INR	0.855
Slope	1.076
Intercept, INR	-0.131
Correlation	0.962
$S_{y.x}$, INR	0.195

Conclusions:
Based on clinical and non-clinical data the i-STAT PT test is insensitive to heparin up to 1.0 U/mL, hematocrit level from 24 – 52%, and fibrinogen concentrations from 70 – 528 mg/dL; and sensitive to all factors impacted by warfarin therapy. Studies using plasma controls and whole blood indicate adequate precision for normal and therapeutic results. Clinical data indicates acceptable correlation to the predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
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Rockville MD 20850

MAY 1 4 2002

Paul VanDerWerf, Ph.D.
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i-STAT Corporation
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Re: k020355
Trade/Device Name: i-STAT® Prothrombin Time Test
Regulation Number: 21 CFR § 864.7750
Regulation Name: Test, Time, Prothrombin
Regulatory Class: II
Product Code: GJS
Dated: May 3, 2002
Received: May 6, 2002

Dear Dr. VanDerWerf:

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 the Code of Federal Regulations, Title 21, Parts 800 to 898. 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 Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 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 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

3 Indications for use

510(k) Number (if known): K020355

Device Name: **Prothrombin Time test.**

The i-STAT PT, a prothrombin time test, is useful for monitoring patients receiving oral anticoagulation therapy such as Coumadin or warfarin.

(Please do not write below this line—continue on another page if needed.)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter-Use _____

(Per 21 CFR 801.109) (Optional Format 1-2-96)

Josephine Bautista

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K020355