K023582

SEP - 8 2003

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: October 23, 2002

Submitted by:
i-STAT Corporation
104 Windsor Center Drive
East Windsor, NJ 08520
Phone: 609-443-9300
FAX: 609-443-9310

Contact:
Paul VanDerWerf, Ph.D.
Vice-President Regulatory Affairs and Quality Assurance
i-STAT Corporation
104 Windsor Center Drive
East Windsor, NJ 08520
Phone 609-443-9300
Fax: 609-443-9310
e-mail: van@i-stat.com

Establishment Registration Number: 2245578

Identification of Device:
Device Name: Activated Clotting Time Test
Proprietary/Trade Name: i-STAT ®Kaolin ACT
Common Name: ACT
Classification: Activated Clotting Time Tests
Device Classification: II
Regulation Number: CFR § 864.7140
Panel: Hematology
Product Code: JBP

Identification of the Predicate Device:
Device Name: Hemochron® Activated Whole Blood Clotting Time (Hemochron KACT)

Intended Use of the Device:
The i-STAT Kaolin Activated Clotting Time (ACT) test is an *in vitro* diagnostic test which uses fresh whole blood to monitor high-dose heparin anticoagulation frequently associated with cardiovascular surgery. The test is to be used with the i-STAT Portable Clinical Analyzer (Models 200 and 300), but not the Philips Medical Systems (formerly Agilent Technologies) Blood Analysis Module (BAM). As part of the i-STAT System, the Kaolin ACT 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 Kaolin ACT test is contained in a single test cartridge. In use, approximately 40 microliters of fresh whole blood are placed in the cartridge. The cartridge is inserted into the thermally controlled i-STAT Model 200 or Model 300 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.

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 an activating agent, a thrombin substrate, and inert matrix components. These reagents allow activation of the coagulation cascade and detection of clot formation.

In the i-STAT ACT 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 reported result is calculated from the time and rate of the substrate conversion and is given in seconds. The reported result correlates to the result of a traditional ACT in which the endpoint is indicated by physical clot formation.

Comparison to Technological Features of the Predicate Device:
The following technological differences between the i-STAT and the Hemochron Systems Activated Clotting Time tests are noteworthy.

- Endpoint detection in both the Hemochron 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 Hemochron, 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 impedance of the magnet's motion through the sample. In the i-STAT test, the generated thrombin converts an added substrate to a species which can be detected electrochemically. The signal for the appearance of this marker is used to assign the endpoint time.
- The volume of blood required for the Hemochron and i-STAT tests is significantly different. The Hemochron requires either 2.0 mL of blood where the i-STAT test requires 0.040 mL. Although such a difference does not necessarily imply systematic differences in the results of test methods, in this case it is a contributor to a between-method bias that is a function of the pre-analytical temperature of the blood. The relatively long time constant for sample heating in the Hemochron results in prolongation of results with hypothermic samples.

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

- The imprecision of the i-STAT test in plasma controls was established using in-house and user studies. Overall the Level 1 and Level 2 Controls read 168 ± 4 seconds (2.1% C.V.) and 407 ± 20 seconds (4.8% C.V.), respectively. This includes within-lot, lot-to-lot, vial-to-vial, analyzer-to-analyzer, and operator-to-operator components of the imprecision.
- Studies using samples *ex-vivo* heparinized whole blood samples with aprotinin added demonstrate that the i-STAT Kaolin ACT test is comparable to the Hemochron Kaolin ACT test, showing approximately half the extension of the Hemochron system to the affect of added aprotinin.
- Studies using *ex-vivo* heparinized whole blood samples establish that the i-STAT Kaolin ACT test responds linearly to the heparin concentration across its reportable range of 50 to 1000 seconds. The average sensitivity across multiple donors is 73 seconds / U/mL heparin. This is equivalent to the sensitivity of the Hemochron Kaolin Activated Clotting Time test.
- Studies show the i-STAT Kaolin ACT test is insensitive to the affect of pre-analytical sample temperature.
- Studies show the i-STAT Kaolin ACT test demonstrates comparable sensitivity to fibrinogen levels from 105 – 514 mg/dL as the Hemochron Kaolin ACT test.
- Studies demonstrate that the i-STAT Kaolin ACT is equivalent to the Hemochron Kaolin ACT in its response to platelet inhibition or removal.

Summary of Clinical Test Performance is Support of Substantial Equivalence Claims:
Studies conducted at three external sites compared the results of the i-STAT Kaolin ACT (y) to those of the predicate device (x) using samples taken during cardiovascular surgery procedures. The identical sample was tested on each instrument. 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	311	352	313
Mean	The average of the comparative method result over the sample population	430	384	391
Range	The range of comparative method results obtained over the sample population	1218	1199	1021
S_x	The standard deviation of the comparative method results across the sample population	300	225	290
Slope	The least squares linear regression estimate of the slope	0.962	1.051	0.962
Bias at 480 seconds	The average difference between the i-STAT Kaolin ACT and the Hemochron Kaolin ACT	30	-11	-47
Correlation	The correlation coefficient calculated from linear regression	0.906	0.940	0.971
s_{xx}%	Relative within sample imprecision of the comparative method over the sample population	9.1%	6.8%	7.6%
s_{yy}%	Relative within sample imprecision of the test method over the sample population	3.6%	4.0%	3.6%

Conclusions:
Based on the non-clinical data the i-STAT Kaolin ACT test responds linearly to heparin concentration in the range from 50-1000 seconds, is insensitive to pre-analytical sample temperature, aprotinin, and fibrinogen levels.. Studies using plasma controls and whole blood indicate adequate precision for normal and prolonged clot times. Clinical data indicates acceptable correlation to the predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

SEP - 8 2003

Mr. Mike Zelin
Chief Technology Officer
i-STAT Corporation
104 Windsor Center Drive
Windsor, NJ 08520

Re: k023582
Trade/Device Name: Kaolin ACT test
Regulation Number: 21 CFR 864.7140
Regulation Name: Activated Whole Blood Clotting Time Tests
Regulatory Class: Class II
Product Code: JBP
Dated: July 24, 2003
Received: July 24, 2003

Dear Mr. Zelin:

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 information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 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
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

3 Indications for use

510(k) Number (if known): K023582

Device Name: **Kaolin ACT test.**

The i-STAT Kaolin Activated Clotting Time (ACT) test is an *in vitro* diagnostic test used to monitor high-dose heparin anticoagulation frequently associated with cardiovascular surgery.

(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)

1/7/03

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K023582