i-STAT Kaolin Activated Clotting Time (^{KAOLIN}ACT) Cartridge

Intended for use with the i-STAT 1 Analyzer (REF 04P75-01 & 03P75-06)

NAME

i-STAT Kaolin Activated Clotting Time (^{KAOLIN}ACT) Cartridge – REF 03P87-25

INTENDED USE

The i-STAT Kaolin Activated Clotting Time (^{Kaolin}ACT) test is an *in vitro* diagnostic test that uses fresh, whole blood, and is used to monitor high-dose heparin anticoagulation frequently associated with cardiovascular surgery.

SUMMARY AND EXPLANATION/CLINICAL SIGNIFICANCE

The ACT is primarily used to monitor a patient's state of anticoagulation due to heparin that is administered during a medical or surgical procedure. It is commonly employed in cardiac catheterization, Percutaneous Transluminal Coronary Angioplasty (PTCA), renal dialysis, hemodialysis, and extra-corporeal circulation during bypass.

TEST PRINCIPLE

The i-STAT Kaolin Activated Clotting Time test, ^{Kaolin}ACT, is a measure of the time required for complete activation of the coagulation cascade.[1]

In traditional ACT tests, coagulation is initiated by mixing a whole blood sample with a particulate activator, and complete activation is indicated when extensive or localized clots form as activated thrombin converts fibrinogen to fibrin. These clots are mechanically detected.

The i-STAT ^{Kaolin}ACT test is similar to traditional ACT tests except that the endpoint is indicated by the conversion of a thrombin substrate other than fibrinogen and an electrochemical sensor is used to indicate the event of this conversion. The substrate used in the electrogenic assay has an amide linkage that mimics the thrombin-cleaved amide linkage in fibrinogen.

The substrate is H-D-phenylalanyl-pipecolyl-arginine-*p*-amino-*p*-methoxydiphenylamine which has the structure:

Phenylalanine - Pipecolic acid - Arginine -- NH - C_6H_4 - NH - C_6H_4 - OCH_3

Thrombin cleaves the amide bond at the carboxy-terminus of the arginine residue (denoted by the two dashes) because the bond structurally resembles the thrombin-cleaved amide linkage in fibrinogen. The product of the thrombin-substrate reaction is the electrochemically inert tripeptide Phenylalanyl - Pipecolyl - Arginine and the electroactive compound NH_3+ - C_6H_4 - NH - C_6H_4 - OCH_3. The formation of the electroactive compound is detected amperometrically, and the time of detection is measured in seconds. The test reports the Activated Clotting Time (ACT) in seconds.

The i-STAT ^{Kaolin}ACT test is calibrated to match the Hemochron Celite FTCA510 using prewarmed reagent tubes. However, users may choose to customize their individual i-STAT locations to report ACT results as calibrated against the Hemochron Celite ACT using non-prewarmed (ambient temperature) tubes. This customization affects the Patient path only and will not be applied to the Control or the Proficiency Testing pathway.

The customization in effect (prewarm or non-prewarm calibration mode) is identified on the analyzer screen. Please note that different locations within a given hospital may utilize different customization profiles. Prior to patient sample testing, ensure the appropriate calibration mode is employed. For a comprehensive discussion of this customization feature, please see the System Manual.

If results appear inconsistent with the clinical assessment, the patient sample should be re-tested using another cartridge.

REAGENTS

Contents

Each i-STAT ^{Kaolin}ACT cartridge provides a sample collection chamber, sensors to detect the coagulation endpoint, and dry reagents necessary to initiate and allow coagulation. Stabilizers and reagents are coated on a section of the sensor channel and include the following reactive ingredients:

Reactive Ingredient	Minimum Quantity
Kaolin	23.4 µg
Thrombin Substrate	0.09 µg

Warnings and Precautions

- For *in vitro* diagnostic use.
- DO NOT REUSE - Cartridges are intended for single-use only.
- Although the sample is contained within the cartridge, cartridges should be disposed of as biohazardous waste according to local, state, and national regulatory guidelines.
- Refer to the i-STAT 1 System Manual for all warnings and precautions.

Storage Conditions

- Refrigerated at 2-8 °C (35-46 °F) until expiration date.
- Room Temperature at 18-30 °C (64-86 °F). Recommended shelf life is 14 days..

INSTRUMENTS

The i-STAT Kaolin Activated Clotting Time (^{KAOLIN}ACT) cartridge is intended for use with the i-STAT 1 analyzer REF 04P75-01 (Model 300-G) and REF 03P75-06 (Model 300W). For a detailed description of the instrument and system procedures, refer to the i-STAT 1 System Manual located at www.pointofcare.abbott

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Arterial or venous whole blood.
Sample Volume: 40 µL

Venipunctures and Arterial Punctures

- Collection technique resulting in good blood flow must be used.
- The sample for testing should be drawn into a **plastic collection device** (either a plastic syringe or plastic evacuated tube).
- The collection device **cannot contain anticoagulants** such as heparin, EDTA, oxalate, or citrate.
- The collection device cannot contain clot activators or serum separators.
- The sample should be immediately dispensed into the sample well of a cartridge.
- If a second measurement is required, a fresh sample must be obtained.

Note: Some experts recommend drawing and discarding a sample of at least 1 mL prior to drawing sample for coagulation testing.[2]

Indwelling line

- Fluid drip through the line must be discontinued.
- If blood must be drawn from an indwelling line, possible heparin contamination and specimen dilution should be considered. The line should be flushed with 5 mL of saline and the first 5 mL of blood or six dead space volumes should be discarded.
- Withdraw the sample for testing into a fresh **plastic** syringe.
- The collection syringe **cannot contain anticoagulants** such as heparin, EDTA, oxalate, or citrate.
- The sample should be immediately dispensed into the sample well of a cartridge.

- If a second measurement is needed, draw a fresh sample.

Extracorporeal line

- Flush the extracorporeal blood access line by withdrawing 5 mL of blood into a syringe and discard the syringe.
- Withdraw the sample for testing into a fresh **plastic** syringe.
- The collection syringe **cannot contain anticoagulants** such as heparin, EDTA, oxalate, or citrate.
- The sample should be immediately dispensed into the sample well of a cartridge.
- If a second measurement is needed, draw a fresh sample.

PROCEDURE FOR PATIENT TESTING

Each cartridge is sealed in a foil pouch for protection during storage--do not use if pouch has been punctured.

- A cartridge should not be removed from its protective pouch until it is at room temperature (18-30 °C or 64-86 °F). For best results, the cartridge and analyzer should be at room temperature.
- Since condensation on a cold cartridge may prevent proper contact with the analyzer, allow refrigerated cartridges to equilibrate at room temperature for 5 minutes for a single cartridge and 1 hour for an entire box before use.
- Use a cartridge immediately after removing it from its protective pouch. Prolonged exposure may cause a cartridge to fail a Quality Check.
- Do not return unopened, previously refrigerated cartridges to the refrigerator.
- Cartridges may be stored at room temperature for the time frame indicated on the cartridge box.

Filling and Sealing the Cartridge (after cartridge has been equilibrated and blood sample has been collected)

1. Place the cartridge on a flat surface.
2. Fill the cartridge immediately after collection. Direct the hub of syringe or tip of the transfer device (pipette or dispensing tip) into the sample well of the cartridge.
3. Slowly dispense sample into the sample well until the sample reaches the fill mark indicated on the cartridge. Cartridge is properly filled when the sample reaches the 'fill to' mark and a small amount of sample is in the sample well. The sample should be continuous, no bubbles or breaks (see System Manual for details).
4. Fold the snap closure of the cartridge over the sample well.

Performing Patient Analysis

1. Press the power button to turn on the handheld.
2. Press 2 for *i-STAT Cartridge*.
3. Follow the handheld prompts.
4. Scan the lot number on the cartridge pouch.
5. Continue normal procedures for collecting the sample, and filling and sealing the cartridge.
6. Push the sealed cartridge into the handheld port until it clicks into place. Wait for the test to complete.
7. Review the results.

For additional information for cartridge testing, refer to the i-STAT 1 System Manual located at www.pointofcare.abbott.

Analysis Time

To detection of end point - up to 1000 sec (16.7 min)

Quality Control
The i-STAT quality control regimen comprises four aspects, with a system design that reduces the opportunity for error, including:

1. A series of automated, on-line quality measurements that monitor the sensors, fluidics and instrumentation each time a test is performed.
2. A series of automated, on-line procedural checks monitors the user each time a test is performed.
3. Liquid materials are available to be used to verify the performance of a batch of cartridges when they are first received or when storage conditions are in question. The performance of this procedure is not a manufacturer's system instruction.
4. Traditional quality control measurements verify the instrumentation using an independent device, which simulates the characteristics of the electrochemical sensors in a way which stresses the performance characteristics of the instrumentation.

For additional information on Quality Control, refer to the i-STAT 1 System Manual located at www.pointofcare.abbott.

EXPECTED VALUES

TEST	UNITS	REPORTABLE RANGE	REFERENCE RANGE *arterial* *venous*
MEASURED			
Kaolin Activated Clotting Time / ^{Kaolin}ACT	seconds	50 – 1000*	74 – 137 (PREWRM) 82 – 152 (NONWRM)

*The range from 77 - 1000 seconds (PREWRM mode) has been verified through method comparison studies.

METROLOGICAL TRACEABILITY

The i-STAT System test for Kaolin Activated Clotting Time measures the time interval required for complete activation, by kaolin, of the coagulation cascade in arterial or venous whole blood (dimension seconds) for *in vitro* monitoring of high-level heparin therapy. Presently, no international conventional reference measurement procedure or international conventional calibrator for ^{Kaolin}ACT is available. ^{Kaolin}ACT values assigned to APOC's controls are traceable to APOC's selected reference measurement procedure, which employs Celite activated glass reagent tubes, an automated timer and traditional viscometric clot detection and is run under specified temperature and sample conditions. i-STAT System controls are validated for use only with the i-STAT System and assigned values may not be commutable with other methods. Further information regarding metrological traceability is available from Abbott Point of Care Inc.

PERFORMANCE CHARACTERISTICS

The typical performance data summarized below was collected in health care facilities by health care professionals trained in the use of the i-STAT System and comparative methods. All data uses the PREWRM calibration, unless otherwise noted.

Precision data* were collected at i-STAT Corporation and during clinical trials following a protocol recommended by i-STAT Corporation and using plasma control material. Similar results can be expected in future performance studies provided the same experimental design and data analysis procedures are followed.

Plasma Control	n	Mean	SD	%CV
Level 1	119	169 seconds	4 seconds	2.0
Level 2	113	409 seconds	21 seconds	5.2

*Representative data, individual laboratories may vary from these results.

Method comparison data were collected using a modification of the CLSI guideline EP9-A[3]. Venous or arterial blood samples were collected in plastic syringes and analyzed in duplicate on the i-STAT System and in duplicate using the comparative methods. All samples were analyzed immediately upon collection. The patient populations in the studies were those in which ACT is routinely used and included both aprotinin and non-aprotinin receiving patients. All were undergoing cardiac surgery. Sample types included baseline, heparin-treated, and heparin-reversed samples.

Deming regression analysis[4] was performed on the first replicate of each sample. In the method comparison table, *n* is the number of specimens in the data set, *Sxx* and *Syy* refer to estimates of the imprecision based on the duplicates of the comparative and i-STAT methods respectively, *Sy.x* is the standard error of the estimate, and *r* is the correlation coefficient.

Method comparisons will vary from site to site due to differences in the sample handling, reagent and instrument systems in use, and other site-specific variables.

	Hemochron FTK-ACT		
CVOR	**Site 1**	**Site 2**	**Site 3**
n	104	118	106
Sxx	9.1%	6.8%	7.6%
Syy	3.6%	4.0%	3.6%
Slope	0.96	1.05	0.96
Intercept	-12	-38	-39
Xmin	68	111	81
Xmax	1286	1310	1102
r	0.906	0.940	0.971

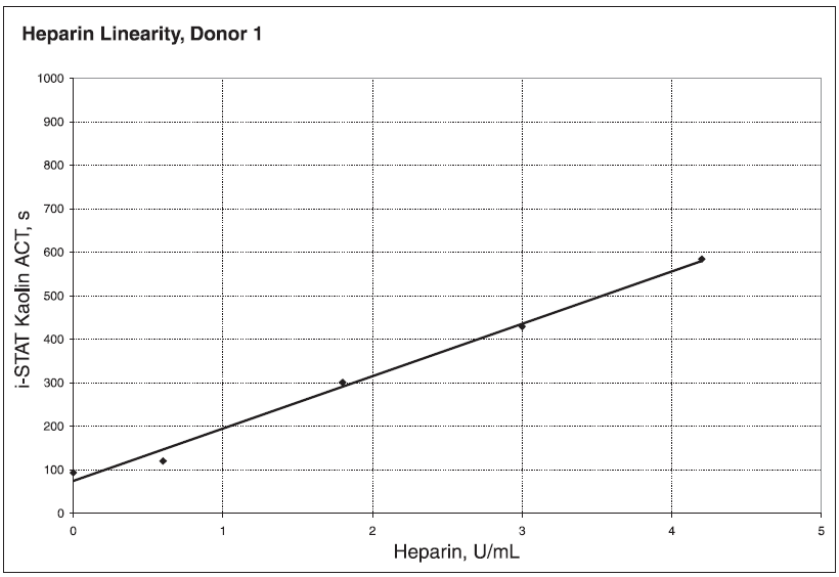
FACTORS AFFECTING RESULTS*

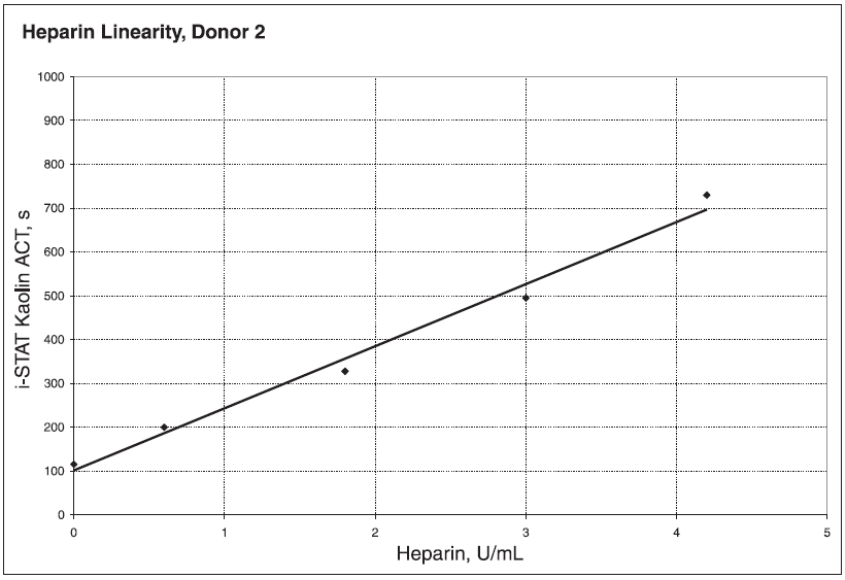
The i-STAT ^{Kaolin}ACT test is not significantly prolonged in the presence of a therapeutic level (200−280 KIU/mL) of aprotinin (Trasylol). If a patient has been administered the maximum aprotinin dosage of 400 KIU/mL, Abbott Point of Care recommends that the first blood sample post administration of the drug be taken after 15 minutes to ensure the full distribution of the drug and to achieve a therapeutic plasma concentration.

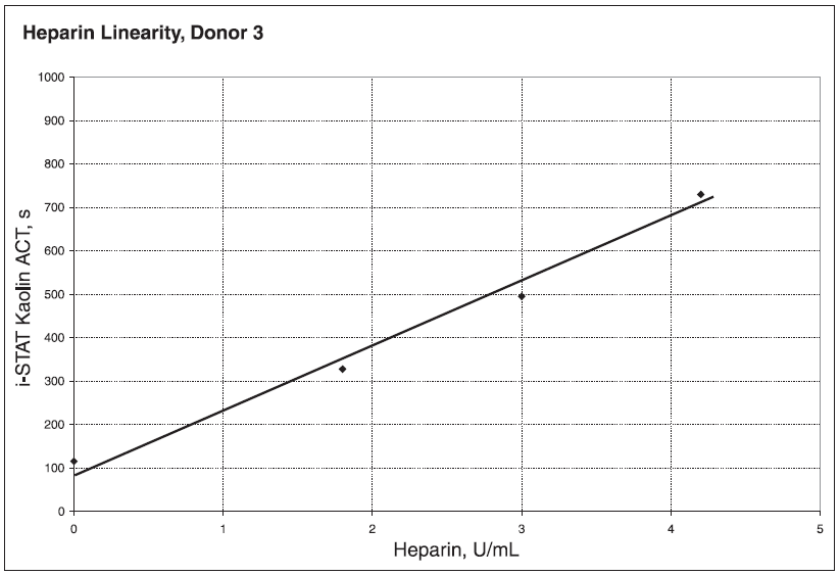
*It is possible that other interfering substances may be encountered. These results are representative and your results may differ somewhat due to test-to-test variation. The degree of interference at concentrations other than those listed might not be predictable.

Heparin sensitivity was demonstrated using whole blood samples to which varying concentrations of heparin were added *in vitro*.

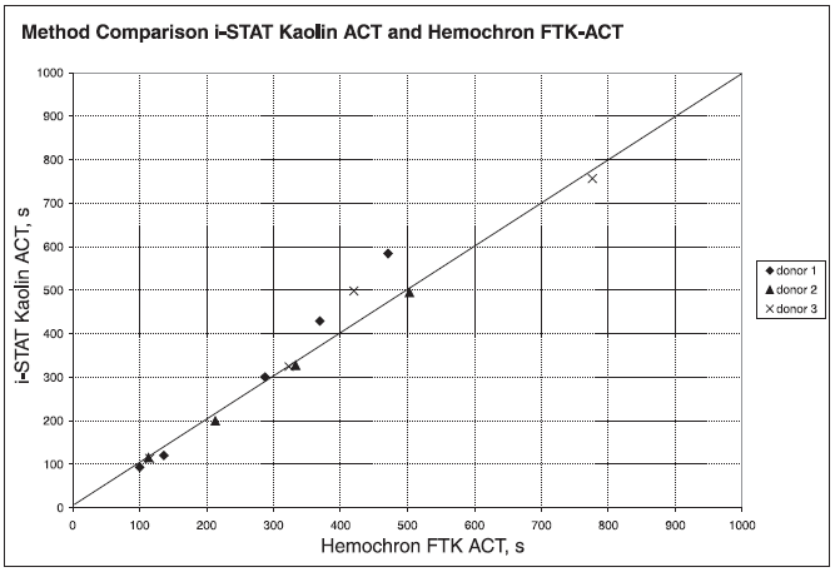
The following three graphs below each indicate the response of a different donor with respect to heparin concentration:

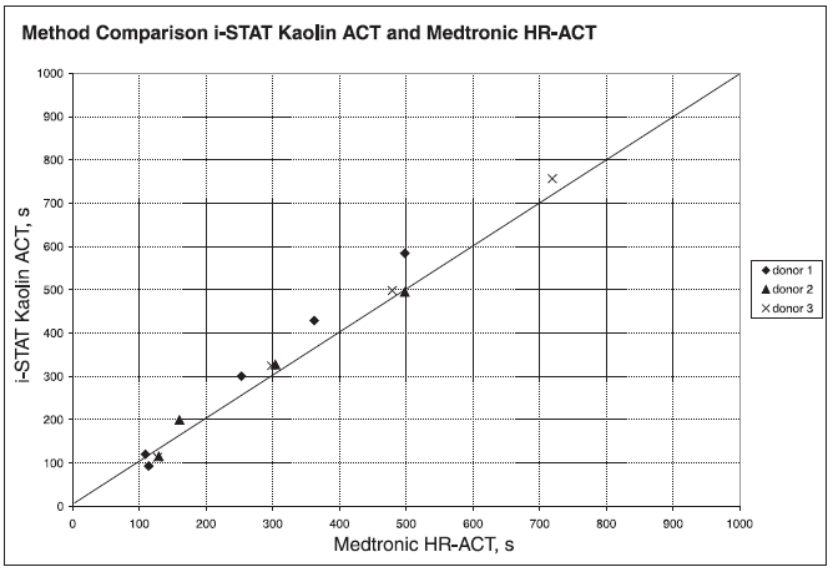






The following two graphs indicate the response of the same three donors with respect to the ACT result on the Hemochron Kaolin FTK-ACT and the Medtronic HR-ACT.





Test Limitations

The i-STAT ^{Kaolin}ACT test is to be used with fresh venous or arterial whole blood samples. The presence of exogenously added heparin, citrate, oxalate, or EDTA will interfere with test results. Poor technique in sample collection may also compromise the results. Samples drawn from insufficiently flushed catheters or from traumatic venipunctures may be contaminated with interfering substances. Samples should be collected into plastic syringes or tubes. Collection into glass may prematurely activate coagulation resulting in accelerated clotting times.

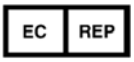
The analyzer should remain on a level surface with the display facing up during testing. If the analyzer is not level, the ACT result may be affected by more than 10%. A level surface includes running the handheld in the downloader/recharger.

Hemodilution may affect test results.

Platelet dysfunction, hereditary or acquired, may affect the results of this test. This includes the administration of pharmacological compounds known as platelet inhibitors which affect platelet function. Factor deficiencies, dysprothrombinemias, other coagulopathies, and other pharmacological compounds may also affect the results of this test.

The i-STAT ACT test is not affected by fibrinogen concentration in the range from 100 - 500 mg/dL, or sample temperature from 15 - 37 ºC.

KEY TO SYMBOLS

Symbol	Definition/Use
	14 days room temperature storage at 18-30 ^{0}C
	Use by or expiration date. An expiration date expressed as YYYY-MM-DD means the last day the product can be used.
	Manufacturer's lot number or batch code. The lot number or batch will appear adjacent to this symbol.
	Sufficient for <n> tests
	Authorized representative for Regulatory Affairs in the European Community.
	Temperature limitations. The upper and lower limits for storage are adjacent to upper and lower arms.
	Catalog number, list number, or reference
	Do not reuse.
	Manufacturer
	Consult instructions for use or see System Manual for instructions.
	*In vitro* diagnostic medical device
	Compliance to the European directive on *in vitro* diagnostic devices (98/79/EC)
	For prescription use only.

Additional Information: To obtain additional product information and technical support, refer to the company website at www.pointofcare.abbott.

References:

1. Hattersly, P. Activated coagulation time of whole blood. Journal of the American Medical Association 136:436-440, 1966.
2. Corriveau, Donna: Fritsma, George (ed.): Hemostasis and Thrombosis in the Clinical Laboratory. Ed, J.B. Lippinncott Company, Philadelphia, 1988, pp 70-71.
3. CLSI. *Method Comparison and Bias Estimation Using Patient Samples*; Approved Guideline. CLSI document EP9-A (ISBN 1-56238-283-7). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087, 1995.
4. P.J. Cornbleet and N. Gochman, “Incorrect Least-Squares Regression Coefficients in Method Comparison Analysis,” Clinical Chemistry 25:3, 432 (1979).

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Celite is a trademark of Celite Corporation, Santa Barbara, CA, for its diatomaceous earth products.

Hemochron is a trademark of International Technidyne Corporation, Edison, NJ.

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