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

Intended for use with the i-STAT Alinity Instrument

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 Alinity System Operations 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 Alinity Instrument (Model No. AN-500). For a detailed description of the instrument and system procedures, refer to the i-STAT Alinity System Operations Manual located at www.pointofcare.abbott

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Arterial or venous whole blood.
Sample Volume: 40 µL

Fill blood collection tubes and syringes to capacity, following manufacturers' instructions.

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

Preparation for Use:

1. Individual cartridges may be used after standing five minutes at room temperature. An entire box of cartridges should stand at room temperature for one hour.
2. All cartridges should be used immediately after opening pouch.
3. If the pouch has been punctured, the cartridge should not be used.
4. Do not return cartridges to the refrigerator after bringing them to room temperature.

How to Perform Patient Testing

1. From the Home screen, touch "**Perform Patient Test**". This initiates the patient testing pathway.
2. To begin, follow instructions on the screen to "**Scan or Enter OPERATOR ID**"
3. Follow instructions on the screen to "**Scan or Enter PATIENT ID**"
4. Continue to follow prompts on the screen to proceed with patient testing. "**Scan (CARTRIDGE POUCH) Barcode**", Scanning is required. Information cannot be entered manually.
5. The screen for selecting sample type will display if more than one sample type is applicable; select sample type if applicable.
6. Follow instructions on the screen to "**Close and Insert Filled Cartridge**". The action buttons at the bottom of the screen allow forward, backward and pause functionality.
7. Once the cartridge is inserted, "**Contacting Cartridge**" will display followed by the countdown bar. The following alerts are also displayed: "**Cartridge locked in instrument. Do not attempt to remove the Cartridge**" and "**Testing - Instrument Must Remain Level**".
8. When the test is complete, the test results are displayed.

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 Alinity System Operations Manual located at www.pointofcare.abbott.

EXPECTED VALUES

TEST	UNITS	REPORTABLE RANGE	REFERENCE RANGE *arterial*	REFERENCE RANGE *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.

Interpretation of results

- Various conditions can cause results to display a symbol or be suppressed. For additional explanation on these results refer to the i-STAT Alinity System Operations Manual.
- An [X] indicates the ACT test was stopped by the operator before the test completed. The ability to stop an ACT test is set via AlinIQ CWi parameter: **Analyte Settings** > **ACT** > **Stop ACT Test**.

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 performance data summarized for Kaolin Activated Clotting Time (^{Kaolin}ACT) was collected by professionals trained in the use of the i‑STAT Alinity System and comparative methods. All data uses the pre-warm calibration.

Precision*

A multiday precision study was performed with plasma control materials using ^{Kaolin}ACT cartridges. Duplicates of each aqueous fluid were tested twice a day for 20 days.

Fluid type	Fluid level	n	Mean (seconds)	SD (seconds)	%CV
Plasma Control	Level 1	80	167	6	3.6
	Level 2	80	455	13	2.9

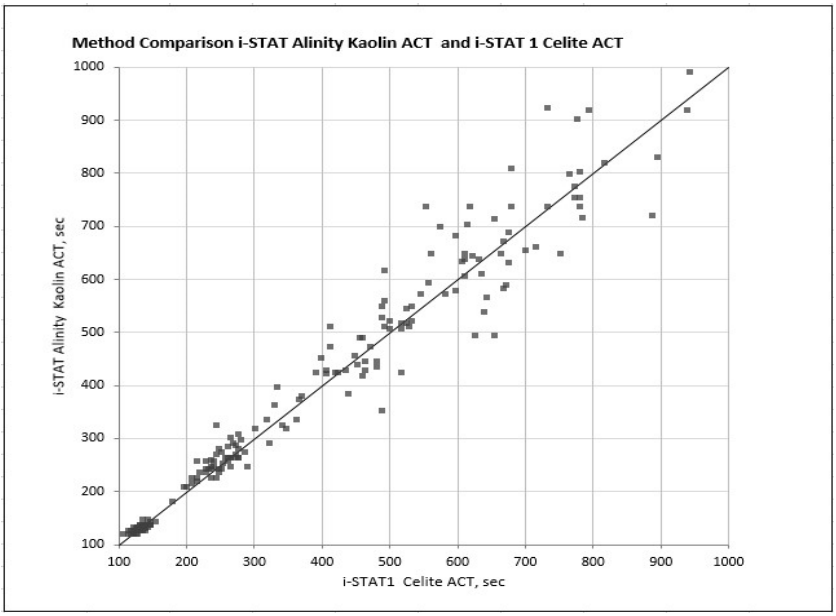
*Representative data, individual laboratories may vary from these results.

Method Comparison

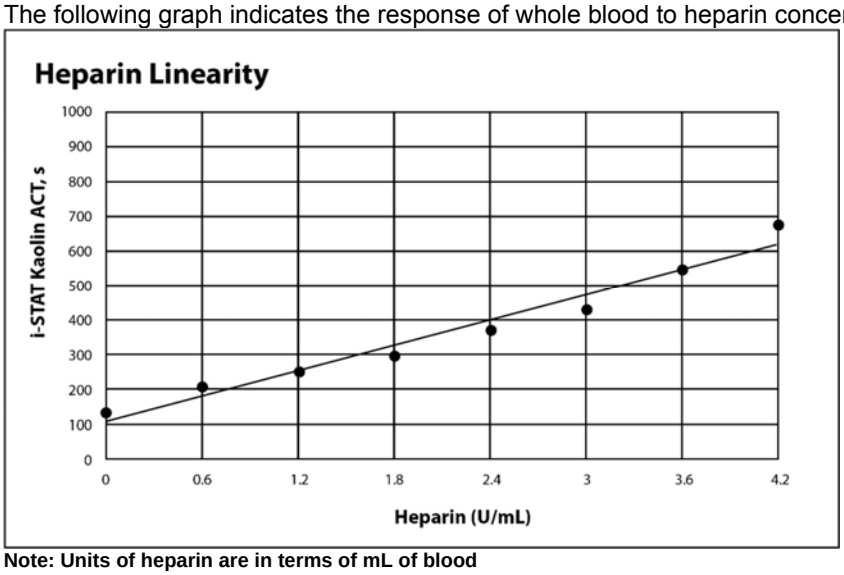
Method comparison was demonstrated in a study comparing the ^{Kaolin}ACT test performed on the i-STAT Alinity to the ^{Celite}ACT test performed on the i-STAT 1 Wireless (i-STAT 1 W). The study was based on CLSI guideline EP09-A3. Non-anticoagulated whole blood altered with several levels of heparin and by hemodilution with lactated Ringer's were evaluated. Samples were analyzed in duplicate on both systems. A Passing-Bablok regression analysis was performed using the first replicate result from the i-STAT Alinity versus the first replicate result from the i STAT 1 W.

In the method comparison table, n is the number of specimens, and r is the correlation coefficient.

n	192
slope	1.02
r	0.98
intercept	-3.74
Xmin (seconds)	119
Xmax (seconds)	990



The following graph indicates the response of whole blood to heparin concentration:



Note: Units of heparin are in terms of mL of blood

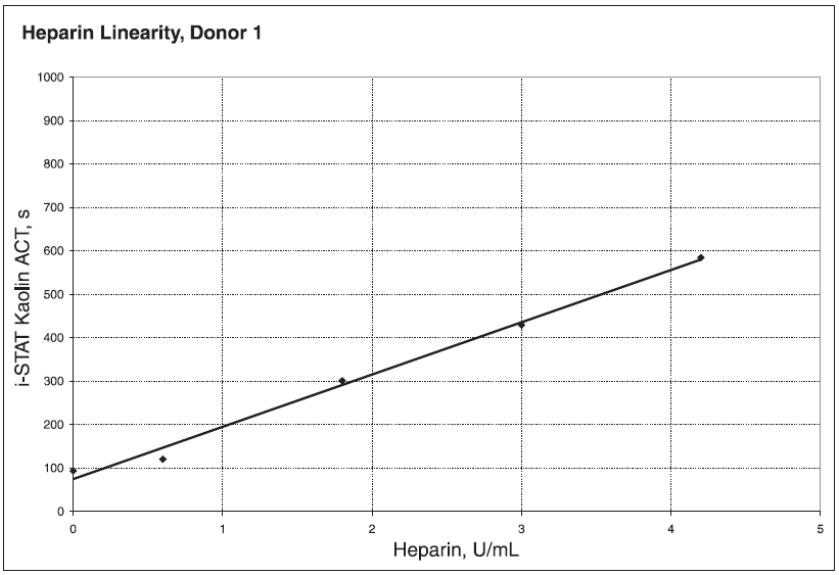
FACTORS AFFECTING RESULTS

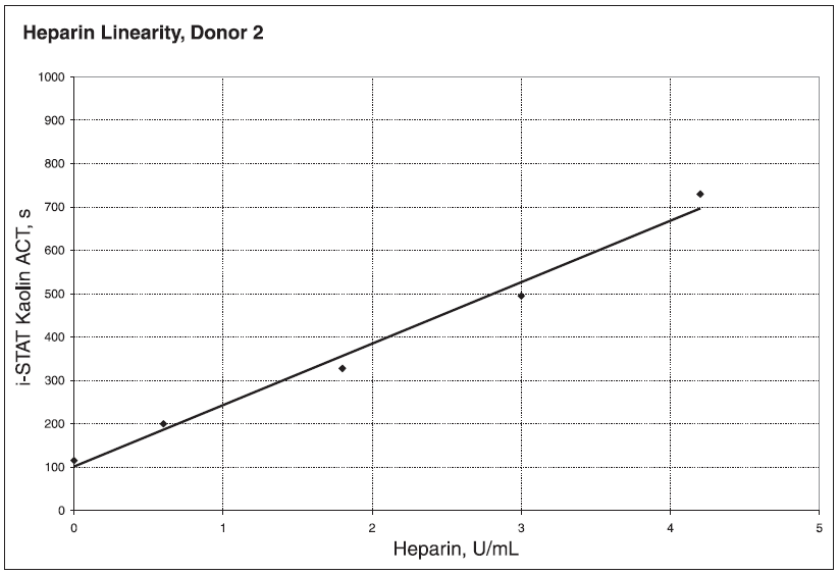
The i-STAT [Kaolin]ACT test is not significantly prolonged in the presence of a therapeutic level (200−280 KIU/mL) of aprotinin (Trasylol). If a patient has been administered the maximum aprotinin dosage of 400 KIU/mL, Abbott Point of Care recommends that the first blood sample post administration of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

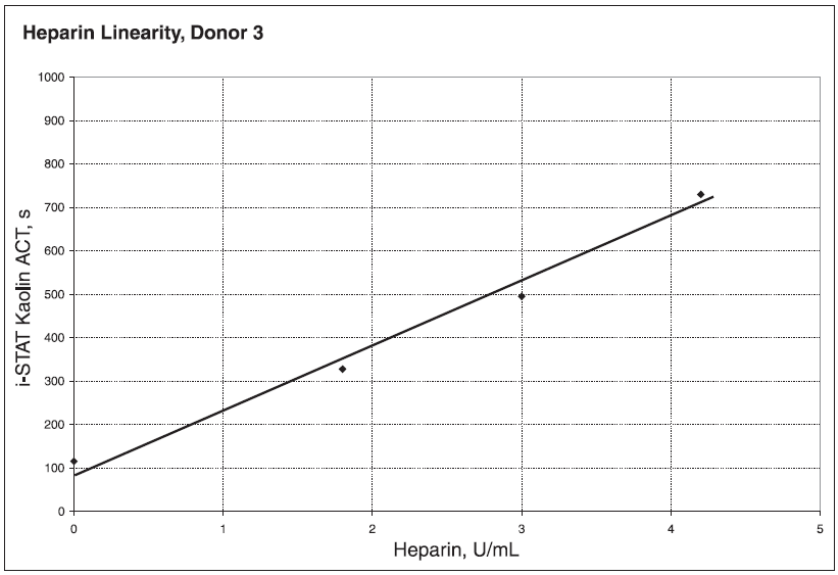
*It is possible that other interfering substances may be encountered. These results are representative and your results may differ somewhat due to test-to-test variation. The degree of interference at concentrations other than those listed might not be predictable.

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

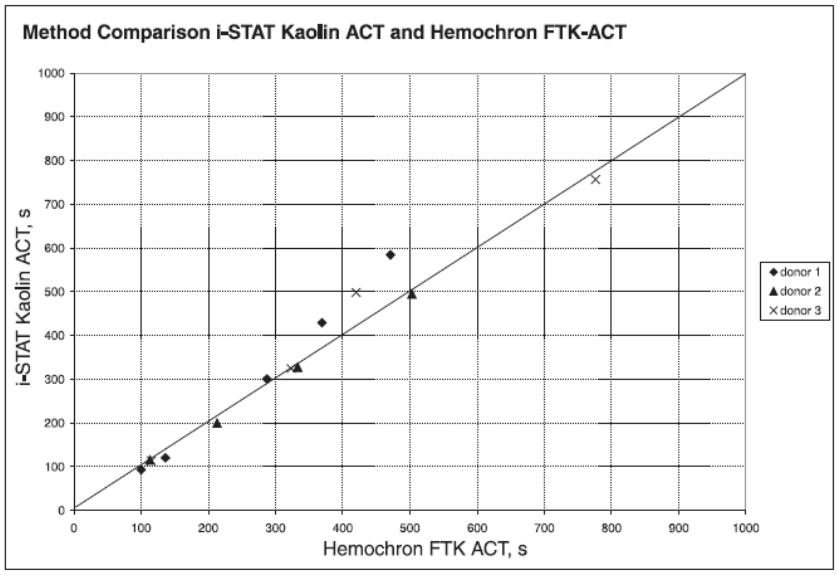
The following three graphs below each indicate the response of a different donor with respect to heparin concentration:

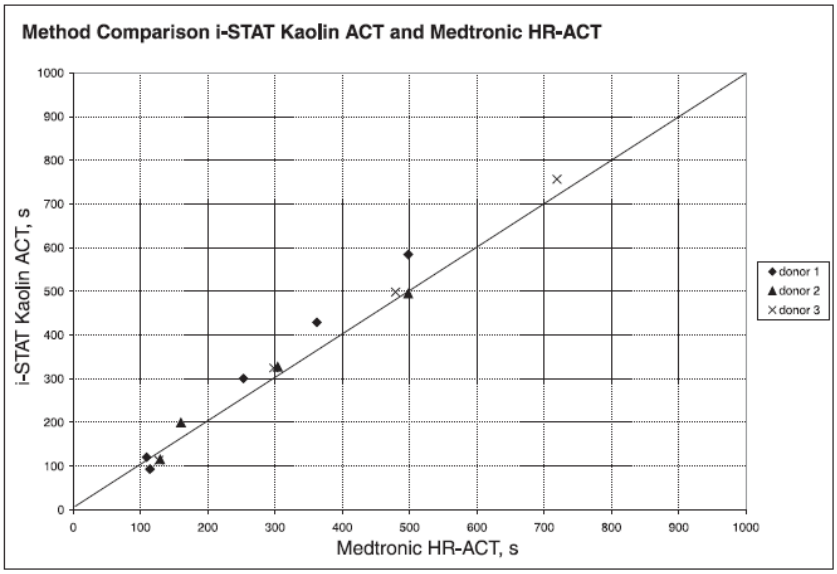






The following two graphs indicate the response of the same three donors with respect to the ACT result on the Hemochron Kaolin FTK-ACT and the Medtronic HR-ACT.





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.

Additional Considerations

ACT Test Calibration Customization Options: Pre-Warm vs. NonWarm

The Activated Clotting Time (ACT) test has been in existence for over 30 years. It is the most popular test for measuring the effect of heparin administered during an interventional procedure. By placing an activator in the test chamber, the blood sample is “activated” to promote clotting. When heparin is present in the sample, the clotting is delayed in proportion to the amount of “anticlotting” effect of the heparin. Since its inception, numerous changes have taken place to ACT tests, including increased automation and decreased sample volume. Today, there are many new, fully automated, low blood volume ACT tests on the market, in addition to the older, macro blood volume, semi-automated tube-based systems (i.e., Hemochron®, Actalyke™). The micro sample ACT systems typically employ test cartridges or cards (instead of tubes), and all have incorporated an automatic test cycle prewarming step that brings the ACT testing chamber to 37 °C prior to initiating the clotting reaction. As blood clotting is an enzymatic process, the temperature at which the clotting cycle takes place has a marked impact on the rate at which the blood clot forms. The ACT tests that incorporate a prewarming step allow the entire clotting reaction to take place at 37 °C. ACT tests that do not use a prewarming step are subject to a delay before the blood specimen reaches (and stabilizes at) 37 °C; the actual

time needed to reach 37 °C is dependent on the starting temperature of the sample test tube. For example, a 30 °C blood sample placed into a (non-prewarmed) 25 °C ACT tube will take a few minutes before the test environment (blood, reagent, tube) stabilizes at 37 °C. The result of this thermal delay is an increase in the reported ACT clot time that will depend on sample tube temperature.

i-STAT Alinity ACT Test Calibration
Currently, the i-STAT Kaolin ACT test is factory calibrated by mathematically adjusting the raw i‑STAT "clot time" to match the Hemochron® Celite tube result. This calibration is performed by testing cartridges and Hemochron Celite tubes side by side, using a range of heparinized, non-hemodiluted whole blood samples, and using Hemochron tubes prewarmed to 37 ºC. Customers who are familiar with macrosample ACT methods like Hemochron and Actalyke™, and who do not preheat their tubes prior to each test, have found that the bias in results between their previous ACT method and the i-STAT ACT (prewarm) may require changing familiar clotting time target values. To ease the changeover to the i-STAT ACT method, i-STAT provides a choice between the current 37 ºC result calibration (pre-warm) and an ambient temperature result calibration (non-warm). The non-warm calibration mode allows an i-STAT ACT cartridge to deliver results closer to macro-sample methods that do not employ automatic prewarming cycles. This is intended to reduce the need to make large changes to ACT target times or ranges.

Since micro-sample methods (Medtronic HR-ACT, Hemochron Jr. ACT+) already incorporate preheating of the test cuvettes, users with ACT target times and ranges based on these methods should continue to use the default i-STAT 37 ºC calibration (pre-warm). To change this customization, see the *Customization Workspace* section of the System Operations Manual.

Verify the instrument for cartridge testing

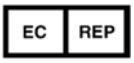
Note: Verification is only required once per cartridge type per instrument.

Prior to using an instrument requiring a specific cartridge type, verify the instrument supports the cartridge:

1. Initiate a liquid quality control test per the instructions in the *Liquid Quality Controls* section of the i-STAT Alinity *System Operations Manual*.
2. Ensure the instrument can successfully scan the cartridge pouch barcode.
3. If the cartridge is not recognized, contact your local representative.

Verify customization on instrument
Prior to testing patient samples, it is recommended to check the result calculation customization set in the instrument. Touch **More Options** > **View Action Ranges and Analyte Information**.

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.

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