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Technical Bulletin: Helena Actalyke Activated Clotting Time System

Procedure compliance, quality control, and platform-specific performance of the Actalyke ACT system

I. Summary

The Actalyke Activated Clotting Time (ACT) system (Helena Laboratories Corporation, Beaumont, TX) is a point-of-care, whole-blood coagulation analyzer used to monitor heparin anticoagulation during various medical and surgical procedures. This bulletin covers four topics that affect the safety and reliability of ACT-guided anticoagulation:

a. Adherence to published procedure, including sample handling, mixing technique, and instrument operation.
b. The multi-tiered quality control program, comprising the Electronic Clotting Tube (ECT), temperature verification, and liquid controls, required to protect the integrity of patient results.
c. Verification of new tube lots through heparin linearity studies before clinical use.
d. The well-documented, system-specific nature of ACT results: different platforms use different activators, detection methods, and clot-formation thresholds, so their numerical results are not interchangeable.

IMPORTANT SAFETY NOTICE: Heparin dosing and anticoagulation reversal decisions must stay within the therapeutic range validated for the specific ACT system in use at each institution. Results from different ACT platforms are not interchangeable. Switching systems without re-validating institution-specific target ranges can lead to inappropriate anticoagulation and expose patients to thrombotic or hemorrhagic complications.

II. Procedure Adherence and Correct Analytical Technique

ACT results are sensitive to pre-analytical, analytical, and post-analytical variables. Procedural inserts 186 (C-ACT, K-ACT, G-ACT) and 187 (MAX-ACT) must be followed without deviation; no quality control program can compensate for a procedural error.

a. Pre-Analytical Requirements

i. **Sample acquisition:** follow the tube-specific procedure for discard volume and draw technique. Heparin contamination at the draw site will prolong results.
ii. **Blood volume:** use the exact volume specified for each tube type.
iii. **Tube handling:** store Actalyke tubes (C-ACT, K-ACT, G-ACT, and MAX-ACT) at room temperature in sealed packaging until immediately before use.
iv. **Tube inspection:** discard any tube showing cracks or structural damage, a damaged or incompletely sealed flip-top cap, missing components, or foreign material. If damage affects multiple tubes from the same lot, notify Helena Technical Services.
v. **Timing:** start the Actalyke timer when blood is added to the tube, not after insertion. Delayed insertion prolongs incubation outside the 37°C ± 0.5°C well and introduces a positive bias.

b. Analytical Requirements

i. **Mixing:** technique is tube-specific. Shake C-ACT and K-ACT tubes end-to-end ten times immediately after filling; tap G-ACT tubes sideways five times; use a gentle side-to-side shake only for MAX-ACT tubes. Incorrect mixing gives incomplete activator distribution and an inaccurate result.
ii. **Instrument warm-up:** allow the instrument to reach 37°C ± 0.5°C before patient testing and confirm the temperature on the readout (see Section III.b).
iii. **Clot detection:** the Actalyke tracks a ferrite rod at two positions; immobilization at the endpoint indicates clot formation. Two-point detection improves sensitivity to early fibrin polymerization and is less susceptible to clot instability at high heparin concentrations.

iv. **S-1 errors:** an S-1 error means the rod did not reach the endpoint within the detection window. Causes include a stuck magnet (from aggressive mixing, or a tube or magnet defect), a clotted tube, a missed start, or a non-human sample with a faster native clot time. A stuck magnet or repeated S-1 error during ECT testing can indicate a need for instrument calibration. If an S-1 error occurs, remove the tube, tap it lightly, and reinsert once; the correction should never be attempted a second time. If the test aborts (E003), discard the tube and repeat with a fresh sample. Never use an uncorrected S-1 result for a clinical decision.

c. **Post-Analytical Requirements**

i. **Repeat testing:** repeat any result inconsistent with the patient's clinical picture, using a fresh sample, before making a heparin or protamine decision.

Per the STS/SCA/AmSECT Clinical Practice Guidelines (Shore-Lesserson et al., 2018): "An ACT ≥400 seconds is recommended for safe institution and maintenance of cardiopulmonary bypass" (Class I, Level of Evidence B). Confirm that any threshold used in your protocol has been validated for the ACT system in use at your institution.

III. Quality Control Program

Reliable Actalyke ACT results depend on three complementary quality control checks, spanning instrument mechanics, thermal performance, and full-system reagent integrity, summarized below and detailed in the sections that follow.

QC Method	Purpose	Action Required
ECT (Electronic Clotting Tube)	Verifies instrument mechanics: magnet movement, motor function, timing circuit, and clot-detection threshold.	Run daily per SOP. Results repeatedly out of range require instrument service before patient testing.
Thermometer verification	Confirms the incubation well reaches 37°C ± 0.5°C; temperature error is a primary source of systematic ACT bias.	Verify at least weekly with the Actalyke thermometer (cat. no. 5757) or an equivalent ±0.2°C reference. Log results; do not test patients if out of range.
Liquid control testing	Verifies the entire analytical system (tubes, reagent, instrument); detects lot-to-lot variation, degraded controls, and operator error.	Run at each new tube lot, new control lot, corrective action, and per institutional QC schedule. Results must fall within the established range.
Heparin linearity	Confirms the dose-response relationship across the clinical heparin range; validates that new tube and heparin lots perform equivalently to established ranges.	Required with each new tube lot before clinical deployment. Use fresh heparinized whole blood at multiple concentrations; document and compare to the expected range.

Electronic Clotting Tube (ECT)

The ECT (Cat no. XL-ECT) electronically simulates the mechanical signature of clot formation, without a blood sample, to verify the instrument's motor, timing circuit, and both magnetic-field detectors. Run it at the start of each shift or day of use, after any corrective action or period of inactivity, and after any mechanical shock or temperature extreme. A result outside ±10 seconds means the instrument must be taken out of service and repaired before further patient testing; ECT testing does not validate reagent or sample-handling performance and must be paired with liquid control testing. Store the ECT in its own tube, not in the instrument, when not in use.

a. **Temperature Verification**

Incubation-well temperature is a primary driver of ACT values: hypothermia inhibits clotting-factor activity and prolongs ACT independent of heparin effect. Machin and Devine (2005, J Extra Corpor Technol) demonstrated this effect across the Hemochron, Medtronic ACT Plus, and Mallinckrodt systems. Measure well temperature at least weekly, and whenever instrument temperature is in question, using the Actalyke thermometer (Cat no. 5757) or an equivalent NIST-traceable reference. The well must read 37.0°C ± 0.5°C; document every check in the QC log and correct any deviation before patient testing proceeds. Because a hypothermic CPB patient's blood is warmed to 37°C in the well, bedside or in-circuit testing without proper incubation reflects the patient's core temperature and must not be used without a validated temperature-correction factor.

b. **Liquid Control Testing**

Human plasma-based liquid controls verify the entire analytical system, tube lot, reagent, sample handling, and instrument, together. Run controls at each new tube lot and control lot, after any corrective action, and per institutional requirements. Results must fall within the range established in the control package insert. Investigate and resolve any out-of-range result, checking instrument temperature, tube lot integrity, control reconstitution technique, operator technique, and calibration status, before reporting patient results. Do not report patient ACT results while liquid controls are out of range.

IV. **New Lot Verification: Heparin Linearity**

A heparin linearity study is required before any new lot of Actalyke tubes enters clinical use, to confirm that the dose-response relationship between heparin concentration and ACT is preserved. This step is not optional: it is the primary safeguard against undetected lot-to-lot performance variation.

a. **Scientific Rationale**

ACT is a functional assay of heparin's antithrombin-mediated inhibition of thrombin and other coagulation factors. The linearity of that response across the clinical heparin range must be reproducible across both tube lots and heparin lots, since heparin sensitivity can vary by brand, source, and lot.

b. **Linearity Verification Protocol**

i. **Sample preparation:** use fresh whole blood from a non-anticoagulated donor, or fresh patient blood drawn during the protamine-recovery period. Add pharmaceutical-grade unfractionated heparin to span the clinical range

ii. **Testing:** run duplicate ACT measurements on the established (validated) lot and the new lot at each heparin concentration.

iii. **Acceptance criterion:** Document acceptance criteria and investigate any systematic deviation before clinical deployment.

iv. **Documentation:** record lot numbers, dates, testing personnel, and the accept or reject decision in the quality control record.

Contact Helena Technical Services (1-800-231-5663) for further assistance.

Why ACT Results Differ Across Systems

Numerical ACT results diverge, reproducibly and predictably, across commercial platforms; this is an expected feature of the assay, not an analytical error. Below outlines sources of that divergence and summarizes the supporting published evidence.

c. **Sources of Inter-System Variability**

i. **Contact activator type and quantity:** ACT begins with contact activation of Factor XII (Hageman factor). Different activators, differing in surface charge, particle size, and specific surface area, activate Factor XII at different rates. Celite (Hemochron C-ACT, Helena C-ACT) gives rapid, robust activation but is prolonged by aprotinin. Kaolin activates Factor XII through a different binding geometry and is unaffected by aprotinin, making it preferred during aprotinin therapy; De Vries et al. (2017) found only 45% correlation between baseline celite and kaolin ACT in 97 cardiac surgery patients. Glass beads tend to produce longer clotting times than celite or kaolin at equivalent heparin concentrations. The Helena MAX-ACT tube blends celite, kaolin, and glass beads to compensate for patient-to-patient variation in activator sensitivity, giving more complete and reproducible activation.

ii. **Clot-detection mechanism:** each platform senses a different point on the fibrin-formation curve. The Actalyke's dual-point electromagnetic detection (0°/46°) catches early fibrin formation, giving systematically shorter results than later-endpoint methods such as the Hemochron 801/Response single-point magnetic tilt. The Medtronic ACT Plus uses plunger impedance, a different mechanical threshold. The Abbott i-STAT uses an amperometric biosensor cartridge with a 0.1 mL sample; Vranken et al. (2021) found a median 87-second bias against the ACT Plus in 100 CPB patients (limits of agreement −124 to +333 seconds).

iii. **Sample volume and activator ratio:** the ratio of blood volume to activator surface area affects Factor XII activation kinetics. Sample volumes range from 2.0 mL (Hemochron 801) to 0.5 mL (Actalyke) to 0.1 mL (i-STAT), a fundamental analytical parameter, not merely a convenience feature.

iv. **Patient and sample condition:** hematocrit (hemodilution lowers coagulation-factor concentration independent of heparin), hypothermia (enzymatically slows clotting independent of heparin; Machin and Devine, 2005,), antithrombin level (low AT-III blunts the ACT response to heparin; Leyvi, Shore-Lesserson et al., 2001, found MAX-ACT significantly less prolonged by hypothermia than standard celite ACT, P = 0.009), and concomitant drugs (aprotinin prolongs celite ACT by 20–30% with little effect on kaolin ACT; direct thrombin inhibitors prolong all systems to varying degrees) interact with platform design to add further variability.

Published Evidence of Inter-System Divergence

System/Platform	Activator(s)	Detection Method	Sample Volume	Typical ACT Range†
Actalyke XL/MINI II (MAX-ACT)	Celite + kaolin + glass beads	2-pt electromagnetic (0°/46°)	0.5 mL	~220–350 s at 3 U/mL heparin
Actalyke (K-ACT)	Kaolin	2-pt electromagnetic	0.5–2 mL	~250–380 s at 3 U/mL heparin
Hemochron 801/Response	Celite or kaolin	Magnetic rotation (tilt)	2 mL	~300–450 s at 3 U/mL heparin
Medtronic ACT Plus	Kaolin	Optical plunger impedance	0.4 mL	~300–480 s at 3 U/mL heparin
Abbott i-STAT (kaolin)	Kaolin	Amperometric electrochemical	0.1 mL	~200–340 s at 3 U/mL heparin

† Approximate values based on published literature; actual values are patient-dependent and influenced by hematocrit, AT-III level, hypothermia, hemodilution, and activator sensitivity. These values are illustrative, not clinical targets. Institutions must establish system-specific therapeutic ranges through prospective validation.

Selected published comparisons, spanning two decades, document the clinical consequences of unrecognized inter-system ACT divergence:

v. Welsby et al. (2002, J Clin Monit Comput): in 81 duplicate CPB/PCI samples from 22 patients, the Actalyke was more precise than the Hemochron Response (±0.1% vs ±4.2% mean duplicate difference) but read 18% lower on average ($p < 0.0001$); the authors estimated that 50% of CPB patients would have received unnecessary additional heparin (mean 1,060 units) had targets remained based on Hemochron 801 values.

vi. Toffaletti et al. (2003, Point of Care: J Near-Patient Testing & Technology): across 272 samples in five clinical groups, the Actalyke MAX-ACT read lower than the Hemochron 801 at every heparin concentration and in every group, leading the authors to establish new system-specific therapeutic ranges for each clinical application.

vii. Leyvi, Shore-Lesserson et al. (2001, Anesth Analg): in 27 CPB patients, celite ACT (Hemochron) was significantly longer than MAX-ACT under hypothermia ($P = 0.009$) but not under normothermia, indicating that the blended activator confers greater stability under CPB conditions of hemodilution and hypothermia.

viii. Jones et al. (2011, J Cardiothorac Vasc Anesth): in 12 bivalirudin-anticoagulated patients, K-ACT ran a mean 94 seconds longer than MAX-ACT (limits of agreement 51–138 seconds) on the same Actalyke XL instrument, showing that assay subtype, not only platform, affects results.

ix. De Vries et al. (2017, Interact CardioVasc Thorac Surg): in 97 randomized cardiac surgery patients, celite and kaolin ACT were not interchangeable at the individual-patient level even on the same Hemochron instrument; bias shifted from +10.3% at baseline to −12.9% at two hours of bypass, with only 45% baseline correlation between methods.

x. Vranken et al. (2021, J Extra Corpor Technol): a median 87-second bias between the ACT Plus and i-STAT in 100 CPB patients ($p < 0.001$); 14 of these patients received additional heparin based on an ACT Plus value that would not have crossed the same threshold on i-STAT.

xi. Ojito et al. (2012, J Extra Corpor Technol): at a fixed heparin concentration of 1.7 U/mL, four platforms ranged from a median of 154 seconds (i-STAT) to 221 seconds (Hemochron Signature Elite) on the same blood samples, a 43% relative spread.

xii. Palmer et al. (2012, J Extra Corpor Technol): in 144 isolated CABG patients, average CPB ACT below 500 or above 700 seconds was associated with significantly more postoperative blood loss ($p = 0.001$), reinforcing the need for a validated, platform-specific therapeutic window.

xiii. Kovacs et al. (2026, Heart Rhythm): in a systematic review of four electrophysiology-specific platform-comparison studies found mean paired ACT differences of 50–60 seconds between platforms (a 15–25% discrepancy at ACT targets of 300–350 seconds) despite generally high correlation. An accompanying international survey of 164 electrophysiologists found that both target ACT and weight-based heparin dose varied systematically by platform in routine practice, and that about one-third of respondents had changed their heparin dosing after switching ACT platforms.

d. **Clinical Implications: Establishing and Maintaining System-Specific Therapeutic Ranges**

The STS/SCA/AmSECT guidelines (Shore-Lesserson et al., 2018) recommend that each institution establish system-specific therapeutic ranges through prospective evaluation of outcomes data (Class IIa, Level of Evidence C); the 400-second CPB minimum is derived largely from Hemochron (celite) data and must be independently validated for other platforms. When adopting or transitioning to the Actalyke MAX-ACT system, institutions should follow a structured validation protocol:

i. Perform a head-to-head comparison with the prior system, using fresh patient blood across the clinical heparin range.

ii. Establish the regression relationship between old and new system values.

iii. Calculate equivalent target thresholds for the new system.

iv. Pilot the new thresholds with prospective outcome monitoring.

v. Document and approve the new ranges through institutional quality governance.

This approach mirrors that used by Toffaletti et al. (2003) at Duke University Medical Center. Patteril et al. (2005, Clin Chim Acta) documented that Duke's transition from the Hemochron 801 to the Actalyke system increased total heparin administered to meet ACT targets, without adverse clinical outcomes, consistent with the Actalyke's lower numerical values reflecting a more sensitive early endpoint, not inadequate anticoagulation, once institution-specific targets were appropriately established.

V. **Actalyke System: Product Overview**

Helena Laboratories offers a complete, integrated ACT test system of analyzers and tube reagents engineered for compatibility and validated performance:

a. **Actalyke XL Analyzer (Cat No. 5770):** full-featured laboratory and OR analyzer with dual test wells, touch-screen interface, barcode reader compatibility, data storage, three user security levels, demographic entry, and optional battery pack. Accepts all Actalyke tube types.

b. **Actalyke MINI II Analyzer (Cat No. 5753/5755):** compact, portable analyzer with a high-visibility display and optional printer. Retains full two-point clot-detection sensitivity and is compatible with all Actalyke tube types; suited to catheterization labs, dialysis units, and satellite locations.

c. **MAX-ACT tubes:** blended activator (celite, kaolin, glass bead); 0.5 mL sample; linearity validated to 6.0 U/mL; indicated for moderate-to-high heparin monitoring (CPB, PCI, ECMO).

d. **K-ACT tubes:** kaolin activator; unaffected by aprotinin; indicated for moderate-to-high heparin monitoring.

e. **C-ACT tubes:** celite (diatomaceous earth) activator; the traditional ACT standard.

f. **G-ACT tubes:** glass bead activator.

g. **ECT (XL-ECT):** Electronic Clotting Tube for daily instrument QC; no blood required.

h. **Actalyke Thermometer** (Cat No. 5757).

VI. **Summary and Recommendations**

Reliable ACT-guided anticoagulation management depends on correct analytical technique, a disciplined quality control program, and institutional understanding of the system-specific performance of the platform in use. Distributors and clinical educators should confirm that all end users:

a. Adhere strictly to published procedure: there are no shortcuts in sample handling, mixing, timing, or blood volume.

b. Operate a formal, documented QC program: ECT and temperature verification daily; liquid controls per institutional schedule; all results logged and retained.

c. Verify new tube lots before clinical use: a heparin linearity assessment is required for each new lot before deployment.

d. Never use cross-platform ACT values interchangeably: Actalyke results cannot be compared directly to any other platform. Each clinical program must establish its own therapeutic ranges for the platform in use.

e. Contact Technical Services with questions: available at 1-800-231-5663 (USA) or 409-842-3714 or by email at techservices@helena.com for procedure questions, QC interpretation, lot-verification guidance, and instrument troubleshooting.

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