Hemochron®
SIGNATURE ELITE

Implementation Guide

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Preface

Introduction

The validation studies described in this section are dependent on requirements approved and dictated by the Laboratory Medical Director and the Accrediting Organization for implementing a new lab instrument or assay. Please consult your local governing agency on best practices when validating diagnostic medical equipment, as such best practices may not be reflected in the descriptions set forth in this section.

The Centers for Medicare and Medicaid Services (CMS) administers the Clinical Laboratory Improvement Amendments (CLIA) which regulates all facilities that perform testing on materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of human beings, to meet certain Federal requirements. If a facility performs tests for these purposes, it is considered a laboratory under CLIA and must apply and obtain a certificate from the CLIA program that corresponds to the complexity of tests performed.

Many private agencies have emerged to promulgate standards for laboratory best practices. In addition, these agencies perform site-visits or inspections to the facility to observe and document compliance of laboratory standards. Currently, these agencies include: The College of American Pathologists (CAP), The Joint Commission (TJC - The Joint Commission on the Accreditation of Healthcare Organizations - or formerly known as JCAHO), and the Commission on Laboratory Accreditation (COLA). These inspecting agencies also offer services to U.S. military hospital laboratories. State governments have a strong role in laboratory standards as well. While the Center for Medicare and Medicaid Services (CMS) regulates laboratory performance by way of the Clinical Laboratory Improvement Act (CLIA) at a national level, each individual State Department of Health (DOH) may modify those regulations and hold the testing facilities in their State to these guidelines that also may be more stringent.

CMS has directed that upon purchasing any new analyzer, immediate testing for patient management is not permitted. Regardless of manufacturer's claims or warranties, a series of quality assurance steps must be conducted to validate instrument performance and ensure analytes are reported with accuracy and precision. These implementation procedures are both essential from a Regulatory perspective and are necessary to assure diagnoses and therapeutic maneuvers remain consistent based on results analyzed from values produced from the new instrument.

Before a new analyzer is used for reporting patient results, the validation and verification of instrument performance must be completed and approved by the Medical Director named on the facility's CLIA license, issued by each State DOH. If the instruments are operating under the Clinical Laboratory's CLIA license, the laboratory Medical Director is required to approve the validation process once completed. If any department holds their own independent license to perform testing, they must comply with the standards set by the accrediting organization identified on the CLIA application.

Quality Assurance / Quality Management System (QA/QM) is a sequential integration of policies and processes that transform a physician's order into laboratory information. The objectives of the QA/QM process are to provide quality accurate diagnostic test results and reduce the potential for medical error that wastes resources and harms patients.

A sound QA/QM System and adherence to regulatory compliance guidelines is essential in providing accurate results yielding quality patient care.

To assist in achieving these objectives, Accriva has developed several tools to assist the Point of Care Coordinator (POCC) when implementing the Hemochron Signature Elite. These tools include: Operator Training documents and Instrument Validation Templates. The Operator Training documents are designed to allow the POCC to adapt the information to reflect their unique testing environment. The Instrument Validation Templates have been designed to submit the data to Technical Support for analysis.

Pre-Implementation Checklist

Facility _____

Implementation date: _____

Product: _____

Qty: _____

Project Leaders

POC: _____

BioMed: _____

Cath Lab Manager: _____

Clinical Specialist: _____

Nurse Educator: _____

IT: _____

_____

	☑	Task	Action Required	Ownership
Instrumentation		**Instrument arrival**	Confirm that all instruments have been received.	
		Bio-Med inspection	Arrange for instruments to be approved in accordance with any Biomedical protocol for new instruments.	
		Battery charging	Charge all Hemochron Signature Elite overnight prior to use.	
Disposables		**Ordering of supplies**	Have appropriate amount of disposable cuvettes/ cartridges for validation.	
		Ordering of control material	Have appropriate amount of liquid control material for validation and training.	
Logistics		**Computer**	Designate computer to install software.	
		Software installation (optional)	Coordinate with IT about installation approvals for new software. The software resides in the computer (not in the network).	
		Download locations	Coordinate with IT to establish IP addresses for all download locations, if applicable.	
		Software training	Training on Accriva software. Set-up.	
Training		**Train-the-trainers (if applicable)**	Determine the Train-the-Trainer personnel, clinical educators and department managers to ensure these personnel have been designated and available for the training.	
		Location	Designate location for training. Ideally away from clinical area.	
		Training checklist and Sign-in sheet	Have checklists and sign-in sheet available.	
		Instrument Training	Training and testing of department personnel on new instruments.	
		Additional staff Training	Training / additional training for personnel who did not complete training or need refresher training.	
Extras		**Storage of QC**	Refrigerate until ready to use, or room temperature for 1 hour prior to testing.	
		Training Accessories	Gauze, syringes, needles, Sani-Wipes, sharps container, biohazard bags, trash cans...	

Operator Training & Competency Certification

Overview

Initial training on the Hemochron Signature Elite is required by all US-based regulatory bodies. This should entail a complete review of the department's Policy and Procedures Manual with respect to the Hemochron Signature Elite instrument and all applicable testing. Documentation of training can be accomplished by the operator participating in a written test after review of the Procedure and certified with a Competency Assessment. The Skills Checklist is a detailed list of the skills necessary to successfully manage testing.

Final validation of competency can be demonstrated by successful testing of an unknown sample.

Continued competency certification is also an annual requirement and the same steps are utilized to satisfy this regulation.

These generic documents are designed to be modified by each site to conform to the site's requirements.

Available As Word Documents:

- (3b) **Skills Checklist**
- (3c) **Competency Assessment**
- (3d) **Competency Test**
- (3e) **Answer Key for Written Test**

Training Log

Facility: _____

Department: _____ **Date:** _____

Trainer: _____

Type of Training: ☐ Initial ☐ Semi-annual ☐ Annual ☐ Remedial

Name (print)	Signature	Operator ID (OID)

Skills Checklist

Employee Name _____ Operator ID _____

Employee Signature: _____ Date: _____
(SIGNATURE)

Evaluator: _____ Date: _____
(SIGNATURE)

Skill

Basic Operation

Performance Acceptable?

1	Instrument is powered “On” by pressing the Start key and holding until logo appears	Y / N
2	Instrument needs charging when “Charge Battery” message is flashing on-screen	Y / N
3	Understands functions of keypad: both alphanumeric and function keys	Y / N
4	Can successfully scan using the barcode reader (OID, cuvettes, PID, LQC)	Y / N
5	Can manually enter OID and PID if scanner is not in use	Y / N
6	Understands dual function of “ABC/123” key	Y / N
7	Can successfully “toggle” between the alphanumeric function and the “NOTE” function	Y / N

*OID is Operator Identification
*PID is Patient Identification
*LQC is Liquid Quality Controls

Skills Checklist (Continued)

Skill		Performance Acceptable?
Electronic Quality Control (EQC)		
1	Can describe the function of EQC	Y / N
2	Knows required time interval for EQC	Y / N
3	Knows that EQC may automatically be performed if instrument is plugged into AC power	Y / N
4	Can demonstrate manual initiation of EQC	Y / N
5	Understands the message “Pass” indicates all EQC functions are acceptable	Y / N
6	Understands what steps to take if EQC fails	Y / N
Liquid Quality Control (LQC)		
1	Understands all materials must equilibrated to room temperature	Y / N
2	Knows there are two levels of LQC	Y / N
3	Knows where the acceptable ranges for LQC are located	Y / N
4	Understands that both levels of LQC must be in range before instrument can be used for patient testing	Y / N
5	Understands the purpose of LQC performance	Y / N
6	Knows the frequency of LQC performance	Y / N
7	Knows LQC can be stored at room temperature up to four weeks	Y / N

Skills Checklist (Continued)

Skill

Cuvettes — **Performance Acceptable?**

1	Knows cuvettes stored in the refrigerator expire on the date stamped on the box and each cuvette pouch	Y / N
2	Understands the cuvettes expire 12 weeks if stored at room temperature	Y / N
3	Understands that room temperature storage dates do not exceed the date stamped on the box	Y / N
4	Understands the expiry date must be written on each foil pouch when removed from the refrigerator	Y / N

Competency Assessment

Competency Period: **Initial** **6-month** **Annual** **Remedial**

Employee Name:_____ Unit:_____

How Competency is measured:

1. Direct observation of routine patient testing including: patient preparation, specimen collection, labeling, handling, processing and testing
2. Monitoring the recording and reporting of test results including critical values as applicable
3. Review of intermediate test results or worksheets, QC records, proficiency testing results, and preventative maintenance records
4. Direct observation of instrument maintenance and function checks, if applicable
5. Assessment of test performance through testing of previously analyzed specimens, internal blind testing, or external proficiency testing samples.
6. Evaluation of problem-solving skills

Method Of Competency Assessment	Performance Acceptable?
1. Direct Observation of Patient Testing	
a. Power Hemochron Signature Elite "On"	Y / N
b. Inserts cuvette	Y / N
c. Scans cuvette pouch to enter lot number	Y / N
d. Scans Operator ID	Y / N
e. Scans Patient ID	Y / N
f. Adds specimen to sample well within 5 minutes	Y / N
g. Take correct action if overfilling of sample well occurs	Y / N
h. Start testing by pressing "Start" button	Y / N
i. Correctly reads results	Y / N

Competency Assessment (Continued)

Method Of Competency Assessment	Performance Acceptable?

2. Monitoring the recording/reporting of patient test results

a. Report patient result according to protocol — Y / N

b. Can successfully retrieve patient result from stored database — Y / N

c. Records correct unit of measure on patient record — Y / N

3. Review at prescribed intervals

a. Liquid Quality Control (LQC) Results — Y / N

b. Electronic Quality Control (EQC) Results — Y / N

c. Proficiency testing — Y / N

4. Problem solving skills

a. Error code received during testing process — Y / N

b. Delay in sample application — Y / N

5. Assessment of test performance (complete one of the following)

a. Comparison of test result performed in duplicate — Y / N

b. Analyze LQC – attach LQC values — Y / N

c. Proficiency Testing sample — Y / N

Results

a. Test Results in duplicate:

Serial Number #1 _____ Result #1 _____

Serial Number #2 _____ Result #2 _____

b. LQC acceptable ranges (Level I or Level II: package inserts):

LQC Level _____ LQC Lot # _____ Exp Date _____

Result: _____ Range _____ACT Seconds

c. Proficiency Test Result: _____ Acceptable Range _____

Proficiency Test Event/Year _____

Competency Assessment (Continued)

Method Of Competency Assessment	Performance Acceptable?

6. Assess miscellaneous skills

a.	Management of questionable patient results	Y / N
b.	EQC Failure causes	Y / N
c.	LQC Failure causes	Y / N
d.	Operator lock-out resolution	Y / N
e.	Written Exam completion (Pass)	Y / N

Written Test Score: _____

Date Exam competed: _____

Employee's Signature: _____ **Date:** _____

Evaluator's Signature: _____ **Date:** _____

Evaluator's signature above indicates the employee has demonstrated abilities necessary for the quality performance of these tasks, at an acceptable level.

The employee's signature indicates the employee is confident with the performance of this procedure, is in agreement, and that all statements are truthful in fact.

Competency Test

Name (Printed): _____ **Date:** _____

Signature: _____ **Operator ID:** _____

Department: _____ **Grade:** _____

For Multiple Choice: Choose ONE best answer to complete each statement.

1. The test cuvettes must be allowed to warm to room temperature prior to use. Once at room temperature, the cuvettes are stable for a maximum of:
   a. 1 week
   b. 2 weeks
   c. 4 weeks
   d. 12 weeks

2. To ensure that the test cuvettes do not exceed their room temperature stability, the "New Expiration Date" must be recorded on their package exterior.
   a. True
   b. False

3. After being removed from the refrigerator, a single liquid control vial and / or single cuvette must be allowed to warm to room temperature for:
   a. 5 minutes
   b. up to 1hr
   c. they should be used right from the refrigerator
   d. 1 month

4. Normal and Abnormal Liquid Quality Control (LQC) must be performed:
   a. Whenever a new lot number of cuvettes is received
   b. When a new shipment of with the same lot number as cuvettes currently in use is received
   c. Every 30 days after initial testing
   d. a, b, and c

5. Control vials are stable at room temperature for a maximum of:
   a. 1 week
   b. 2 weeks
   c. 4 weeks
   d. 12 weeks

Competency Test (Continued)

6. **The Electronic Quality Control (EQC) must be run:**
   a. Once weekly
   b. Once daily
   c. Every 12 hours
   d. Every 8 hours of system operation

7. **The operator has the ability to initiate the EQC at any time unless the device is processing a sample.**
   a. True
   b. False

8. **While filling the test cuvette, you observe an excess of blood in the sample well. You should:**
   a. Pull out the cuvette and start over
   b. Push the excess sample into the overflow area
   c. No action is required
   d. Press “CANCEL”

9. **If the message “CHARGE BATTERY” is displayed on the screen, the Hemochron Signature Elite must be plugged into an AC outlet prior to performing the next test.**
   a. True
   b. False

10. **Once the cuvette is removed after completing a test:**
    a. The result remains displayed on the screen
    b. The result disappears from the screen and cannot be retrieved
    c. The result disappears from the screen and can be retrieved using the “Database” key

11. **A result flagged with < or > indicates the following:**
    a. The cuvette is defective
    b. The test result is outside the cuvette’s measuring range.
    c. The analyzer needs to be checked with the Electronic Quality Control (EQC)
    d. The sample should be redrawn and re tested.

12. **Results that appear inconsistent with the patient’s therapy should be viewed as questionable and another sample should be redrawn and tested.**
    a. True
    b. False

Competency Test (Continued)

13. **If the sample is obtained before the message "Add Sample...Press Start" is displayed, the blood will begin to clot and the result may not be accurate.**
    a. True
    b. False

14. **When the device displays the message "Start Timed Out", it means that the specimen has not been added to the sample well within five minutes. To run a test, a new cuvette needs to be inserted into the device, a new specimen must be obtained from the patient, and if required, the operator ID, and patient ID or QC information needs to be re-entered.**
    a. True
    b. False

15. **The EQC test may fail for the following reasons:**
    a. Operator initiated test at 6 hours
    b. The instrument was turned off for 8 hours
    c. Cuvette was left in the Hemochron Signature Elite after testing and not removed before EQC began
    d. EQC was not specified in Configuration Manager

Grader's Name (Printed): _____

Grader's Signature: _____

Answer Key for Competency Test

1. D
2. A
3. B
4. D
5. C
6. D
7. A
8. B
9. A
10. C
11. B
12. A
13. A
14. A
15. C

Validation Studies

Overview

The following information represents the common procedures as specified by the Accrediting Organizations (AOs) for initial validation of each Hemochron Signature Elite:

- Trueness/Precision
- Method Correlation between the "Old" method and the Hemochron Signature Elite
- Reference Interval (Normal Values) Studies

For continued compliance

- Six-month Instrument Correlation: correlating all instruments performing the same test
- Optional: Heparin Response Studies

Trueness & Precision Study Protocols

Testing Method

Operators should be familiar with the technique required to manage the LQC material prior to performing this test.

1. **The process should be done across several days (i.e., 5 days) and by multiple operators to accommodate different techniques and environments.**
2. **The suggested process involves testing Liquid Quality Control material at 2 levels twice per day for a total of 10 results for each level.**
3. **The data collected can be analyzed by Accriva upon request. A template to be electronically sent must be completed entirely or will be returned for correction.**

Procedure

1. **Ensure cuvettes and LQC material are valid and have not expired.**
   a. Make sure the room temperature storage date for the cuvettes (12 week dating) is used if cuvettes are stored at room temperature;
   b. Also make sure the room temperature storage date for the LQC material (4 weeks) is used if the LQC materials are stored at room temperature.
2. **If stored refrigerated, remove necessary supplies and allow to reach room temperature. This process may take up to one hour.**
3. **Follow instructions for testing LQC materials as outlined in the Package Inserts for the LQC material.**
4. **Record results as directed by policy.**
5. **Data analysis: the CV% for each level of LQC should not exceed 14%.**

Optional: Entering Data into the Template for Data Submission to Accriva

The template will be electronically sent to the requesting individual and has key sections in red that must be completed before any data analysis. Instructions for completing the template are included. Technical Support is available for data analysis templates or any assistance:

- Email: **ilsd_techsupport@ilww.com**
- Phone number: **1-800-579-2255**

If the CV exceeds 14%, repeat the testing after reviewing management of the LQC material and the correct operation of the Hemochron Signature instrument.

Method Correlations

Overview

The correlation between the current method and the Hemochron Signature Elite is the Method Correlation. This is accomplished by testing 20 to 40 samples that span the clinical treatment range for that designated application.

The data will demonstrate the average difference (bias: positive or negative) to aid in the determination of the new target time or therapeutic range.

The data can be analyzed by Technical Support.

Contact Information:

- Email: **ilsd_techsupport@ilww.com**
- Phone number: **1-800-579-2255**

Method Correlation Protocol:

ACT+, ACT-LR, Whole Blood APTT and Whole Blood PT

Pre-evaluation

Prior to initiating the Method Correlation Protocol, review the following:

1. **Be familiar with all functions of the Hemochron Signature Elite and review the Operator's Manual.**
2. **Ensure both the Hemochron Signature Elite instrument and the method currently in use are performing correctly by checking Quality markers such as Electronic Quality Control (EQC), Liquid Quality Control (LQC).**
3. **Read all package inserts.**
4. **Review this entire protocol before beginning the evaluation.**

Patient Population

A sufficient number of patient samples must be obtained to span the entire normal and therapeutic range. CLSI EP-09 recommends a total of 40 patient samples.

Patient results must span the entire treatment range to include baseline or pre-heparinization, post-heparin administration and reversal with protamine, if applicable.

Material Preparation

Prior to initiating the Method Correlation Protocol, review the following:

1. **Cuvettes can be stored at refrigerated temperatures (2-8°C or 35-46°F). If refrigerated, allow cuvette to come to room temperature. This may take up to one hour.**
2. **Testing is performed with cuvettes at room temperature (15-30°C or 59-82°F).**

Method Correlation Protocol: ACT+ / ACT-LR / APTT / PT (Continued)

Test Procedure and Blood Collection

1. **Insert room temperature cuvette into the Hemochron Signature Elite.**
2. **Follow site policy for entering cuvette lot information, Operator ID (OID) and Patient ID (PID).**
3. **Prepare the reference instrument for testing**
4. **Collect whole blood samples in a non-heparinized syringe.**
   a. If obtaining blood by venipuncture, the needle must not be smaller than 23 guage.
   b. If collecting from an indwelling line, ensure sufficient waste is removed from the system before obtaining the specimen for testing.
5. **Add specimen to the sample well of the cuvette and test according to procedure.**
6. **Add the sample to the reference method and test according to procedure.**
7. **Record the results from the reference method and the Hemochron Signature Elite on a data collection sheet.**
   - NOTE: When comparing APTT, use the plasma-equivalent (P-E) seconds. When comparing PT, use the INR.
8. **Optional: the customer may request support with the data analysis by contacting Technical Support:**
   - Email: **ilsd_techsupport@ilww.com**
   - Phone number: **1-800-579-2255**

Interpretation of results:

Method correlations demonstrate the statistical similarity of two different test systems.

The target time or therapeutic ranges are adjusted by the average difference between the current system and the Hemochron Signature Elite.

The average difference and the bias graph provide the best approximation of how the target times or therapeutic ranges may be altered.

Some facilities may choose not to change the target times or therapeutic ranges due to a lack of statistical difference between methods. The Medical Director must approve of any changes in target times or therapeutic range.

Method Correlation Protocol:

Citrate APTT & Citrate PT

Pre-evaluation

1. Be familiar with all functions of the Hemochron Signature Elite and review the Operator's Manual.
2. Ensure both the Hemochron Signature Elite instrument and the method currently in use are performing correctly by checking Quality markers such as Electronic Quality Control (EQC), Liquid Quality Control (LQC) and maintenance records.
3. Read all package inserts.
4. Review this entire protocol before beginning the evaluation.

Patient Population

A sufficient number of patient samples must be obtained to span the entire normal and therapeutic range. CLSI EP-09 recommends a total of 40 patient samples.

The patient samples must span the entire range of treatment to include baseline or pre-anticoagulant administration, if possible, and post-treatment.

Material Preparation

1. Cuvettes can be stored at refrigerated temperatures (2-8°C or 35-46°F). If refrigerated, allow cuvette to come to room temperature. This may take up to one hour.
2. Testing is performed with cuvettes at room temperature (15-30°C or 59-82°F).

Method Correlation Protocol: Citrate APTT & Citrate PT (Continued)

Test Procedure and Blood Collection

1. **Collect whole blood samples in a 3.2% citrate vacutainer tube or a non-heparinized syringe;**
   a. If collecting from an indwelling line, ensure sufficient waste is removed from the system before obtaining the specimen for testing;
   b. If collected into a syringe, transfer the specimen immediately to a 3.2% citrate tube.
2. **Insert room temperature cuvette into the Hemochron Signature Elite.**
3. **Follow policy for entering cuvette lot number, Operator ID (OID) and Patient ID (PID).**
4. **Add specimen to the sample well of the cuvette when indicated and test according to procedure.**
   - NOTE: If only a single citrate tube was collected, always test sample using Hemochron Signature Elite before centrifuging as sample cannot be re-mixed after centrifugation.
5. **If two citrate tubes were collected, process the second tube according to protocol.**
6. **Process and test using the reference method according to protocol.**
7. **Record the results from the reference method and the Hemochron Signature Elite.**
   - NOTE: If correlating Cit APTT, use the plasma-equivalent (P-E) seconds from the Hemochron Signature Elite. If correlating the Cit PT, use the INR results for correlation.
8. **Optional: the customer may request support with the data analysis by contacting Technical Support:**
   - Email: **ilsd_techsupport@ilww.com**
   - Phone number: **1-800-579-2255**

Interpretation of results:

Method correlations demonstrate the statistical similarity of two different test systems.

Citrated APTT: The therapeutic range may be adjusted by the average difference between the current system and the Hemochron Signature Elite using the P-E results. The average difference and the bias graph provide the best approximation of how the target times or therapeutic ranges may be altered.

Some facilities may choose not to change the target times or therapeutic ranges due to a lack of statistical difference between methods. The Medical Director must approve of any changes in target times or therapeutic range.

Citrated PT: The test has been designed to closely match most clinical laboratory instruments when comparing INR results. The Medical Director of each site will decide if the method meets their expectations.

Reference Interval Studies (Normal Values Range)

Overview

The Reference Interval has to be established prior to using the new method to report patient results.

The Reference Interval study must be performed to determine the range for healthy individuals and this range must be included on the result reports.

CMS/ CLIA “Brochure #2 Verification of Performance” and CLSI Document C28 both suggest that as few as 20 individuals may be sufficient to verify the reference interval.

The final decision for the total number of individuals to be tested will be made by the Medical Director.

Reference Interval Studies (Normal Values Range) Protocol:

ACT+, ACT-LR, APTT & PT

Pre-evaluation

Prior to beginning the Reference Interval Study Protocol, review the following:

1. Be familiar with all functions of the Hemochron Signature Elite and review the Operator's Manual.
2. Ensure the Hemochron Signature Elite instrument has been fully validated and performing correctly by checking Quality markers such as Electronic Quality Control (EQC), Liquid Quality Control (LQC) and maintenance records.
3. Read all package inserts.
4. Review this entire protocol before beginning the evaluation.

Donor Population

1. A sufficient number of normal donor samples must be obtained.
2. CMS/CLIA Brochure #2 and CLSI Document C28-A3 suggest the evaluation may be completed using as few as 20 normal donors.

Material Preparation

1. Cuvettes can be stored at refrigerated temperatures (2-8°C or 35-46°F). If refrigerated, allow cuvette to come to room temperature. This may take up to one hour.
2. Testing is performed with cuvettes at room temperature (15-30°C or 59-82°F).

Reference Interval Studies (Normal Values Range) Protocol:

ACT+, ACT-LR, APTT & PT (Continued)

Test Procedure & Blood Collection

1. **Insert room temperature cuvette into the Hemochron Signature Elite.**
2. **Follow site policy for entering the cuvette lot number, Operator ID (OID) and Patient ID (PID).**
3. **Collect whole blood samples in a non-heparinized syringe.**
   a. If obtaining blood by venipuncture, the needle must not be smaller than 23 Gauge;
   b. If collecting from an indwelling line, ensure sufficient waste is removed from the system before obtaining the specimen for testing.
4. **Add specimen to the sample well of the cuvette and test according to procedure.**
5. **Record the Hemochron Signature Elite results as specified by policy.**

Results

1. **Record Hemochron Signature Elite results.**
2. **Once the appropriate number of data points have been collected:**
   a. Review data for any results inconsistent with product performance.
   b. Remove outliers if appropriate - each facility will determine what constitutes an outlier.
   c. If outliers exceed 10% of all results, the evaluation may not be valid.
3. **Optional: the customer may request data analysis by contacting Technical Support:**
   - Email: **ilsd_techsupport@ilww.com**
   - Phone number: **1-800-579-2255**

Interpretation of Results:

The Reference Interval is required on all patient results by all regulatory agencies.

The site may use the manufacturer's data as provided in the package insert for the method or data from a text book or peer-reviewed journal provided the verification of this data is documented by performing the Reference Interval study in some form.

Reference Interval Studies (Normal Values Range) Protocol:

Citrate APTT & Citrate PT

Pre-evaluation

1. Be familiar with all functions of the Hemochron Signature Elite and review the Operator's Manual.
2. Ensure the Hemochron Signature Elite instrument has been fully validated and performing correctly by checking Quality markers such as Electronic Quality Control (EQC), Liquid Quality Control (LQC).
3. Read all package inserts.
4. Review this entire protocol before beginning the evaluation.

Donor Population

1. A sufficient number of normal donor samples must be obtained.
2. CMS/CLIA Brochure #2 and CLSI Document C28-A3 suggest the evaluation may be completed using as few as 20 normal donors.

Material Preparation

1. Cuvettes can be stored at refrigerated temperatures (2-8°C or 35-46°F). If refrigerated, allow cuvette to come to room temperature. This may take up to one hour.
2. Testing is performed with cuvettes at room temperature (15-30°C or 59-82°F).

Reference Interval Studies (Normal Values Range) Protocol:

Citrate APTT & Citrate PT (Continued)

Test Procedure & Blood Collection

1. **Collect whole blood samples in a 3.2% citrate vacutainer tube or non-heparinized syringe.**
   a. When obtaining blood by venipuncture, the needle must not be smaller than 23 Gauge;
   b. If collecting from an indwelling line, ensure sufficient waste is removed from the system before obtaining the specimen for testing;
   c. If collected into a syringe, transfer the specimen immediately to a 3.2% citrate tube;
   d. Gently mix before testing.
2. **Insert room temperature cuvette into the Hemochron Signature Elite to be tested.**
3. **Follow site policy for entering cuvette lot number, Operator ID (OID) and Patient ID (PID).**
4. **Add specimen to the sample well of each cuvette and test according to procedure.**
5. **Record the results.**
6. **Optional: the customer may request the data analysis be performed by contacting Technical Support:**
   - Email: **ilsd_techsupport@ilww.com**
   - Phone number: **1-800-579-2255**

Interpretation of Results:

The Reference Interval is required on all patient results by all regulatory agencies.

Each site may use the manufacturer's data as provided in the package insert for each method or data from a text book or peer-reviewed journal provided the verification of this data is documented by performing the Reference Interval study in some form.

Instrument Correlation

Overview

Instrument correlation is a mandatory comparison among instruments performing the same test at six-month intervals. The purpose of this comparison is to assure patient care will be uniform regardless of which instrument is employed to perform patient testing.

Each manufacturer provides a specification for this agreement. Hemochron Signature Elite instruments must agree within 10% when testing the same patient sample simultaneously.

Instrument Correlation Protocol

Pre-evaluation

1. Be familiar with all functions of the Hemochron Signature Elite and review the Operator's Manual.
2. Ensure the Hemochron Signature Elite instrument has been fully validated and performing correctly by checking Quality markers such as Electronic Quality Control (EQC), Liquid Quality Control (LQC).
3. Read all package inserts.
4. Review this entire protocol before beginning the evaluation.

Patient Population

1. Samples should represent the patient treatment range.
2. The Medical Director will determine the number of patient samples to be performed.

Material Preparation

1. Cuvettes can be stored at refrigerated temperatures (2-8°C or 35-46°F). If refrigerated, allow cuvette to come to room temperature. This may take up to one hour.
2. The number of Hemochron Signature Elite instruments to be tested is determined by each facility.
3. Testing is performed with cuvettes at room temperature (15-30°C or 59-82°F).

Instrument Correlation Protocol (Continued)

Test Procedure & Blood Collection

1. **Insert room temperature cuvette into the Hemochron Signature Elite to be tested.**
2. **Enter cuvette lot number, Operator ID (OID) and Patient ID (PID) according to site policy.**
3. **Collect whole blood samples in a non-heparinized syringe.**
   a. If obtaining blood by venipuncture, the needle must not be smaller than 23 Gauge;
   b. If collecting from an indwelling line, ensure sufficient waste is removed from the system before obtaining the specimen for testing.
4. **Add specimen to the sample well of each cuvette and test according to procedure.**
5. **Record the results from all instruments.**
6. **Optional: the customer may submit the data analysis to Technical Support:**
   - Email: **ilsd_techsupport@ilww.com**
   - Phone number: **1-800-579-2255**

Interpretation of Results:

Instrument correlations demonstrate the statistical similarity of the test to demonstrate agreement regardless of which instrument is used for testing.

Any instrument that exceeds the allowable 10% variance when testing the same patient sample at the same time as the other instruments should be removed from patient testing until the reason for the unacceptable variance is resolved.

Optional: Heparin Response Studies

Overview

The Heparin Response studies are designed to evaluate the response of the system (Hemochron Signature Elite and cuvette) to increasing concentrations of heparin.

This is not an evaluation of instrument “Linearity” as the donor varies in heparin sensitivity and heparin response is never linear. Linearity testing is also not required by any regulatory agency for whole blood coagulation assays.

This test is not an evaluation of the Analytical Measurement Range as this is not a requirement by any accrediting organization for whole blood coagulation assays.

There are three separate heparin response studies for the Hemochron Signature Elite as each test is designed for an optimal heparin concentration.

Heparin Response Protocol: ACT+

Intended Use

The Heparin Response Study can be used to evaluate system performance. This in vitro testing consists of testing the baseline or non-heparinized sample and then adding whole blood to serial dilutions of heparin (range: 1.0 U/mL to 6.0 U/mL).

The Analytic Measurement Range (AMR): 68 – 1005 Celite-equivalent seconds.

This Study may not be required by the inspecting agency; each site should determine if this study is mandatory.

As each individual has a unique response to heparin as the ACT results in the higher concentrations may exceed the AMR and will yield an "Out of Range-Hi" message on the Hemochron Signature Elite. These results can be recorded as such but must be understood this result is a reflection of the donor's sensitivity to heparin and not an instrument malfunction.

While the procedure is written for a total volume of 1 mL of donor blood, better results are obtained by using larger volumes of donor blood and the accordingly adjustment also made in heparin amount to maintain the same heparin concentration.

Materials

- **Hemochron Jr ACT+ cuvettes**
- **Plastic test tubes with caps**
- **USP Heparin (concentration 1000 IU/mL)**
- **Normal saline**
- **Syringe needle (not less than 23 Gauge)**
- **Plastic syringe (capacity to be determined by total volume necessary)**
- **Precision pipettes capable of measuring to a minimum of 10 µL**
- **Plastic transfer pipettes**
- **Graduated pipettes able to measure in 1 mL increments**

Heparin Response Protocol: ACT+ (Continued)

Procedure

1. Obtain 5 Hemochron Jr ACT+ cuvettes (optional: 7 cuvettes for the full study) for each Hemochron Signature Elite or Hemochron Signature+ instrument being tested. The cuvettes must be at room temperature before opening the pouch
2. Dilute the heparin to a concentration of 100 U/mL. This is accomplished by adding 9 mL normal saline to 1 mL of the USP heparin (concentration 1000 U/mL). The diluted heparin preparation must be well-mixed and at room temperature prior to use.
3. Label 5 (optional: 7 tubes) plastic test tubes in the following manner: "A" (or add the sample directly to the testing well), "B", "C", "D" and "E" (optional: F, G).
4. Dispense the following quantities of the diluted heparin into the respective test tubes. The final concentration of heparin in the plastic test tubes after the addition of 1 mL fresh whole blood can be found in ***Table 1***.

Table 1 – Basic Dilution Guide*

Tube	Amount of Heparin (µL)	Whole Blood (mL)	Heparin (Units/1 mL Blood)
A	0	1.0	0
B	10	1.0	1.0
C	20	1.0	2.0
D	30	1.0	3.0
E	40	1.0	4.0
F (optional)	50	1.0	5.0
G (optional)	60	1.0	6.0

* Better performance may be observed by using larger quantities of blood; the heparin amount must be increased proportionately to maintain the final concentrations as listed.

5. Draw the necessary blood volume via venipuncture using the syringe method; dispense the appropriate volume of blood into each tube that contains the described amount of diluted heparin.
6. For the tubes containing heparin, mix the diluted heparin with the blood by gentle end-to-end inversion in the capped plastic tube before use.
7. Tube "A" must be tested immediately. Transfer to the testing well of the cuvette by a plastic transfer pipette.
   NOTE: in lieu of a tube, the sampling may be directly from the syringe.
8. Test the remaining tubes in the order of lowest to highest concentration of heparin; mix each tube thoroughly before testing.

Heparin Response Protocol: ACT+ (Continued)

Procedure (continued)

9. Record the results for each instrument tested.
10. The resulting data may be recorded ***Table 2.***

Notes

- The actual ACT+ results obtained will vary among donors due to the individual responses to heparin. The optional heparin concentrations of 5.0 U/mL and 6.0 U/mL may yield results that exceed the reportable range of the system.
- The heparin manufacturer source and lot number of the heparin may also affect results.
- The maximum concentration of heparin at which donor blood will clot is dependent upon physiologic characteristics of the donor.

Table 2 – Data Collection

Tube	Amount of Heparin (µL)	Whole Blood (mL)	Total Heparin Concentration	Results
A			0	
B			1.0	
C			2.0	
D			3.0	
E			4.0	
F (optional)			5.0	
G (optional)			6.0	
Heparin Manufacturer			Lot No.	Exp Date

Heparin Response Protocol: ACT+ (Continued)

Serial Number _____ **Date** _____

Cuvette Lot Number _____ **Exp. Date** _____

Tube	Amount of Heparin (µL)	Whole Blood (mL)	Total Heparin Concentration	Results
A			0	
B			1.0	
C			2.0	
D			3.0	
E			4.0	
F (optional)			5.0	
G (optional)			6.0	
Heparin Manufacturer			Lot No.	Exp Date

Serial Number _____ **Date** _____

Cuvette Lot Number _____ **Exp. Date** _____

Tube	Amount of Heparin (µL)	Whole Blood (mL)	Total Heparin Concentration	Results
A			0	
B			1.0	
C			2.0	
D			3.0	
E			4.0	
F (optional)			5.0	
G (optional)			6.0	
Heparin Manufacturer			Lot No.	Exp Date

Heparin Response Protocol: ACT-LR

Intended Use

The Heparin Response Study can be used to evaluate system performance. This in vitro testing consists of adding whole blood to serial dilutions of heparin (range: up to 2.5 U/mL).

The Analytic Measurement Range (AMR): 65 – 400 Celite-equivalent seconds.

This Study may not be required by the inspecting agency; each site should determine if this study is mandatory.

As each individual has a unique response to heparin as the ACT results in the higher concentrations may exceed the Analytic Measurement Range (AMR) and will yield an "Out of Range-Hi" message on the Hemochron Signature Elite. These results can be recorded as such but must be understood this result is a reflection of the donor's sensitivity to heparin and not an instrument malfunction.

This procedure has been written using 1 mL of donor blood. Optimal results are obtained using larger volumes of donor blood but the heparin volumes must be adjusted to maintain the heparin concentrations.

Materials

- **Hemochron Jr ACT-LR cuvettes**
- **Plastic test tubes with caps**
- **USP Heparin (concentration 1000 IU/mL)**
- **Normal saline**
- **Syringe needle (not less than 23 Gauge)**
- **Plastic syringe (capacity to be determined by total volume necessary)**
- **Precision pipettes capable of measuring to a minimum of 10 µL**
- **Plastic transfer pipettes**
- **Graduated pipettes able to measure in 1 mL increments**

Heparin Response Protocol: ACT-LR (Continued)

Procedure

1. Obtain 5 Hemochron Jr ACT-LR cuvettes (optional: 7 ACT-LR cuvettes for the full study) for each Hemochron Signature series instrument being tested. The cuvettes must be at room temperature before opening the pouch.
2. Dilute the heparin to a concentration of 100 U/mL. This is accomplished by adding 9 mL normal saline to 1 mL of the USP heparin (concentration 1000 U/mL). The diluted heparin preparation must be well-mixed and at room temperature prior to use.
3. Label 5 (optional: 7) plastic test tubes in the following manner: "A" (or add the sample directly to the sample well from the syringe), "B", "C", "D" and "E" (optional: F, G). Dispense the following quantities of the diluted heparin into the respective test tubes.
4. The final concentration of heparin in the plastic test tubes after the addition of 1 mL fresh whole blood can be found in ***Table 1***.

Table 1 – Basic Dilution Guide*

Tube	Amount of Heparin (µL)	Whole Blood (mL)	Heparin (Units/1 mL Blood)
A	0	1.0	0
B	2.5	1.0	0.25
C	5.0	1.0	0.5
D	10.0	1.0	1.0
E	15.0	1.0	1.5
F (optional)	20.0	1.0	2.0
G (optional)	25.0	1.0	2.5

* Better performance may be observed by using larger quantities of blood; the heparin amount must be increased proportionately to maintain the final concentrations as listed.

5. Draw the necessary blood volume via venipuncture using the syringe method; dispense the appropriate volume of blood into each tube that contains the described amount of diluted heparin.
6. For the tubes containing heparin, mix the diluted heparin with the blood by gentle end-to-end inversion in the capped plastic tube before use.
7. Tube "A" must be tested immediately. Transfer to the testing well of the cuvette by a plastic transfer pipette.
   NOTE: in lieu of a tube, the sampling may be directly from the syringe.
8. Test the remaining tubes in the order of lowest to highest concentration of heparin; mix each tube thoroughly before testing.

Heparin Response Protocol: ACT-LR (Continued)

Procedure (continued)

9. Record the results for each instrument tested.
10. The resulting data may be recorded on ***Table 2.***

Notes

- The actual ACT-LR results obtained will vary among donors due to the individual responses to heparin. The optional heparin concentrations of 2.0 U/mL and 2.5 U/mL may yield results that exceed the reportable range of the system.
- The heparin manufacturer source and lot number of the heparin may also affect results.
- The maximum concentration of heparin at which donor blood will clot is dependent upon physiologic characteristics of the donor.

Table 2 – Data Collection

Tube	Amount of Heparin (µL)	Whole Blood (mL)	Total Heparin Concentration	Results
A			0	
B			0.25	
C			0.5	
D			1.0	
E			1.5	
F (optional)			2.0	
G (optional)			2.5	
Heparin Manufacturer			Lot No.	Exp Date

Heparin Response Protocol: ACT-LR (Continued)

Serial Number _____ **Date** _____

Cuvette Lot Number _____ **Exp. Date** _____

Tube	Amount of Heparin (µL)	Whole Blood (mL)	Total Heparin Concentration	Results
A			0	
B			0.25	
C			0.5	
D			1.0	
E			1.5	
F (optional)			2.0	
G (optional)			2.5	
Heparin Manufacturer			Lot No.	Exp Date

Serial Number _____ **Date** _____

Cuvette Lot Number _____ **Exp. Date** _____

Tube	Amount of Heparin (µL)	Whole Blood (mL)	Total Heparin Concentration	Results
A			0	
B			0.25	
C			0.5	
D			1.0	
E			1.5	
F (optional)			2.0	
G (optional)			2.5	
Heparin Manufacturer			Lot No.	Exp Date

Heparin Response Protocol: APTT & Citrate APTT

Intended Use

The Heparin Response Study can be used to evaluate system performance. This in vitro testing consists of adding whole blood to serial dilutions of heparin (range: up to 1.5 U/mL).

APTT Analytic Measurement Range (AMR): 20 – 399.9 plasma-equivalent (P-E) seconds.

Cit APTT AMR: 20.0 – 396.9 P-E seconds

This Study may not be required by the inspecting agency; each site should determine if this study is mandatory.

As each individual has a unique response to heparin as the APTT results in the higher concentrations may exceed the AMR and will yield an "Out of Range-Hi" message on the Hemochron Signature Elite. These results can be recorded as such but must be understood this result is a reflection of the donor's sensitivity to heparin and not an instrument malfunction.

The procedure has been written for the donor blood volume of 1 mL. Optimal results can be obtained when using larger volumes of donor blood but the heparin volumes must be adjusted to maintain the desired concentrations.

Citrate APTT testing is collected into 3.2% sodium citrate tubes and gently mix the sample or place on a hematology-type rocker prior to dispensing into each tube.

Materials

- **Hemochron® APTT cuvettes or Cit APTT cuvettes**
- **Plastic test tubes with caps**
- **USP Heparin (concentration 1000 IU/mL)**
- **Normal saline**
- **Syringe needle (not less than 23 Gauge)**
- **For APTT: Plastic syringe (capacity to be determined by total volume necessary)**
- **Precision pipettes capable of measuring to a minimum of 10 µL**
- **Plastic transfer pipettes**
- **Graduated pipettes able to measure in 1 mL increments**
- **For Cit APTT: appropriate number of 3.2% sodium citrate vacutainer tubes**

Heparin Response Protocol: APTT & Citrate APTT (Continued)

Procedure

1. Obtain 5 APTT cuvettes or Cit APTT cuvettes (optional: 6 APTT cuvettes for the full study) for each HEMOCHRON Signature series instrument being tested. The cuvettes must be at room temperature before opening the pouch.

2. Dilute the heparin to a concentration of 100 U/mL. This is accomplished by adding 9 mL normal saline to 1 mL of the USP heparin (concentration 1000 U/mL). The diluted heparin preparation must be well-mixed and at room temperature prior to use.

3. Label 5 (optional: 6) plastic test tubes in the following manner: "A" (for APTT: dispense the sample directly from the syringe; for Cit APTT: remove sample directly from the citrate tube) , "B", "C", "D" and "E" (optional: F).

4. Dispense the following quantities of the diluted heparin into the respective test tubes. The final concentration of heparin in the plastic test tubes after the addition of 1 mL fresh whole blood can be found in ***Table 1***.

Table 1 – Basic Dilution Guide*

Tube	Amount of Heparin (µL)	Whole Blood (mL)	Heparin (Units/1 mL Blood)
A	0	1.0	0
B	2.5	1.0	0.25
C	5.0	1.0	0.5
D	7.5	1.0	0.75
E	1.0	1.0	1.0
F (optional)	1.5	1.0	1.5

* Better performance may be observed by using larger quantities of blood; the heparin amount must be increased proportionately to maintain the final concentrations as listed.

5. Draw the necessary blood volume via venipuncture using the syringe method; dispense the appropriate volume of blood into each tube that contains the described amount of diluted heparin.

6. For Cit APTT: either collect several sodium citrate vacutainers or collect the necessary amount by syringe and transfer immediately to the required number of citrate vacutainers.

7. For the tubes containing heparin, mix the diluted heparin with the blood by gentle end-to-end inversion in the capped plastic tube before use.

8. For Cit APTT: Test by transferring the sample using a transfer pipette from 3.2% Citrate tube.

Heparin Response Protocol: APTT & Citrate APTT (Continued)

Procedure (continued)

10. Test the remaining tubes in the order of lowest to highest concentration of heparin; mix each tube thoroughly before testing.

11. Record the results for each instrument tested.

12. The resulting data may be recorded on ***Table 2.***

Notes

- The actual APTT results obtained will vary among donors due to the individual responses to heparin. The optional heparin concentrations of 1.5 U/mL may yield results that exceed the reportable range of the system.
- The heparin manufacturer source and lot number of the heparin may also affect results.
- The maximum concentration of heparin at which donor blood will clot is dependent upon physiologic characteristics of the donor.

Table 2 – Data Collection

Tube	Amount of Heparin (µL)	Whole Blood (mL)	Total Heparin Concentration	Results
A			0	
B			0.25	
C			0.5	
D			0.75	
E			1.0	
F (optional)			1.5	
Heparin Manufacturer			Lot No.	Exp Date

Heparin Response Protocol: APTT & Citrate APTT (Continued)

Serial Number _____ **Date** _____

Cuvette Lot Number _____ **Exp. Date** _____

Tube	Amount of Heparin (µL)	Whole Blood (mL)	Total Heparin Concentration	Results
A			0	
B			0.25	
C			0.5	
D			0.75	
E			1.0	
F (optional)			1.5	
Heparin Manufacturer			Lot No.	Exp Date

Serial Number _____ **Date** _____

Cuvette Lot Number _____ **Exp. Date** _____

Tube	Amount of Heparin (µL)	Whole Blood (mL)	Total Heparin Concentration	Results
A			0	
B			0.25	
C			0.5	
D			0.75	
E			1.0	
F (optional)			1.5	
Heparin Manufacturer			Lot No.	Exp Date