INR (PT) Testing by Hemochron Signature Elite ™
Department of Clinical Laboratories
The Ohio State University Wexner Medical Center

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Point of Care Testing	Procedure	01/05/2011	POC-7 Revision 8

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Approval*:
Point of Care Coagulation Division Director University Hospitals Laboratory Medical Director

Approval and Acknowledgements
Refer to QPulse system and Document Details report for laboratory directors(s)' electronic signature approval, employee acknowledgment and effective date.

1. **PRINCIPLE:**
   1.1. The HEMOCHRON PT test measures the extrinsic coagulation pathway and is sensitive to coagulation factors VII, X, V, II and fibrinogen.
   1.2. HEMOCHRON Microcoagulation Systems utilize a mechanical endpoint clotting mechanism in which testing occurs within the disposable INR cuvette. Following whole blood sample introduction, the instrument precisely measures 15 microliters of blood and automatically moves it into the test channel within the cuvette. The remainder of the blood sample, not needed for testing, is automatically drawn into the waste channel of the cuvette.
   1.3. Sample/reagent mixing and test initiation are performed automatically, requiring no operator interaction. After mixing with the reagent, the sample is moved back and forth within the test channel and monitored by the analyzer for clot formation. The clot detection mechanism consists of two LED optical detectors aligned with the test channel of the cuvette. The speed at which the blood sample moves between the two detectors is measured. As clot formation begins, blood flow is impeded and the movement slows. The instrument recognizes that a clot endpoint has been achieved when the movement decreases below a predetermined rate. Electronic optical detection of a fibrin clot in the blood sample automatically terminates the test. The Signature Elite mathematically converts the whole blood values to International Normalized Ratio (INR) and plasma equivalent value.
   1.4. The prothrombin time can be prolonged in certain clinical states, i.e. warfarin therapy, intestinal reabsorption disorders, Vitamin K deficiency, liver failure, and DIC. The prothrombin time is also used to monitor warfarin (Coumadin) therapy because of its sensitivity to variations in the concentration of the Vitamin-K dependent factors II, VII and X. Because of the variations in the prothrombin time results with different thromboplastins and instruments, it is recommended that the prothrombin time results be converted to an International Normalized Ratio (INR). The INR corresponds to the value of the ratio of the patient's PT and the geometric mean PT of the normal reference population raised to the ISI (International Sensitivity Index) power.

2. **SCOPE OF DOCUMENT:**
   2.1. This document applies to all pre procedural areas that perform POC INR testing.

3. **RESPONSIBILITY:**
   3.1. The POCT coordinators and manager are responsible for maintaining this document and ensuring biennial review. The coagulation laboratory division director is responsible for approving all changes, and reviewing at least biennial. The laboratory medical director is responsible for establishing and approving all changes before activating document.

4. **SPECIMEN COLLECTION:**
   4.1. All institutional policies and procedures should be followed in the collection of blood samples.
   4.2. Patient preparation: Verify patient identification using at least 2 identifiers.
      4.2.1. During surgical procedures, patients are identified per OSU Time Out.
   4.3. Specimen Type: Venous whole blood collected in a Vacutainer tube containing sodium citrate (3.8% or 3.2%). The sodium citrate tube must be filled until flow stops to ensure a 9:1 (blood: anticoagulant) ratio.
      4.3.1. For specimens collected from an IV system, obtain at least 5 ml of dead space volumes of blood and discard prior to collection of the test sample in order to eliminate the risk of excess dilution and contamination of the sample with heparin.
   4.4. Blood samples for testing should be labeled with the patient's label. Samples should sit on a rocker for at least 5 minutes prior to testing to allow for adequate mixing of the sodium citrate with the sample. Optimal results are obtained when samples are tested within 1 hour, and specimens maintained at room temperature until tested.
   4.5. Unacceptable specimen:
      4.5.1. Blood obtained from heparinized access line, lock or indwelling heparin lock.
      4.5.2. Clotted specimens.
      4.5.3. Incorrect sodium citrate tube volume (under or over filled tube).

5. **REAGENTS/SUPPLIES:**

5.1. Room temperature (15-30°C) is monitored each day of use by the testing department and recorded on temperature log. The temperature log is reviewed monthly by the POC department.
5.1.1. If a minimum/maximum thermometer is used to perform continuous monitoring of temperature between daily temperature readings or following a laboratory downtime (e.g. laboratory closure for weekend or holiday), both the low and high temperatures must be recorded. To ensure correct temperature readings, the minimum/maximum thermometer device must be reset prior to the monitoring period.

5.2. ITC Hemochron Signature Elite™
5.2.1. The ITC Hemochron Signature Elite must be used at room temperature 15-30°C (59-86°F).
5.2.2. There are no humidity requirements to use the ITC Hemochron Signature Elite.
5.2.3. If the HEMOCHRON test system becomes inoperable, do not use the system and contact the Point-of-Care department at 614-685-6610 immediately. A loaner device may be available for use.

5.3.Citrated INR cuvettes
5.3.1. The citrated PT/INR cuvette is a self-contained disposable test chamber preloaded with dried preparation of thromboplastin, calcium salts, stabilizers, and buffers. Each cuvette is individually packaged in a pouch.
5.3.2. Each lot of cuvettes should be validated for performance when a new shipment is received and once per 30 calendar days thereafter by:
5.3.2.1. Running two liquid quality control levels.
5.3.2.2. Running one patient specimen on new lot of cuvette and on the previous lot of cuvette-compare results. Acceptable results are within 20%.
5.3.3. Acceptable performance ranges for the cuvettes are included with each quality control product kit.
5.3.4. Cuvettes can be stored in the refrigerator (2-8°C) up to the manufacturer expiration date. Do not use beyond manufacturer expiration date. The cuvettes are stored in the POC department refrigerator which is monitored by Isensix.
5.3.5. Upon removal from refrigerator, the cuvettes are stored at room temperature (15-30$_0$C). Room temperature re-dating is to a maximum of 12 weeks, but must never exceed the marked manufacturer expiration date.

5.4. ***Direct*Check ™ liquid controls**
5.4.1. INR controls: Level 1 (DCJCPT-N) and Level 2 (DCJCPT-A)
5.4.2. Both controls consist of dried fixed bovine red blood cells, buffered sheep and horse plasma. The diluent portion in the dropper vial contains distilled water, sodium chloride, Tween 20, anticoagulant and calcium chloride. The diluent rehydrates the dried blood once the vial is cracked.
5.4.3. When refrigerated (2-8°C) the vials are stable until the marked expiration date. Vials may also be stored at room temperature (15-30°C) for up to 4 weeks, but must never exceed the marked expiration date.

6. SPECIAL SAFETY PRECAUTIONS:

WARNING: BODY FLUID PRECAUTION

6.1. Blood is a body fluid capable of transmitting infectious diseases. Universal precautions for the prevention of the transmission of blood borne pathogens must be in effect at all times.
6.2. Personal protective equipment: wear gloves throughout the specimen collection and testing process. If a tube piercer is not present to obtain a drop of blood, use gauze to avoid any blood and body fluid exposure when removing the cap from the tube.

7. CALIBRATION/PROGRAMMING/CLEANING:

7.1. Calibration: The instrument is self-calibrated, as all instrument functions are continuously monitored and verified by the instrument software when a test is performed. The instrument does not required additional calibration by the user.
7.2. Correlation: performed biannually. Refer to POC Quality Management Plan.
7.3. Routine Cleaning:
7.3.1. Inspect and clean the cuvette opening at least monthly.

7.3.2. If disinfection is needed, disinfect with a 0.5% solutions of sodium hypochlorite (Orange Sani Wipes).
7.3.3. DO NOT submerse the unit in any liquids.
7.4. System Self-Check: Each ITC Hemochron Signature Elite is equipped to perform a self-check every time the instrument is activated and a test is performed. When a test is initiated by insertion of a cuvette, the system automatically checks:
7.4.1. Verification of adequate battery power to complete a full test.
7.4.2. Verification of the test type on the screen display to ensure that the Liquid Electronic Diodes (LED's) used for identifying the tests are functioning properly.
7.4.3. Verification that the cuvette temperature is warmed to 37°C ±1°C. If this temperature is not achieved or is exceeded, an appropriate error message will be displayed and testing is prohibited.
7.4.4. Verification that the internal timers function correctly for each test. If the system timer and assay timer disagree, a real-time clock error message is displayed and the test result is not reported.
7.4.5. Verification that the sample is present and is of sufficient size to run the test. This ensures that the pumps and sample sensing LED's are functioning properly and that the cuvette is adequately sealed. If these instrument and sample parameters are not appropriate, the test is terminated and an error message is displayed.
7.5. Performance verification after a repair or on a new instrument
7.5.1. Perform a precision study which includes measuring a combined total of 20 INR measurements, a combination of EQC and Liquid QC, as follows:
7.5.1.1. Measure 10 EQC measurements—validates the low and high INR timing measurement ranges with internal electronic QC processes (all must PASS).
7.5.1.2. Measure 5 Liquid QC Level 1—validates the low INR timing measurement ranges with external liquid QC processes (results must be within package inert limits).
7.5.1.3. Measure 5 Liquid QC Level 2—validates the high INR timing measurement ranges with external liquid QC processes (results must be within package insert limits).
7.5.2. Liquid Quality Controls for the instrument will be documented and assessed for acceptability within the manufactures range.
7.5.3. Instruments may be requested to be returned to the vendor for repairs. If available, loaner instruments may be given to the department while their instrument is out for repair.
7.5.3.1. If a loaner is put in use, two levels of QC must be performed prior to patient testing.
7.6. Start Up/Shut Down
7.6.1. To start up or shut down the Signature Elite, press and hold the START button.

8. QUALITY CONTROL:

8.1. **Internal Electronic Control**: Automatically performed every 8 hours of use by the department/unit
8.1.1. Turn on the instrument by pressing and holding the START button. EQC will automatically start if it is due.
8.1.2. To manually run EQC
8.1.2.1. Select QC button.
8.1.2.2. Select option #1 for EQC.
8.1.3. Instrument automatically runs a system check and both low and high electronic controls.
8.1.4. Electronic QC indicates "PASS" if the normal level (30-second) and the abnormal level (300-second) plus the internal temperature check meet manufacturer's acceptable performance criteria.
8.1.5. If the internal Electronic QC fails, repeat EQC once and if it fails again contact the POC department at 685-6610. Do not use the instrument.
8.2. **External Liquid Controls (LQC)**:
8.2.1. ***Direct*Check ™ liquid controls** –
8.2.1.1. INR controls: Level 1 (DCJCPT-N) and Level 2 (DCJCPT-A) are performed:
8.2.1.1.1. On each analyzer once a month by testing personnel.
8.2.1.1.2. On new cuvette lots and new shipments of cuvette lots.
8.2.1.1.3. To confirm acceptable range of new lots of QC before use.
8.2.1.2. Acceptance limits and how confirmed
8.2.1.2.1. Liquid control ranges are confirmed per shipment of QC. Each box of control is barcoded to input the lot number and expected ranges to establish control limits.

8.2.1.2.2. Five vials of QC of each level are run to verify new lot of QC compared to manufacturer's ranges. Record results in Sig Elite QC Lot Verification Worksheet.

8.2.2. LQC Procedure

8.2.2.1.1. Remove controls from the refrigerator and bring to room temperature (this could take up to 60 minutes).

8.2.2.1.2. Visually inspect the QC material to ensure that the ampule is intact.

8.2.2.1.3. Ensure the cuvette is at room temperature and do not open the sealed pouch until ready for use.

8.2.2.1.4. Place the cartridge into the cartridge slot of the Hemochron analyzer.

8.2.2.1.5. Scan the cuvette lot number.

8.2.2.1.6. Enter badge ID number on the keypad or scan the barcode on the ID badge. Press and hold ENTER button if using the keypad to manually enter ID.

8.2.2.1.7. **Press the QC** button at the bottom of the instrument so the instrument goes into QC mode.

8.2.2.1.8. Select the QC level to tag the sample as QC: Select option #1 for normal QC, **or** #2 for abnormal QC.

8.2.2.1.9. Choose the correct QC lot number or scan the appropriate QC barcode to download the lot number and expiration of the control being used.

8.2.2.1.10. Remove the outer plastic seal from the ampule of the control material and place in a protective sleeve provided with each box of controls.

8.2.2.1.11. Holding the vial upright, gently tap the ampule to allow the liquid contents to settle to the bottom of the vial.

8.2.2.1.12. Crush the inner glass ampule three times to ensure complete breakage of the ampule.

8.2.2.1.13. Shake the control vigorously to mix until the red blood cells are uniformly dispersed and the control is completely reconstituted, approximately 10 seconds.

8.2.2.1.14. While inverting the vial (dropper tip down), use a downward snapping motion of the wrist to ensure control material flows to the tip of the dropper.

8.2.2.1.15. Remove the cap from the vial.

8.2.2.1.16. Discard the first drop of the control ampule, then add one drop of control material to the sample well of the cartridge.

8.2.2.1.17. Fill the cuvette sample well to the top. Should a large dome extend over the top of the center sample well, push it over into the outer sample well.

8.2.2.1.18. **Immediately** Press the START key.

8.2.2.1.19. Dispose of the vial appropriately into bio hazardous waste.

8.2.2.1.20. Wait for a single beep signaling the conclusion of the test.

8.2.2.1.21. Results are displayed as the standardized INR for PT/INR.

8.2.2.1.22. Note the results to ensure that the controls have passed and are within acceptable range. Ranges are lot specific documented in the package insert and may vary slightly from lot-to-lot.

8.2.2.1.23. Controls must be acceptable prior to reporting patient results.

8.2.3. Trouble shooting unacceptable QC

8.2.3.1. If the control result is below the acceptable range:

8.2.3.1.1. The reconstituted control was not thoroughly mixed.

8.2.3.1.2. The time period between control material mixing and addition to test cuvette is too long.

8.2.3.2. If the control result is above the acceptable range:

8.2.3.2.1. The inner glass ampule was not adequately crushed.

8.2.3.2.2. Reconstituted control was not thoroughly mixed.

8.2.3.2.3. Vial cap is removed prior to inverting, allowing diluent to leak from the vial.

8.2.3.3. If instrument continues to fail either level of liquid QC, do not use the instrument and contact the POC department.

8.2.3.4. Corrective action is documented in QML.

8.2.3.5. The QC is reviewed by the manager and the coagulation division director. The results are maintained on the L: Drive.

8.2.4. Quality Control Download:

8.2.4.1. Download Quality Control data from instrument each time QC is performed:

8.2.4.1.1. Attach the Ethernet cable into the Ethernet port.
8.2.4.1.2. Press the Data Base button at the bottom of the instrument.
8.2.4.1.3. Press the #6 (POCT>>NET).
8.2.4.1.4. The stored data will upload to the system network.

9. **TEST PROCEDURE:**
9.1. Samples should sit on a rocker for at least 5 minutes prior to testing to allow for adequate mixing of the sodium citrate with the sample. Optimal results are obtained when samples are tested within 1 hour, and specimens maintained at room temperature until tested.
9.2. Press and hold START button to turn the instrument on. The Hemochron Signature Elite will complete a system check.
9.3. Ensure the cuvette is at room temperature and do not open the sealed pouch until ready for use.
9.4. Insert the INR cartridge into the Hemochron Signature Elite.
9.5. Scan the cuvette lot number.
9.6. Enter the operator ID (OID).
9.7. Enter the Patient ID using the keypad or scanning the barcoded wristband or label of the patient.
9.8. The instrument will signal when ready with an audible tone, and the screen will display the messages "Add Sample".
9.8.1. The instrument will remain in the ready mode for five minutes. At the end of five minutes, a "Start Timeout" will occur indicating that the current cuvette must be discarded and a new cuvette placed in the instrument.
9.9. Dispense one drop of blood into the sample well of the prewarmed cuvette, using **fresh whole citrated blood.** Should a large drop of blood extend above the top of the center sample well, creating a dome, simply push it over into the outer sample well with the pipette.
9.10. **NOTE: When transferring blood into the sample well, DO NOT force blood into the hole located on the center of the sample well, and DO NOT generate air bubbles in the sample well.**
9.11. Press the START key.
9.12. Test completion will be indicated by a single beep.
9.13. PT results are converted to a standardized INR value which is transmitted into the electronic medical record (EMR) via Telcor/Sunquest interface after downloading the instrument.
9.13.1.1. Attach the Ethernet cable into the Ethernet port.
9.13.1.2. Press the Data Base button at the bottom of the instrument.
9.13.1.3. Press the #6 (POCT>>NET).

10. **CALCULATIONS:**
10.1. No calculations are required. All results are automatically converted to a standardized INR value.

11. **REPORTING RESULTS:**
11.1. Refer to master test list for reference intervals.
11.2. Refer to master test list for Analytical measurement range (technical range).
11.3. Refer to master test list reportable range (reportable range) CRR.
11.4. Refer to Critical Result/ Critical Value policy for critical values.
11.5. Patient Data:
11.5.1. The analyzer will transmit patient results into the LIS and EMR via Telcor ethernet connectivity.
11.5.2. In case of a system downtime the results will be stored in the Signature Elite and will transmit to the medical record once the system is up and running and the instrument is downloaded. Alternately, the testing personnel can document the INR results in the patient's IHIS flowsheet.

12. **INTERPRETATION OF RESULTS**

12.1. If the patient's INR is greater than 3.0, the physician must place an order in IHIS for PT/INR and send the specimen to the main lab for confirmation.
12.2. If a critical value is obtained, document the first and last name of the physician notified in the Critical Results section in the Complex Vitals flowsheet.
12.3. INR values between 0.5-0.8 and 10-12 are displayed as "INR<0.8" and "INR>10" respectively. INR values under 0.5 and over 12 are displayed as "Out of Range-Lo" and "Out of Range-Hi" respectively.

12.4. All test results should be scrutinized in light of a specific patient's condition and anticoagulant therapy. Any results exhibiting inconsistency with the patient's clinical status should be repeated, supplemented with additional test data, or sent to the main lab for testing.

13. **LIMITATION OF PROCEDURE:**
13.1. If an instrument breaks and no backup is available, send specimens to the main lab.
13.2. Interferences may occur in patients with antiphospholipid antibodies or antiphospholipid syndrome.
13.3. Poor technique including blood collection and transfer of blood to the sample well may affect the quality of the results.
13.4. Samples with hematocrits less than 20% or greater than 55% are not recommended due to an optical density outside the level of detection of the instruments.

14. **REFERENCES:**
14.1. ITC Hemochron Signature Elite™ Operator's Manual, 2004
14.2. ITC Hemochron Signature Elite™ Whole Blood Microcoagulation System Configuration Manager Software, 2005.
14.3. Product Inserts for the following ITC Hemochron Signature Elite™ Cartridges and Controls:
14.3.1. DirectCheck Whole Blood Controls for Hemochron Jr Microcoagulation Systems, 2006
14.3.2. ITC Hemochron Citrate Prothrombin Time (PT) Cartridges
14.4. CLSI Point-of-Care In Vitro Diagnostic (IVD) Testing; Approved Guideline, current version
14.5. CLSI Collection, Transport, and Processing of Blood Specimens for Coagulation Testing and General Performance of Coagulation Assays; Approved Guideline-Third Edition, current version
14.6. Bull BS, Korpman RA, Huse WM, Briggs BD; Heparin Therapy During Extracorporeal circulation: I. Problems Inherent in Existing Protocols. J Thorac Cardiovasc Surg 1975; 69:674-684.
14.7. Doty DB, Knott HW, Hoyt JL, Koepke JA: Heparin dose for accurate anticoagulation in cardiac surgery. J Cardiovasc Surg 20:597-604, 1979.
14.8. Esposito RA, Culliford AT, Colvin SB, Thomas SF, Lackner II, Spencer FE: The role of the activated clotting time in heparin administration and neutralization for cardiopulmonary bypass. J Thorac Cardiovasc Surg 85: 174-175, 1983.
14.9. Gambino R: Monitoring heparin therapy. Lab Report for Physicians 4:17-20, 1982.
14.10. Hattersley P: Activated Coagulation Time of Whole Blood. JAMA 1966: 136-436.
14.11. Wang J-S, Lin C-Y, Hung W-T, Thisted RA, Karp RB: In vitro effects of aprotinin on Activated Clotting Time measured with different activators. J Thorac Cardiovasc Surg 104, 4: 1135-1140, 1992.

15. **RELATED DOCUMENTS**
15.1. Refer to QPulse System or Document Detail Report for related Laboratory Policies, Procedures, and Master Forms.