

ProTime® Microcoagulation System

Clinical and Laboratory Standards Institute (CLSI) Formatted Procedure

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Refer to the ProTime® Operator's Manual and cuvette package insert for complete instructions for test and instrument performance.

I. PURPOSE

The ProTime Microcoagulation System is a portable, AC or battery-operated instrument with a disposable cuvette for quantitative determination of prothrombin time (PT) from fingerstick whole blood or anticoagulant-free venous whole blood. The product is intended for in vitro diagnostic use in the management of patients treated with oral anticoagulants.

II. PRINCIPLE

The ProTime Microcoagulation System measures the PT using fibrin clot formation and detection. The ProTime cuvette is a self-contained, micro volume reaction cell constructed of precision molded plastic.

There are two user options within the ProTime Microcoagulation System: the standard ProTime cuvette and the ProTime3 cuvette. These cuvettes differ from each other in the amount of blood collected.

The standard ProTime cuvette has five micro-channels which contain the dried reagents required to perform triplicate testing of the prothrombin time assay and two levels of controls. The ProTime3 cuvette has three functional micro-channels. Two micro-channels perform the controls, and one micro-channel performs the prothrombin time assay. The standard ProTime uses the Tenderlett® Plus device for performing the fingerstick and it is designed to hold 65 µl of blood (approximately 3 drops) needed to fill all five micro-channels. The ProTime3 uses the Tenderlett Plus LV (lower volume) device for performing the fingerstick and it collects the 27 µl of blood (approximately 1 large drop) needed to fill the three micro-channels of the ProTime3 cuvette.

The instrument draws the precise volume of blood into the micro-channels of either cuvette, which contain thromboplastin and other reagents. An array of LEDs detects the motion of sample/reagent mixtures as they move through a precision restriction in each channel. The blood is pumped back and forth until a clot forms, obstructing the channels and slowing the flow of blood. The instrument detects the clot when the blood movement decreases below a predetermined rate.

III. SPECIMEN

A. Patient Preparation

Either the Tenderlett Plus (ProTime) or Tenderlett Plus LV (ProTime3) is supplied for finger incision and blood collection. The Tenderlett Plus will collect approximately 65 µl of blood, while the Tenderlett Plus LV will collect approximately 27 µl of blood. Samples should be analyzed immediately after collection. No additional sample preparation is required. Refer to the Test Procedure in the package insert for full instructions on hand preparation, finger incision and blood collection. Refer also to CLSI H4, "Procedures for the Collection of Diagnostic Blood Specimens by Skin Puncture."

For venous samples, collect venous whole blood (approximately 100µl) into an anticoagulant-free plastic syringe. Refer to CLSI H3, “Procedure for the Collection of Diagnostic Blood Specimens by Venipuncture.”

B. Specimen Type

Fingerstick whole blood is the recommended specimen. Anticoagulant-free venous whole blood may be used if the sample is collected into a plastic syringe. (Glass activates the clotting process and could therefore interfere with the results.)

NOTE: Whole blood collected with citrate, heparin, oxalate or EDTA anticoagulants are NOT suitable for use with the ProTime Microcoagulation System. Serum or plasma samples are not appropriate samples.

C. Sample Collection Procedure/Handling Conditions

Patient specimens and used cuvettes are potentially infectious. Use universal precautions in the handling of cuvettes and blood collection materials in accordance with local standards of biohazard control.

D. Preparation for Finger Incision

Warming the hands increases blood flow and makes it easier to collect an adequate volume of blood. Follow these steps to help ensure a good sample:

- Wash hands in warm water.
- Rub hands together to stimulate blood flow.
- Cleanse middle or ring finger with an alcohol pad and dry with sterile gauze.
- Apply firm pressure to the palm and finger. Massage the hand to push blood into the fingertips.

E. Sample Collection: Fingerstick Procedure

Wait for screen that instructs to “Incise Finger” to appear before incising finger.

CAUTION: Blood collection must be finished within 2 minutes and 10 seconds to prevent early clotting of the sample. The ProTime device will keep time.

- Place the Tenderlett Plus device firmly against the side of the finger. Place thumb on top of the device and press the red trigger using the other thumb while holding the Tenderlett in place.
- Wipe away the first trace of blood. The use of gauze is recommended. Cotton swabs should not be used as loose fiber strands can potentially activate clotting.
- Gently massage from the base of the finger to force blood to the tip. Form a large drop of blood.
- Touch the large drop of blood to the collection cup. Keep adding blood until the blood level passes the line on the collection cup.
- Ensure the blood extends all the way to the bottom of the cup. Add another drop if you are not sure you have enough.

F. Sample Collection: Venous Procedure

Wait for the screen that instructs to “Incise Finger” to appear before obtaining venous sample.

CAUTION: Blood collection must be finished within 2 minutes and 10 seconds to prevent early clotting of the sample. The ProTime device will keep time.

- Follow standard phlebotomy protocol for obtaining venous sample using a syringe.
- Obtain a minimum 100 µl sample.
- Using the syringe, administer blood to the collection cup. Keep adding blood until the blood level passes the line on the collection cup (fills the Tenderlett LV cup).
- Ensure the blood extends all the way to the bottom of the cup. Add another drop if you are not sure you have enough.

G. Cuvette Notes/Interferences

- Make sure cuvettes have been brought to room temperature prior to testing.
- Cuvettes are for single use only. Do not re-use a cuvette once it has been inserted into the analyzer.
- Do not begin sample collection OR add sample to Tenderlett Plus cup before instrument instructs to “Incise Finger.”
- Always wipe away first trace of blood after incising finger.
- Do not use samples collected with citrate, heparin, oxalate or EDTA anticoagulants.

H. Operational Precautions

- Use universal precautions when handling blood.
- Place the ProTime cuvette into the analyzer within 8 hours of opening the package. If more than 8 hours elapse, discard the cuvette and use a new cuvette.
- Make sure to remove the Tenderlett Plus cup when instrument instructs to do so.

IV. EQUIPMENT/MATERIALS/REAGENTS

Each box of ProTime cuvettes contains 25 individually pouched cuvettes and 25 individually pouched Tenderlett Plus devices. Cuvette and Tenderlett Plus pouches are stamped with a lot number and expiration date.

CAUTION: All used cuvettes and Tenderlett Plus devices should be considered as potentially infectious, handled using universal precautions and disposed of by following your standard waste facility disposal policy.

A. Materials

- ProTime Instrument
- AC/DC Power Module (optional)
- ProTime Cuvette
- Tenderlett Plus collection device

B. Additional Materials Required

- Alcohol pad
- Gauze

C. Reagent Preparation

ProTime cuvettes are ready-to-use. No additional preparation is required. Remove cuvette from refrigeration and allow it to come to room temperature prior to testing.

D. Storage Requirements

Store the foil-pouched cuvettes refrigerated (2-8°C, 35-46°F). An unopened cuvette is stable when stored at 2-8°C until the date printed on the pouch. Unopened cuvettes may be stored at room temperature for 60 days. Once the pouch has been opened, the cuvette must be used within 16 hours.

V. QUALITY CONTROL (QC)

The ProTime instrument performs a self-check before every test and has been designed with redundant systems to ensure proper instrument functions. The self-check at start-up checks temperature, timing functions, battery level, and optical, electrical and mechanical functions. No additional calibration or functional procedures are required.

Each ProTime cuvette has two levels of integral reagent controls that are run with every patient sample. The built-in controls indicate proper sample collection and correct test procedure, ensuring assay reliability and performance. Both control channels contain human coagulation factors designed to normalize the clotting time of the blood sample. In addition, the level 2 control channel has extra reagent which causes an extended clotting time. If the built-in controls do not perform as expected, the result is invalid and the instrument will display an error code. The use of external quality control material is not required but available if needed.

The ProTime cuvette includes a barcode that contains the cuvette lot number and expiration date and the lot specific algorithm for calculating the results in each channel. The barcode also contains the lot specific requirements for the integral control channels to meet in order for the instrument to report a patient result.

(Add your institution's policy here, if applicable.)

A. Use of Optional External DirectCheck Whole Blood Controls (DCPRO) Handling and Storage

When refrigerated (2–8°C, 35-46°F) the DCPRO vials are stable until the marked expiration date. The quality control product should never be exposed to temperatures in excess of 37°C, 98.6°F. Reconstituted vials should be used immediately. DCPRO may also be stored at room temperature for up to 4 weeks. (The marked expiration date must not be exceeded.) A re-dating label is provided and should be marked with 4 weeks dating if room temperature storage is selected.

Materials Provided

DCPRO quality controls are designed for use with the ProTime Microcoagulation System. Each kit contains a single level of quality control reagent consisting of 15 dropper vials of 0.5 cc dried whole blood control in a glass ampule and 0.7 cc of diluent. There are four reusable protective sleeves provided for use in crushing the vials.

Materials Required But Not Provided

- ProTime instrument
- ProTime / ProTime 3 cuvette
- Tenderlett Plus/ Tenderlett Plus LV sample collection device

Preparation of Control Material

Remove the control vials from the refrigerator and allow them to come to room temperature prior to use.

Q.C. Test Procedure

NOTE: Reconstitution and mixing of the whole blood control material should be accomplished quickly and without delay in any step. Once the dried control material has been reconstituted, the sample should be used immediately, as clotting will occur.

- Turn on the ProTime instrument and from the “Main Menu” select “Run LQC.” After self-check is completed, the instrument will display, “Insert Cuvette.”
- Insert cuvette into slot in the front of the instrument. The printing should be face up and the barcode should be face down.
- After warming, the instrument will signal ready by prompting for sample collection.
- Reconstitute the (room temperature) dropper vial contents as follows:
- Remove the label from the vial. Insert vial into protective sleeve. While holding the vial upright, tap the vial on a table top to settle the glass ampule to the bottom of the vial. Crush the inner glass ampule by either bending the vial over the edge of a table top or by crushing the vial between two fingers. Immediately repeat the crushing action two to three additional times to ensure complete breakage of the glass ampule. Quickly invert the dropper vial end to end 10 times.
- While inverting the vial (dropper tip down), use a downward snapping motion to the wrist to ensure the control material flows to dropper tip. Remove and retain the vial cap. Squeeze the vial to discard the first drop of the control material into the vial cap. Immediately dispense as many drops of control material as needed to fill the Tenderlett Plus collection cup until it passes the line or to completely fill the Tenderlett Plus cup.
- Snap the Tenderlett Plus to the ProTime instrument, you should hear a soft click.
- Follow the display to start the test. When prompted, remove the Tenderlett Plus from ProTime instrument.
- Remove the control vial from the protective sleeve. Dispose of the vial and vial cap appropriately and retain the protective sleeve for reuse.
- Record results.

CAUTION: No human material is used in the control product. However, all blood products should be handled with care, and should be discarded in accordance with your institution's policy on disposal of medical waste.

B. Out-of-Range Quality Control Procedure

In cases where quality control results are outside of an acceptable range, the cause is likely attributable to one of the following categories:

- Test technique
- Control material
- Cuvette
- Instrument
- If results are outside of the acceptable range, the following items should be verified immediately:
 - Control material expiration dates
 - Proper technique
 - Presence of bubbles in the sample cup or cuvette channels
- If none of the above parameters are suspect, repeat the test using control materials with the identical lot number.
- If this repeat does not fall within the expected range, verify the above parameters again. Obtain a cuvette from a different lot number and repeat the test using a control with the same lot number.
- Obtain control material with a different lot number and repeat the controls again.
- If this repeated control does not fall within the expected range, contact your laboratory consultant or call ITC Technical Support.
- Additional test should not be performed until control values obtained are within range.

The liquid quality control products are helpful when an instrument problem is suspected. It is recommended that multiple tests be performed with the quality control products, and that the data be discussed with an ITC Technical Support representative prior to sending the instrument to ITC for service. Call toll free in the U.S. (800) 631-5945, or (732) 548-5700 if calling from outside the U.S or e-mail us at techsupport@itcmed.com.

VI. Patient ID (PID) and/or Operator ID (OID) Entry

Go to the "Main Menu" screen and choose the "Set Up" option. Scroll and select "SET PID/OID" to access this option. The PID can be up to 12 digits in length and the OID up to 6 digits in length.

- Selecting PID/OID ON enables both a patient ID and operator ID to be entered.
- Selecting PID ON enables only a patient ID to be entered.
- Selecting OID ON enables only an operator ID to be entered.
- Selecting OFF disables both the patient ID and operator ID.

VII. STEP-BY-STEP TEST PROCEDURE

A. Turn on the ProTime Instrument

Press the 0 button to start. ProTime does a self-check procedure which may take up to 60 seconds. ProTime will prompt you through the test. Watch the screen and follow the prompts.

B. Insert a Cuvette

Wait for the prompt. Insert the cuvette into the slot with the printed side face up and the barcode down. If either OID or PID is required, ProTime will prompt for this information. Use the select button to scroll through the digits 0 – 9 under the cursor. Press the “0” button to accept and advance to the next digit. Continue until entry is complete. Press the “0” button to confirm entry. While the cuvette is warming, prepare the finger. Wait for the prompt before incising the finger and collecting blood.

C. Prepare for Finger Incision and Collect the Blood Sample

- Snap Tenderlett Plus to ProTime instrument
- Hold the device at an angle and place the front end of the device into the slot in the instrument.
- Press down to click the Tenderlett Plus in place. You should hear a soft click. Proper engagement of the Tenderlett Plus to the cuvette is critical to prevent a sample error.

D. Start the Test

Press the 0 button to start the test. This signals the ProTime instrument to draw the sample into the cuvette. It takes only a few seconds for the ProTime device to draw the blood into the cuvette. Watch the screen for the next prompt.

E. Remove the Tenderlett Plus

Remove the Tenderlett Plus from the ProTime instrument when prompted to do so.

CAUTION: Remove Tenderlett Plus immediately. The ProTime instrument allows you 6 seconds. Failure to do so will result in an error message.

F. Read the Result

Results will be displayed on test completion. If the ProTime device is connected to a printer or computer and the “AUTO SEND” feature is turned on, the result will automatically be transmitted to a serial printer or computer by using the PROCABLE.

Press the SELECT button to go to the MAIN MENU if you want to review the data in memory, print results, transfer results to a computer or perform set up functions. Press the 0 button to tune off the ProTime instrument.

VIII. CALCULATIONS

The INR and PT seconds are displayed for each result. There are no user defined calculations required.

IX. READING and REPORTING RESULTS

The ProTime device reports results as International Normalized Ratio (INR) and PT seconds. The ProTime system calculates INR directly from whole blood clotting time based on a conversion equation that was established in clinical trials. The result in plasma equivalent seconds is then calculated from the INR result.

Since results reported in PT seconds depend on the sensitivity (ISI) of the reagent employed, the clinician has the option of changing the ISI value in ProTime so that the ProTime results reported in PT seconds closely match the results reported by the hospital laboratory. To change the ISI used in the calculation, access the "PROGRAM MODE" by selecting "SET UP" in the "MAIN MENU" and enter the ISI of the local laboratory reagent. The INR result is unaffected by changing the ISI setting.

A. Reportable Ranges

In clinical trials, no significant difference was observed between fingerstick and venous specimens run on the ProTime system. The ProTime instrument measured patients with an INR range of 0.8 to 7.0. If $INR > 7.0$, the numerical result is marked with "**". An error message is displayed if $INR > 10.0$.

The ProTime system measures both normal and therapeutic prothrombin times in fresh whole blood. Results are displayed in plasma equivalent seconds and INR. Expected values for patients taking oral anticoagulants depend on the patient's disease state and the target values established by the physician.

B. Procedures for Abnormal Results

As with all diagnostic tests, 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 or supplemented with additional test data.

(Identify your procedure for reporting abnormal/unexpected results here.)

PROCEDURAL NOTES:

- DO NOT use cuvettes past their expiration date or if they have been stored improperly.
- DO NOT force a cuvette into the instrument. If resistance to insertion is encountered, gently remove the cuvette and examine the cuvette slot. Remove any obstruction before attempting to insert the cuvette.
- DO NOT use excessive force in depressing any of the soft touch keys.
- DO NOT disturb the instrument while a test is in progress.

- DO NOT expose the ProTime instrument to extremes in temperature (above 35°C, 95°F). Such exposure could affect the performance of any type of electronic equipment.
- DO NOT attempt to open the ProTime instrument other than for battery replacement, as there are no user-serviceable parts.
- DO NOT remove the AC/DC power module from the ProTime instrument by pulling on the cord.
- The ProTime instrument is designed for use only with ProTime cuvettes.
- Results from the ProTime device can be affected by poor technique during blood collection and delivery to the sample cup. The accuracy of the test is largely dependent upon the quality of the sample collection and the transfer of the blood to the cuvette. Tests may be affected by (but not limited to) any of the following conditions:
 - Delay of longer than 2 minutes from obtaining sample to running test
 - Foaming of the sample (air bubbles)
 - Clotted or partially clotted blood
 - All biohazard safety guidelines pertaining to the handling of human blood, such as the CDC guidelines of universal precautions, should be strictly adhered to when collecting, handling blood specimens and operating the ProTime.
 - Used ProTime cuvettes and Tenderlett Plus devices should be considered as potentially infectious. They should be handled according to individual institutional policies concerning the disposal of potentially infectious materials.

X. LIMITATIONS

The ProTime instrument uses only fresh capillary or venous whole blood. Plasma or serum cannot be used. Glass tubes or syringes must not be used to collect venous samples. Use only plastic syringes without anticoagulants to collect venous samples.

- Poor fingerstick blood collection technique may affect results.
- Results may be affected in patients receiving supra-therapeutic heparin or who have an abnormal response to heparin.
- Correlation of results reported by ProTime to laboratory results depends on the precision of the laboratory method and on the ISI value of the laboratory reagent and instrument system.
- As with all diagnostic tests, ProTime test results should be scrutinized in light of a specific patient's condition and therapy. Any results exhibiting inconsistency with the patient's clinical status should be repeated or supplemented with additional test data.

XI. MAINTENANCE

A. Cleaning

- DO NOT immerse the ProTime instrument or allow fluid to enter the cuvette housing. Inspect and clean the outside of the cuvette slot as required. Remove residual dried blood or other foreign matter on the outside of the instrument using gauze dampened with a 10% dilution of household bleach in water or with gauze dampened with isopropyl alcohol or other disinfectant.
- DO NOT use other solvents or strong cleaning solutions as they may damage the plastic components of the instrument.

B. Battery Care

The ProTime instrument is designed to run either on AC power supplied by the AC/DC power module or on the rechargeable battery supplied within the unit.

C. Rechargeable Battery Facts

Batteries discharge naturally over time (approximately 5% per month). Battery capacity (the amount of charge the battery will hold) is lower at low temperatures.

The ProTime instrument uses a rechargeable NiMH (Nickel Metal Hydride) type battery. The maximum capacity of any rechargeable battery will gradually decrease over time. To ensure maximum life of the rechargeable battery, follow the guidelines below.

A new instrument, an instrument that is used infrequently, or an instrument with a new replacement battery, should be plugged in for at least 8 hours before use to ensure that the battery is completely charged. The instrument screen will show CHARGING BATTERY when the AC/DC power module is connected to the AC power cord and the ProTime instrument. The screen will show CHARGE COMPLETE when the battery is fully charged. The AC/DC power module may be disconnected after the CHARGE COMPLETE message is seen. The AC/DC power module that has been supplied by ITC has been selected specifically for use with your ProTime Microcoagulation System. Do not use any other AC/DC power module. When the battery indicator on the screen shows less than 25% charge remaining, the instrument should be plugged in. To maximize battery life, allow your ProTime instrument to discharge completely before re-charging. Avoid charging the ProTime instrument for frequent, short periods of time (such as charging for a few minutes, removing from the AC/DC power module, and then recharging again).

D. Battery Replacement

Refer to the instructions provided with the replacement battery. The used battery should be disposed of in accordance with local regulations for NiMH batteries.

E. Service

Other than replacement of the rechargeable battery as described above, the ProTime instrument is not user serviceable. Should service be required, please contact Technical Support at 1-732-548-5700, 1-800-631-5945, or e-mail us at techsupport@itcmed.com. If you are advised to return the instrument to ITC for service or repair prior to shipping, please clean the instrument as described above.

F. Instrument Downtime

During instrument downtime, patient samples will be tested on alternate ProTime instruments. If all instruments are down, patient samples will be tested in the clinical laboratory.

XII. PROFICIENCY TESTING

(Proficiency testing is only required in some states for CLIA-waived systems. Delete if this does not apply to your institution.)

Proficiency testing will be performed at least twice per year using linearity kit samples obtained from an outside testing institution. The results will be returned to the outside testing institute by the specified date. If the results from both the primary and secondary machines are not at least 80% acceptable, the unacceptable grade will be reported to your technical consultant or medical director.

XIII. EMPLOYEE CERTIFICATION

Employee certification is completed upon in-servicing, and should be renewed at the institution's required frequency for all certified operators of the ProTime system. Documentation of certification is maintained in the employee's personnel folder.