SPECIMEN COLLECTION AND HANDLING

Materials Provided

- Preloaded PT, dark purple–top test tube (A201) for fresh whole blood, or
- Preloaded PT, light purple–top test tube (A202) for citrated whole blood

Materials Required

- HEMOCHRON *Response*, 8000, 801 or 401
- 5 cc syringe (for use with PT for fresh whole blood), or
- Sodium citrate (3.8% or 3.2%) blood collection tube for use with PT for citrated whole blood

Before performing any test, the user should refer to the appropriate HEMOCHRON operator's manual for detailed operating instructions. For blood collection, adhere to the appropriate technique (A, B or C):

A. Indwelling venous blood-line (Do not obtain blood from a heparinized access line, or indwelling heparin lock):

1. Discontinue fluids drip, if required.
2. Use a two-syringe technique - discard the first 5 cc draw. Obtain a 3 cc sample with the second syringe for testing.

B. Extracorporeal blood line port

1. Flush the extracorporeal blood access line by withdrawing and discarding 5 cc of blood.
2. Draw a 3 cc sample with a second syringe for testing.

C. Venipuncture

Obtain a 3 cc sample with a syringe.

NOTE: *Fresh whole blood samples must be tested immediately after collection. If the blood has been collected into a sodium citrate tube, it is important that the specimen be tested within one hour of drawing. Keep the specimen at room temperature - do not heat or ice.*

TEST PROCEDURE

NOTE: *The PT test tubes must be at room temperature prior to use. Once removed from the refrigerator, this may take up to 60 minutes.*

For use with fresh whole blood (A201 - dark purple top tube)

1. From the collection syringe, dispense exactly 2.0 cc of blood into the PT tube. At the same time, depress the **START** key of the appropriate test well.
2. Immediately agitate the test tube vigorously from end to end ten times.
3. Insert the PT test tube into the appropriate test well. Quickly rotate the tube clockwise. See appropriate instrument operator's manual for additional information.
4. Repeat steps 1 through 3 for a duplicate PT test tube if desired.
5. At the indicator tone, record the test results.

NOTE: *If using a HEMOCHRON 8000 or Response instrument, the whole blood and plasma equivalent clotting times will be displayed automatically. If using a HEMOCHRON 801 (serial number T or later) depressing the* ***SELECT*** *key while the tube is still in the test well will alternate between whole blood and plasma equivalent values.*

For use with citrated whole blood (A202 - light purple top tube)

1. Collect blood in a sodium citrate blood collection tube.
2. Follow directions for fresh whole blood above.

CAUTION: *Every precaution should be taken to use proper technique with syringes to avoid accidental needlesticks.*

PRODUCT USE WARNING

NOTE: *Observe universal precautions at all times.*

1. The blood specimen should be transferred using an appropriate transfer needle to pierce the stopper.
2. Always use a two-hand technique to transfer blood. One hand securely holds the tube while the second hand dispenses the blood specimen.
3. The PT test tubes are made of glass. They can be broken or cracked if mishandled. Do not drop or toss tubes.
4. The PT test tubes contain a material of biological origin (thromboplastin). Do not handle, aerosol, or ingest.
5. All used test tubes containing human derived blood should be discarded in approved biohazard containers.

PERFORMANCE CHARACTERISTICS

Normal Range

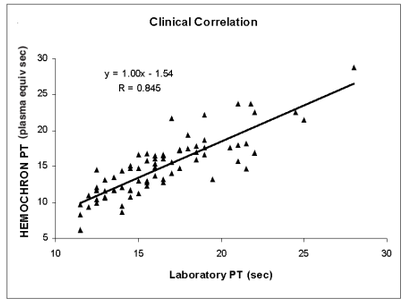
The HEMOCHRON PT was evaluated in normal volunteer donors. The normal range of response was:

	PT (A201) Fresh Whole Blood	PT (A202) Citrated Whole Blood
mean ± SD (sec)	55 ± 5	62 ± 5.6
Normal Range	up to 70 sec	up to 75 sec
Normal Range (INR)	≤ 1.3	≤ 1.3

For optimal test performance, it is recommended that each institution establish their own normal range.

Clinical Correlation of the HEMOCHRON PT and the Plasma PT

Correlation of the HEMOCHRON PT (A201) values were obtained for "matched" blood samples from patients on oral anticoagulant therapy. The plasma PT was determined using a reference thromboplastin reagent (Ortho Brain Thromboplastin, Ortho Diagnostic Systems, Inc., Raritan, NJ) and a photo–optical detection device (Koagulab, Ortho Diagnostic Systems, Inc., Raritan, NJ) . The data is expressed in the graph as the HEMOCHRON plasma equivalent values at ISI=2.0, and laboratory PT values at ISI=2.0.



HEMOCHRON PT Conversion Chart

A201 PT (fresh whole blood) ISI = 2.0 for plasma equivalent Mean Normal PT = 12.0 seconds			A202 PT (citrated whole blood) ISI = 2.0 for plasma equivalent Mean Normal PT = 13.5 seconds		
Whole Blood Result	Plasma Equiv. Value	INR	Whole Blood Result	Plasma Equiv. Value	INR
55	10.7	0.8	60	12.7	1.0
58	11.3	0.9	65	13.5	1.1
61	11.9	1.0	70	14.3	1.2
64	12.4	1.1	75	15.0	1.3
67	12.9	1.2	80	15.7	1.5
70	13.4	1.3	85	16.3	1.6
73	13.9	1.3	90	16.9	1.7
76	14.3	1.4	95	17.4	1.8
79	14.8	1.5	100	18.3	2.0
82	15.2	1.6	105	18.6	2.0
85	15.6	1.7	110	18.9	2.1
88	16.0	1.8	115	19.2	2.2
91	16.4	1.9	120	19.5	2.2
94	16.7	1.9	125	19.8	2.3
97	17.1	2.0	130	20.0	2.4
100	17.4	2.1	135	20.3	2.4
103	17.8	2.2	140	20.5	2.5
106	18.1	2.3	145	20.8	2.6
109	18.4	2.3	150	21.0	2.6
112	18.7	2.4	155	21.2	2.7
115	19.0	2.5	160	21.4	2.7
118	19.3	2.6	165	21.6	2.8
121	19.6	2.7	170	21.8	2.8
124	19.8	2.7	175	22.0	2.9
127	20.1	2.8	180	22.2	2.9
130	20.4	2.9	185	22.4	3.0
133	20.6	3.0	190	22.6	3.0
136	20.9	3.0	195	22.8	3.1
139	21.1	3.1	200	22.9	3.1
142	21.4	3.2	205	23.1	3.2
145	21.6	3.2	210	23.3	3.2
148	21.8	3.3	215	23.4	3.2
151	22.1	3.4	220	23.6	3.3
154	22.3	3.4	225	23.7	3.3
157	22.5	3.5	230	23.9	3.4

Continued from page 3

A201 PT (fresh whole blood) ISI = 2.0 for plasma equivalent Mean Normal PT = 12.0 seconds			A202 PT (citrated whole blood) ISI = 2.0 for plasma equivalent Mean Normal PT = 13.5 seconds		
Whole Blood Result	Plasma Equiv. Value	INR	Whole Blood Result	Plasma Equiv. Value	INR
160	22.7	3.6	235	24.0	3.4
163	22.9	3.6	240	24.2	3.5
166	23.1	3.7	245	24.3	3.5
169	23.3	3.8	250	24.4	3.5
172	23.5	3.8	255	24.6	3.6
175	23.7	3.9	260	24.7	3.6
178	23.9	4.0	265	24.8	3.6
181	24.1	4.0	270	24.9	3.7
184	24.3	4.1	275	25.1	3.7
187	24.5	4.2	280	25.2	3.8
190	24.6	4.2	285	25.3	3.8
193	24.8	4.3	290	25.4	3.8
196	25.0	4.3	295	25.5	3.9
199	25.1	4.4	300	25.7	3.9
202	25.3	4.5	305	25.8	3.9
205	25.5	4.5	310	25.9	4.0
208	25.6	4.6	315	26.0	4.0
211	25.8	4.6	320	26.1	4.0
214	26.0	4.7	325	26.2	4.1
217	26.1	4.7	330	26.3	4.1
220	26.3	4.8	335	26.4	4.1
223	26.4	4.8	340	26.5	4.2
226	26.6	4.9	345	26.6	4.2
229	26.7	5.0	350	26.7	4.2
232	26.9	5.0	355	26.8	4.2
235	27.0	5.1	360	26.9	4.3
238	27.2	5.1	365	27.0	4.3
241	27.3	5.2	370	27.1	4.3
244	27.4	5.2	375	27.2	4.4
247	27.6	5.3	380	27.2	4.4
250	27.7	5.3	385	27.3	4.4
253	27.8	5.4	390	27.4	4.4
256	28.0	5.4	395	27.5	4.5
259	28.1	5.5	400	27.6	4.5
262	28.2	5.5	405	27.7	4.5
265	28.4	5.6	410	27.8	4.6
268	28.5	5.6	415	27.8	4.6
271	28.6	5.7	420	27.9	4.6
274	28.7	5.7	425	28.0	4.6
277	28.9	5.8	430	28.1	4.7
280	29.0	5.8	435	28.1	4.7
283	29.1	5.9	440	28.2	4.7
286	29.2	5.9	445	28.3	4.7
289	29.3	6.0	450	28.4	4.8
292	29.5	6.0	460	28.5	4.8
295	29.6	6.1	470	28.7	4.9
298	29.7	6.1	480	28.8	4.9
301	29.8	6.2	490	29.0	5.0
			500	29.1	5.0

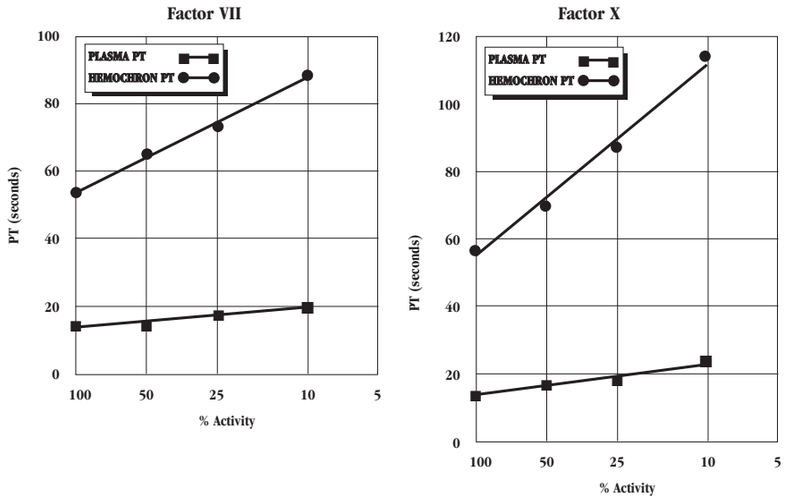
The plasma equivalent values depicted in the charts (p. 4 and 5) and reported by the HEMOCHRON instruments are based on a laboratory reagent with an ISI of 2.0. The thromboplastin contained in the PT tubes (A201 or A202) has an ISI of 1.13±0.17.[7]

Coagulation Factor Sensitivity

One of the most common applications of the PT test is monitoring oral anticoagulation therapy. These drugs exert an anticoagulant effect by inhibition of the synthesis of specific vitamin K dependent clotting factors, namely factors II, VII, IX and X. A measure of the value of the PT test is its sensitivity to these clotting factor deficiencies.

The following sensitivity curves were determined using the citrated HEMOCHRON PT (A202), a reference plasma PT, and a coagulation factor deficient whole blood. The reference PT was performed using a reference

thromboplastin (Pacific Hemostasis, Ventura, CA) and a mechanical clot detection instrument (BBL, Cockeysville, MD). The slope of the curve is a measure of the sensitivity of the test to coagulation factor deficiencies. For both factors VII and X, the HEMOCHRON PT was more sensitive than the corresponding plasma PT.



International Normalized Ratios

The therapeutic range of the PT for oral anticoagulant therapy is traditionally expressed as a ratio of patient PT to the normal PT. Due to the variable procoagulant nature of different thromboplastins each manufacturer of thromboplastin reagent identifies the potency of their preparation compared to the British Comparative Standard (BCT). Such a comparison is the basis for assigning the International Sensitivity Index (ISI) of the reagent. The ISI may then be used to convert patient/normal ratios to International Normalized Ratios (INR). The INR reported is designed to be independent of the plasma reference used and has been correlated to systems using an ISI of 1.0. Reports* have emphasized the persistence of inconsistencies between INR test systems. Institutions may wish to establish their own target range of therapeutic anticoagulation based on their patient population and laboratory INR test system.

Precision

Reproducibility was determined using HEMOCHRON Quality Control for PT. Day to day variation was determined by repeated testing of normal and abnormal level controls on multiple days:

A201 (PT for fresh whole blood)

	Normal			Abnormal		
	(N)	Mean (sec)	CV (%)	(N)	Mean (sec)	CV (%)
Day 1	5	64	9	5	140	7
Day 2	5	64	3	5	146	6
Day 3	5	63	3	5	141	4
Combined	15	64	5	15	142	6

A202 (PT for citrated whole blood)

	Normal			Abnormal		
	(N)	Mean (sec)	CV (%)	(N)	Mean (sec)	CV (%)
Day 1	5	53	2	5	125	8
Day 2	5	49	8	5	116	9
Day 3	5	48	6	5	123	4
Combined	15	50	7	15	121	8

LIMITATIONS OF THE PROCEDURE

The PT test is affected by poor technique including sample collection[9] and test procedure. Proper specimen/reagent mixing is required for precise and accurate testing. The following may affect results or be misleading in test interpretation:

1. Unsuspected anticoagulation with either heparin or warfarin.
2. Warfarin resistant patients.[10]
3. Studies indicate interferences may occur in patients with antiphospholipid antibodies or antiphospholipid syndrome.[11,12,13]
4. Test kits that have been improperly stored, have been affected by heat, or expired.

Test results which do not agree with expected values should be verified and, thereafter, evaluated by alternative diagnostic means.

QUALITY CONTROL

Routine quality control (QC) testing and tracking should be a part of a comprehensive quality assurance program. HEMOCHRON Whole Blood Coagulation System Quality Control products are available to make routine QC convenient and affordable.

Daily Instrument QC

At a minimum, all HEMOCHRON instruments should be quality controlled at two levels of performance, including both the normal and abnormal ranges, once every 8 hours of operation.

To assist in accomplishing daily QC, Electronic System Verification Tubes are available to provide multiple level (normal and abnormal) quality control checks on the instrument. Electronic System Verification should be performed once every 8 hours during which the instrument is utilized. This will ensure proper instrument operation.

QC of HEMOCHRON Test Tubes

Each box of HEMOCHRON test tubes should be validated at least once, prior to use. This can be accomplished by using the appropriate HEMOCHRON Liquid Quality Control. Acceptable performance ranges for the test tubes are included in the HEMOCHRON Quality Control Product Kit. After each individual box of test tubes has been verified, the "Performance Verified" label provided should be completed and placed on the box . This box is now "IN CONTROL" and will not require further liquid control unless a shift in clinical results is experienced.

***NOTE:** If multiple boxes are received within the same shipment, it is recommended to validate each box upon opening, prior to use.*

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HEMOCHRON®

Whole Blood Coagulation Systems

Prothrombin Time Test (PT)

Package Insert

INTENDED USE

The HEMOCHRON® Prothrombin Time (PT) test is designed for performing a one-stage prothrombin time test. The PT test is intended solely for use with HEMOCHRON models 401, 801, 8000 or *Response*. The prothrombin time test is performed using fresh or citrated whole blood at the patient's bedside. The PT test is commonly used for deficiency coagulation screening and warfarin monitoring.

For *in vitro* Diagnostic Use

SUMMARY AND EXPLANATION

Bedside whole blood coagulation systems eliminate many variables known to affect the reliability of plasma prothrombin time testing, including specimen collection, handling and processing.[1] The PT is a test of the extrinsic coagulation pathway. The test system is especially valuable during procedures/therapies that require monitoring of oral anticoagulants or for hemostasis assessment before and after blood transfusions.

Traditionally, the events leading to the formation of a fibrin clot have been simplified in coagulation theory into two coagulation pathways; the intrinsic and extrinsic.[2,3] The PT test was first described in 1935 with thromboplastin as the only active ingredient.[4,5] The prothrombin time measures the extrinsic coagulation pathway and is sensitive to coagulation factors VII, X, V, II, and fibrinogen (I). The prothrombin time test may be prolonged in patients with liver disease or vitamin K deficiency. The test is widely used to monitor oral anticoagulant therapy.[6]

The HEMOCHRON PT test tube contains lyophilized rabbit brain tissue thromboplastin. Upon delivery of the whole blood specimen into the PT test tube, it is then inserted into the test well of the HEMOCHRON instrument for temperature control and end–point detection. Many test variables such as temperature degradation, adverse transport manipulation, or cold or glass activation, are eliminated for more precise and accurate prothrombin time testing.

The PT may be performed at the patient site with a fresh whole blood sample using the HEMOCHRON dark purple-top PT tubes (A201). When testing away from the point-of-care, the PT may be performed with a citrated blood sample using the HEMOCHRON light purple-top PT tubes (A202).

REAGENTS

PT for Fresh Whole Blood (A201)

The HEMOCHRON PT dark purple–top test tube contains:

- a lyophilized preparation of acetone dried rabbit brain thromboplastin, stabilizers and buffers

PT for Citrated Whole Blood (A202)

The HEMOCHRON PT light purple–top test tube contains:

- a lyophilized preparation of acetone dried rabbit brain thromboplastin, calcium salt, stabilizers and buffers

***CAUTION:** Sodium azide (0.05%) is added to the test tubes as a preservative. Reagents containing sodium azide should be discarded in accordance with your institution's policy on disposal of medical waste.*

STORAGE AND STABILITY

When refrigerated (2-8° C), the PT test tubes are stable until the marked expiration date. This product may also be stored at a controlled room temperature (15-30° C). Room temperature dating is to a maximum of four weeks, but must never exceed the marked expiration date. If stored at room temperature, redating on the enclosed label is necessary. The label should be affixed to the outside of the product box, covering the stamped expiration date. The test tubes should not be exposed to temperatures in excess of 37° C.