STORAGE AND STABILITY

When refrigerated (2-8° C), the OneStep APTT 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.

SPECIMEN COLLECTION AND HANDLING

Materials Provided

- Preloaded OneStep APTT, navy blue-top test tube (A103) for fresh whole blood, or
- Preloaded OneStep APTT, light grey-top test tube (A104) for citrated whole blood

Materials Required

- HEMOCHRON *Response*, 8000, 801 or 401
- 5 cc syringe for use with OneStep APTT for fresh whole blood, or
- Sodium citrate blood collection tube for use with OneStep APTT 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.

CAUTION: *Blood collection should be performed by a qualified medical professional.*

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 APTT test tubes must be at room temperature prior to rehydration. Once removed from the refrigerator this may take up to 60 minutes.*

For use with fresh whole blood (A103 - navy blue-top tube)

1. If using a HEMOCHRON 401 or 801, depress the **SELECT** key twice until **APTT** appears on the display. If using a HEMOCHRON 8000 or *Response* refer to the instrument operator's manual for test selection procedure.
2. From the collection syringe, dispense exactly 2.0 cc of blood into the APTT tube. At the same time, depress the **START** key of the appropriate test well.
3. Immediately agitate the test tube vigorously from end to end ten times.
4. Insert the APTT test tube into the appropriate test well. Quickly rotate the tube clockwise. See appropriate instrument operator's manual for additional information.
5. When running in duplicate, repeat steps 1 to 4 for the second OneStep APTT tube.
6. At the indicator tone, record the test results displayed as the whole blood APTT in seconds. While the tube is still in the test well, depress the **START** key to obtain a plasma equivalent time. Depressing the **SELECT** key will alternate between the whole blood and plasma equivalent values until the tube is removed from the well.

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 (A104 - light grey-top tube)

1. From the sodium citrate blood collection tube, withdraw 3 cc of citrated blood into a 5 cc syringe.
2. Follow instructions above for A103 APTT test procedure.

NOTE: *The plasma conversion programmed into the instrument does not apply to the OneStep APTT (A104) for use with citrated whole blood. Refer to the conversion chart in this package insert for plasma equivalent values for A104.*

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 APTT test tubes are made of glass. They can be broken or cracked if mishandled. Do not drop or toss tubes.
4. The APTT test tubes contain a material of biological origin (platelet factor 3 substitute). 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 OneStep APTT was evaluated in normal volunteer donors. The normal range of response was:

Test	**n**	**Mean (secs)**	**SD (secs)**	**Range (mean ± 2 SD) (secs)**
Fresh APTT (A103)	69	123	7	109-137
Citrated APTT (A104)	52	136	11	114-158

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

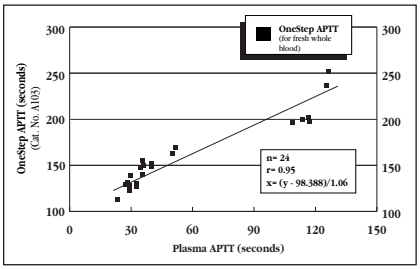
Precision

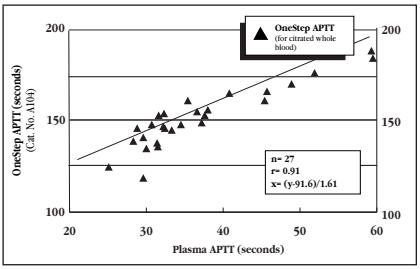
The precision of the OneStep APTT was evaluated by performing multiple assays of Control Plasma on five separate test days using well-maintained instruments with the following results:

OneStep APTT (A103)	**n**	**Mean (secs)**	**SD (secs)**	**CV (%)**
Normal	20	99	4.0	4.0
Abnormal	20	187	5.5	2.9
OneStep APTT (A104)	**n**	**Mean (secs)**	**SD (secs)**	**CV (%)**
Normal	20	112	3.2	2.8
Abnormal	20	170	3.0	1.4

Correlation of the HEMOCHRON OneStep APTT and the Plasma APTT

HEMOCHRON APTT values and plasma APTT values were obtained for matched blood samples from heparinized and non-heparinized patients (n=27). The reference plasma APTT was determined using an ellagic acid activated APTT reagent, (Dade International, Deerfield, IL) and a photo-optical coagulation instrument (Medical Laboratory Automation, Inc., Pleasantville, NY)





Conversion Chart

HEMOCHRON APTT values may be readily converted to conventional plasma APTT values using the conversion chart below. Due to the known variability of APTT reagents,[7,8] the user should note that different plasma APTT reagents will result in different conversion factors.

* Plasma equivalent APTT values less than 24 seconds are not routinely available and should be reported as "less than 24 seconds".
** Plasma APTT values greater than 120 seconds are not routinely available using photo-optical systems. Values are calculated from regression analysis.

HEMOCHRON APTT CONVERSION CHART

OneStep APTT (fresh)	Plasma	OneStep APTT (citrated)	Plasma	OneStep APTT (fresh)	Plasma	OneStep APTT (citrated)	Plasma
100	*24.0	100	*24.0	129	28.5	129	*24.0
101	*24.0	101	*24.0	130	29.5	130	*24.0
102	*24.0	102	*24.0	131	30.5	131	24.5
103	*24.0	103	*24.0	132	31.5	132	25.5
104	*24.0	104	*24.0	133	32.5	133	26.0
105	*24.0	105	*24.0	134	33.0	134	26.5
106	*24.0	106	*24.0	135	34.0	135	27.0
107	*24.0	107	*24.0	136	35.0	136	28.0
108	*24.0	108	*24.0	137	36.0	137	28.5
109	*24.0	109	*24.0	138	37.0	138	29.0
110	*24.0	110	*24.0	139	38.0	139	29.5
111	*24.0	111	*24.0	140	39.0	140	30.5
112	*24.0	112	*24.0	141	40.0	141	31.0
113	*24.0	113	*24.0	142	40.5	142	31.5
114	*24.0	114	*24.0	143	41.5	143	32.0
115	*24.0	115	*24.0	144	42.5	144	33.0
116	*24.0	116	*24.0	145	43.5	145	33.5
117	*24.0	117	*24.0	146	44.5	146	34.0
118	*24.0	118	*24.0	147	45.5	147	34.5
119	*24.0	119	*24.0	148	46.5	148	35.5
120	*24.0	120	*24.0	149	47.5	149	36.0
121	24.0	121	*24.0	150	48.0	150	36.5
122	24.0	122	*24.0	151	49.0	151	37.0
123	24.0	123	*24.0	152	50.0	152	38.0
124	24.0	124	*24.0	153	51.0	153	38.5
125	25.0	125	*24.0	154	52.0	154	39.0
126	25.5	126	*24.0	155	53.0	155	39.5
127	26.5	127	*24.0	156	54.0	156	40.0
128	27.5	128	*24.0	157	55.0	157	41.0

OneStep APTT (fresh)	Plasma	OneStep APTT (citrated)	Plasma
158	56.0	158	41.5
159	56.5	159	42.0
160	57.5	160	42.5
161	58.5	161	43.5
162	59.5	162	44.0
163	60.5	163	44.5
164	61.5	164	45.0
165	62.5	165	46.0
166	63.5	166	46.5
167	64.0	167	47.0
168	65.0	168	47.5
169	66.0	169	48.5
170	67.0	170	49.0
171	68.0	171	49.5
172	69.0	172	50.0
173	70.0	173	51.0
174	71.0	174	51.5
175	71.5	175	52.0
176	72.5	176	52.5
177	73.5	177	53.5
178	74.5	178	54.0
179	75.5	179	54.5
180	76.5	180	55.0
181	77.5	181	56.0
182	78.5	182	56.5
183	79.0	183	57.0
184	80.0	184	57.5
185	81.0	185	58.0
186	82.0	186	59.0
187	83.0	187	59.5
188	84.0	188	60.0
189	85.0	189	60.5
190	86.0	190	61.5
191	86.5	191	62.0
192	87.5	192	62.5
193	88.5	193	63.0
194	89.5	194	64.0
195	90.5	195	64.5
196	91.5	196	65.0
197	92.5	197	65.5
198	93.5	198	66.5
199	94.5	199	67.0
200	95.0	200	67.5
201	96.0	201	68.0
202	97.0	202	69.0
203	98.0	203	69.5
204	99.0	204	70.0
205	100.0	205	70.5
206	101.0	206	71.5
207	102.0	207	72.0
208	102.5	208	72.5
209	103.5	209	73.0
210	104.5	210	74.0
211	105.5	211	74.5
212	106.5	212	75.0
213	107.5	213	75.5
214	108.5	214	76.5
215	109.5	215	77.0
216	110.0	216	77.5
217	111.0	217	78.0
218	112.0	218	78.5
219	113.0	219	79.5
220	114.0	220	80.0
221	115.0	221	80.5
222	116.0	222	81.0
223	117.0	223	82.0
224	117.5	224	82.5
225	118.5	225	83.0
226	119.5	226	83.5
227	**120.5	227	84.5
228	**121.5	228	85.0
229	**122.5	229	85.5

OneStep APTT (fresh)	Plasma	OneStep APTT (citrated)	Plasma
230	**123.5	230	86.0
231	**124.5	231	87.0
232	**125.0	232	87.5
233	**126.0	233	88.0
234	**127.0	234	88.5
235	**128.0	235	89.5
236	**129.0	236	90.0
237	**130.0	237	90.5
238	**131.0	238	91.0
239	**132.0	239	92.0
240	**133.0	240	92.5
241	**133.5	241	93.0
242	**134.5	242	93.5
243	**135.5	243	94.5
244	**136.5	244	95.0
245	**137.5	245	95.5
246	**138.5	246	96.0
247	**139.5	247	97.0
248	**140.5	248	97.5
249	**141.0	249	98.0
250	**142.0	250	98.5
251	**143.0	251	99.0
252	**144.0	252	100.0
253	**145.0	253	100.5
254	**146.0	254	101.0
255	**147.0	255	101.5
256	**148.0	256	102.5
257	**148.5	257	103.0
258	**149.5	258	103.5
259	**150.5	259	104.0
260	**151.5	260	105.0
261	**152.5	261	105.5
262	**153.5	262	106.0
263	**154.5	263	106.5
264	**155.5	264	107.5
265	**156.0	265	108.0
266	**157.0	266	108.5
267	**158.0	267	109.0
268	**159.0	268	110.0
269	**160.0	269	110.5
270	**161.0	270	111.0
271	**162.0	271	111.5
272	**163.0	272	112.5
273	**163.5	273	113.0
274	**164.5	274	113.5
275	**165.5	275	114.0
276	**166.5	276	115.0
277	**167.5	277	115.5
278	**168.5	278	116.0
279	**169.5	279	116.5
280	**170.5	280	117.5
281	**171.0	281	118.0
282	**172.0	282	118.5
283	**173.0	283	119.0
284	**174.0	284	119.5
285	**175.0	285	**120.5
286	**176.0	286	**121.0
287	**177.0	287	**121.5
288	**178.0	288	**122.0
289	**179.0	289	**123.0
290	**179.5	290	**123.5
291	**180.5	291	**124.0
292	**181.5	292	**124.5
293	**182.5	293	**125.5
294	**183.5	294	**126.0
295	**184.5	295	**126.5
296	**185.5	296	**127.0
297	**186.5	297	**128.0
298	**187.0	298	**128.5
299	**188.0	299	**129.0
300	**189.0	300	**129.5

Heparin Sensitivity

Single Donor Sample

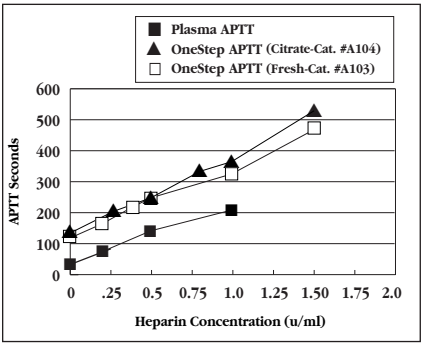
The APTT is commonly used to monitor heparin anticoagulation. Comparative heparin sensitivity curves were obtained using the indicated HEMOCHRON OneStep APTT for fresh and citrated samples and a reference plasma APTT which was determined using an ellagic acid APTT reagent and a photo-optical instrument as described on page 4.

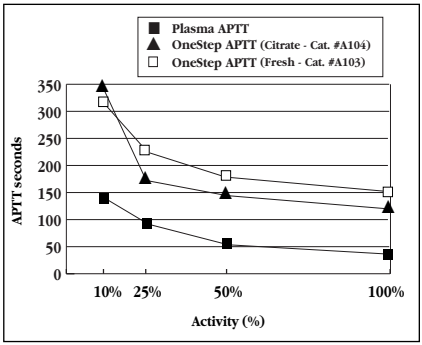
The reference plasma APTT and the HEMOCHRON OneStep APTT prolonged upon addition of heparin. At increasing heparin concentrations the HEMOCHRON OneStep APTT displayed linear prolongation up to 1.5 units/ml heparin while the reference plasma APTT did not detect an endpoint.

Coagulation Factor Sensitivity

Single Donor Sample

The APTT is commonly used to screen for intrinsic factor deficiencies. The OneStep APTT and plasma APTT show similar rates of clotting time increase as the percent activity decreases. Comparative sensitivity curves were obtained using the indicated OneStep APTT and the reference plasma APTT was determined using a particulate activator (Activated Thrombofax, Ortho Diagnostic Systems, Inc., Raritan, NJ) and a photo-optical instrument (Koagulab, Ortho Diagnostic Systems, Inc., Raritan, NJ).





LIMITATIONS OF THE PROCEDURE

The APTT 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. Lupus anticoagulant.
3. Test kits that have been improperly stored, 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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5. Brinkhous KM, Langdell RD, Penick GD, Graham JB, Wagner RH: Newer approaches to the study of hemophilia and hemophilioid states. JAMA 154:481, 1954.
6. Bell WN, Alton HG: A brain extract as a substitute for platelet suspensions in the thromboplastin generation test. Nature 174:880, 1954.
7. Bjornsson TD, Nash PV: Variability in heparin sensitivity of APTT reagents. Am J Clin Path 86:199, 1986.
8. Shojania AM, Tetreault J, Turnbull G: The variations between heparin sensitivity of different lots of activated partial thromboplastin time reagents produced by the same manufacturer. Am J Clin Path 89:19, 1988.
9. Blood collection guidelines are described in NCCLS document H21-A, "Collection, transport and processing of blood specimens for coagulation testing and general performance of coagulation assays."

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HL0795 6/01

HEMOCHRON®

Whole Blood Coagulation Systems

OneStep™ Activated Partial Thromboplastin Time (APTT)

Package Insert

INTENDED USE

The HEMOCHRON® APTT is a quantitative, whole blood coagulation test of the intrinsic coagulation pathway. The APTT test is intended solely for use with HEMOCHRON models 401, 801, 8000 or *Response*. The test can be performed at the bedside using fresh or citrated whole blood with the OneStep™ APTT. The OneStep APTT test monitors heparin anticoagulation and assesses hemostasis, and should be used only in accordance with established HEMOCHRON procedural guidelines.

For *in vitro* Diagnostic Use

SUMMARY AND EXPLANATION

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.[1,2] The activated partial thromboplastin time (APTT) test is a measure of the intrinsic coagulation pathway, which involves all the coagulation factors except factors VII and III (tissue factor).

The HEMOCHRON APTT tests are performed using a whole blood sample on the HEMOCHRON whole blood coagulation instrument. Two APTT configurations are available which use a single step procedure (e.g. no incubation step) to meet the differing needs of various settings in which the HEMOCHRON may be utilized.

The APTT may be performed at the patient site with a fresh whole blood sample using the HEMOCHRON OneStep APTT (A103). Alternatively, the APTT may be performed with a citrated blood sample using the HEMOCHRON OneStep APTT (A104).

The APTT, first described in 1961[3], evolved from the partial thromboplastin time test decribed in 1953.[4,5] The APTT uses a phospholipid derived from either brain or lung tissue to mimic the role of the platelets in the coagulation process.[6] Through the use of a reagent activator, Factor XII is converted to the active enzyme XIIa, which in turn activates Factor XI. This is followed by a succession of coagulation factors converting to active enzymes via the intrinsic pathway. Ultimately, this process, referred to as the coagulaton cascade, leads to the conversion of fibrinogen into a fibrin clot.

The HEMOCHRON OneStep APTT utilizes a kaolin activator to initiate the coagulation process as well as a platelet factor 3 substitute. This reagent system provides linearity to heparin up to 1.5 units per ml of blood, allowing HEMOCHRON OneStep APTT results to be reported up to a plasma equivalent of 250 seconds (A104 for citrated blood) or 300 seconds (A103 for fresh whole blood).

REAGENTS

APTT for use with fresh whole blood (A103)

The HEMOCHRON OneStep APTT, navy blue stopper test tube contains:

- Lyophilized preparation of colloidal kaolin, platelet factor 3 substitute, stabilizers and buffers.
- Thimerosal (0.02%) is added as a preservative.

APTT for use with citrated whole blood (A104)

The HEMOCHRON OneStep APTT, light grey stopper test tube contains:

- Lyophilized preparation of colloidal kaolin, platelet factor 3 substitute, calcium salts, stabilizers and buffers.
- Thimerosal (0.02%) is added as a preservative.

CAUTION: *The HEMOCHRON APTT test tubes contain 0.02% thimerosol as a preservative. Reagents containing thimerosol should be discarded in accordance with your institution's policy on disposal of medical waste.*