CE IVD

Precision in Hemostasis

Behnk Elektronik

BE APTT SL APTT Silica + CaCl2

Reagent for chronometric determination of Activated Partial Thromboplastin Time in human citrated plasma

REF 771250: AC (5 x 3 mL), CC (2 x 10 mL)
REF 771251: AC (8 x 10 mL), CC (8 x 10 mL)

| INTENDED USE

Reagent (Silica activator) and Calcium Chloride 0.025M solution for *in vitro* chronometric determination of Activated Partial Thromboplastin Time (APTT) in human citrated plasma.
Suitable for use with manual procedure on semi automated coagulometer, or on automated coagulation analyzer.
This device is intended for the evaluation of the function of the intrinsic pathway of the coagulation cascade (except platelets, Factor VII) and the monitoring of patients with heparin therapy.
It can also be used in conjunction with the relevant deficient plasmas, for the determination of the activity of coagulation Factors VIII, IX, XI and XII.
For clinical laboratory use by healthcare professionals.

PRINCIPLE [2]

BE APTT SL reagent contains a standardized amount of cephalin (platelet substitute) and an activator (silica). The reaction medium in contact with the CaCl solution recalcifies the plasma and triggers the coagulation reaction. Silica has the advantage of not sedimenting (standardized activation of Factor XII).

GENERALITIES [11]

A prolongation of the APTT happens in the following cases:
- Congenital Deficiencies
  - ✓ If the prothrombin time (PT) is normal, Factor VIII, IX, XI, XII may be Deficient.
  - ✓ If all these factors are normal, a deficiency in the following should be considered: prekallikrein (Fletcher factor) or HMW kininogen (Fitzgerald factor).
- Acquired Deficiencies and Abnormal Conditions
  - ✓ Liver diseases.
  - ✓ Consumptive coagulopathy.
  - ✓ Fibrinolysis.
  - ✓ Circulating anticoagulants (LA type or circulating anticoagulant against a factor).
  - ✓ During heparin or oral anticoagulant therapy.
  - ✓ Treatment with thrombin inhibitors (*e.g.* hirudin, argatroban, ...).

| REAGENTS

AC	APTT SL	Reagent	ATTENTION
Cephalin (rabbit cerebral tissues)		2.5%	
Activator (Silica)		< 0.1%	
Buffer		19%	
Excipients (non active ingredients)		qsp 100%	



According to (EC) 1272/2008 regulation,
Before reconstitution:
Attention: GSH07, Skin Sens.1: H317 - May cause an allergic skin reaction.
P261: Avoid breathing dust, P302+P352: After contact with skin, wash with plenty of water, P333+313: If skin irritation or a rash occurs, get medical advice, P501: Dispose of contents and container in accordance with dangerous waste regulations.
Classification based on: Silica < 1%. For more details refer to current Safety Data Sheet (SDS).
After reconstitution: the working reagent is not classified as dangerous.

CC	APPT SL	CaCl
Calcium chloride Solution		0.025M

According to (EC) 1272/2008 regulation, CC reagent is not classified as dangerous.

SAFETY CAUTIONS

- Refer to current Safety Data Sheet (SDS) available on request or on www.behnk.de.
- Verify the integrity of the contents before use.
- Waste disposal: Respect legislation in force in the country.
- All specimens or reagents of biological origin should be handled as potentially infectious. Respect legislation in force in the country.

Any serious incident that has occurred in connection with the device is notified to the manufacturer and the competent authority of the Member State in which the user and/or patient is based.

PREPARATION OF REAGENTS

AC: Reconstitute the lyophilizate with the amount of demineralized water indicated on the label. Cap the vial and mix gently until complete dissolution.
CC: Ready for use.

STABILITY AND STORAGE

Unopened vials, stored away from light at 2-8 °C are stable until the expiry date stated on the label.
AC: Stability after reconstitution:

• 2-8 °C	30 days
• On board Stability (OBS)*	6 days (AC and CC)
• Laboratory mode**	30 days

* 16-22 °C, stirred
** Laboratory mode = 8 hours on board; 16 hours well capped in the original vial at 2-8 °C.

CC: Once opened, if stored at 2-8 °C and free from contamination, CC content is stable until the expiry date stated on the label.

Do not use any reagent after expiry date.

SAMPLES COLLECTION AND HANDLING [1] [8] [9] [10]

Careful venipuncture in conformity with recommendations for Haemostasis tests.
Citrated plasma:
Collect blood (9 parts) in 0.109 M (*i.e.* 3.2 %) trisodium citrate anticoagulant (1 part).
Use collection tubes made of plastic or siliconized glass.
When monitoring heparin therapy, use preferably CTAD tubes to prevent heparin inactivation. Follow instructions of tube manufacturer.
Centrifuge within 1 hour after collection for 10 minutes at 2500 g.
Stability in plasmas:
- ✓ For 4 hours at 15-25°C

If, on heparin therapy:
- ✓ For 2 hours at 15-25°C (with Citrate anticoagulant)
- ✓ For 4 hours at 15-25°C (with CTAD tubes)

LIMITS [3] [5] [12-17]

Traumatic venipuncture may contaminate the specimen with tissue thromboplastin and shorten the APTT.
When monitoring heparin therapy, any release of Platelet Factor 4 (PF4) which is a potent inhibitor of heparin, represents a major source of error.
When using APTT assay to monitor unfractionated heparin therapy (UFH), it needs to consider factors and pre-analytical variables which may affect results. For more details refer to Performances file available on request.
Drugs: No interference was found at therapeutic concentrations using common drug panels.
CRP binds to phospholipids. High levels can result in a prolongation of the clotting time.
For a more comprehensive review of factors affecting this assay refer to the publication of Young D.S.

MATERIAL REQUIRED BUT NOT PROVIDED

Basic medical analysis laboratory equipment.
Automated or semi-automated coagulation analyzer.
Demineralized water for reconstitution of reagent.
REF 050813: Magnetic stirrers 8 x 1.5 mm, for Behnk Thrombolyzer series.

REFERENCE RANGE [1] [5] [6] [7]

The reference values vary according to the reagent-instrument combinations and local conditions (population, etc.).
In general, the low limit value is 20-25 sec and the high limit value < 35 sec.
Therefore, it is necessary for each laboratory to establish its own reference intervals on a panel of normal plasmas.
In this case, the reference interval is equivalent to the mean +/- 2 standard deviations (+/-2 SD).
For example, on 58 normal plasmas tested, the average observed is 31.1 sec with a standard deviation of 1.6 sec.
The APTT is normally prolonged in newborns babies and shortened in older populations.

QUALITY CONTROL

REF 773100: BE Trol 1; REF 773101: BE Trol 2
Controls are required for checking the accuracy and reproducibility of the results.
The control intervals should be adapted to each laboratory's individual requirements.
Values obtained should fall within the defined limits.
Follow the applicable government regulations and local guidelines for quality control.

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CALIBRATION [4]

Reference plasma: use normal human plasma from healthy individuals, men or women aged between 18 and 55, who are not taking any medication and blood donors. Results depend on the method used. The validity of the results depends on the correct timing, the correct reagent volume/specimen volume ratio and temperature.

PROCEDURE

Manual method on semi-automated systems:

- Plasma: 100 µL
- AC Reagent (mix before use): 100 µL

Mix and incubate for 180 sec at 37°C.

- CC Reagent (37°C): 100 µL

The automatic countdown timer will start immediately after CC reagent addition and stop when the clot is formed.

Automated method on Behnk Thrombolyzer series:

Refer to the full detailed application specific to the automated system.

- Performances and stability data have been validated on Thrombolyzer Compact X (available on request). These data are valid for all instruments in the Thrombolyzer series.

With manual procedure and on other automated coagulation analyzer, performances and stability data must be validated by user.

CALCULATION [5]

Results may be expressed as follows:

- In seconds (Patient time and Reference normal plasma time).
- In ratio Patient time/Reference normal plasma time.
- Reference plasma, see § Calibration.

PERFORMANCES

On the automated Thrombolyzer Compact X analyzer:

Precision: Repeatability (Within run) and Reproducibility (Between run):

Within run N = 20	Level 1	Level 2	Level 3
Mean (sec)	36.3	66.6	70.5
S.D. (sec)	0.33	1.49	0.59
C.V. (%)	0.9	2.2	0.8

Between run N = 20	Level 1	Level 2	Level 3
Mean (sec)	42.2	63.4	69.1
S.D. (sec)	0.99	1.19	0.77
C.V. (%)	2.3	1.9	1.1

Comparison with commercially available reagent, same method: 202 plasmas located between 21 sec and 69 sec were tested:

y = 1.2809 x – 6.4957 R= 0.8673

Interferences:

Total bilirubin	Positive interference from 124 µmol/L
Turbidity	No interference up to 731 mg/dL of triglycerides
Hemoglobin	No interference up to 261 µmol/L

Other substances may interfere with the results (see § Limits)

REFERENCES

(1) *Clinical Guide to Laboratory Test, 4th Ed, N.W. TIETZ (2006) p.46-47.*
(2) *Struver G.P., Bittner D.L. Am. J. Clin. Path. 1962, **38**, 473-481.*
(3) *Young DS. Effects on Clinical Laboratory Tests – Drugs Disease, Herbs & Natural Products, https://clinfx.wiley.com/ aaccweb/aacc/, accessed in September 2021. Published by AACC Press and John Wiley and Sons, Inc.*
(4) *Bell W.N., Alton H.G., Nature, 1954, **174**, 880-881.*
(5) *CAWKWELL R.D.: "Patient's age and the activated partial thromboplastin time test". Thromb. Haemostasis, 39, 780-781, 1978.*
(6) *ANDREW M., PAES B., MILNER R., JOHNSTON M., MITCHELL L., TOLLEFSEN D.M., POWERS P.: "Development of the human coagulation system in the full-term infant". Blood, 70, 1, 165-172, 1987.*
(7) *LEVIN HILLMAN C.R., LUSHER J.M.: "Determining the sensitivity of coagulation screening reagents: a simplified method". Lab. Med., 13, 3, 162-165, 1982.*
(8) *« Etude des différents paramètres intervenant dans les variables préanalytiques (revue de littérature) ». Sang Thromb. Vaiss., **10**, p.5-18 (1998).*
(9) *CONTANT G., GOUAULT-HEILMANN M., MARTINOLI J.L.: "Heparin inactivation during blood storage: its prevention by blood collection in citric acid, theophylline, adenosine, dipyridamole - C.T.A.D. mixture". Thromb. Res., 31, 365-374, 1983.*
(10) *Van den Besselaar AMHP, Meeuwisse-Braun J, Jansen-Gruter R, et al. Monitoring heparin therapy by the activated partial thromboplastin timedie effect of pre-analytical conditions. Thromb Haenwst. 1987; 57:226-231*
(11) *SAMAMA M., CONARD J., HORELLOU M.H., LECOMPTE T. : "Physiologie et exploration de l'hémostase". Paris: Doin, 152-153, 1990.*
(12) *Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996; 34:385-386.*
(13) *Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001; 38:376-385.*
(14) *Devreese KMJ, Verfaillie CJ, De Bisschop F et al. Interference of Creactive protein with clotting times. Clin Chem Lab Med 2015; 53(5): e141–e145.*
(15) *Price EA, Jin J, Nguyen HM, et al. Discordant aPTT and Anti-Xa Values and Outcomes in Hospitalized Patients Treated with Intravenous Unfractionated Heparin. Ann Pharmacother 2013; 47:151-8.*
(16) *Vandiver JW, Vondracek TG. Antifactor Xa Levels versus Activated Partial Thromboplastin Time for Monitoring Unfractionated. Pharmacotherapy 2012 ;32(6) :546-558.*
(17) *Marlar RA, Clement B, Gausman J, et al. Activated Partial Thromboplastin Time Monitoring of Unfractionated Heparin Therapy: Issues and Recommendations. Semin Thromb Hemost 2017;43(3):253-260.*

| = Significant modifications

IFU_771250-771251-EN_V04_20260703

Table of symbols

Manufacturer	Expiry date	*In Vitro* Diagnostic	Temperature limitation	Catalogue number	See insert	Batch number	Store away from light	Sufficient for	Dilute with	Demineralized water	Biological hazard

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