APTT Lyophilized silica - 0008468710

ENGLISH - Insert revision 02/2003 CE

Intended use

For the *in vitro* determination of Activated Partial Thromboplastin Time (APTT) in citrated plasma on IL Coagulation Systems as a general screening procedure for the evaluation of the intrinsic coagulation pathway and to monitor patients receiving heparin anticoagulant therapy.

Summary and principle

In the APTT test a contact activator is used to stimulate the production of Factor XIIa by providing a surface for the function of high molecular weight kininogen, kallikrein and Factor XIIa. This contact activation is allowed to proceed at 37°C for a specific period of time. Calcium is then added to trigger further reactions and the time required for clot formation is measured. Phospholipids are required to form complexes which activate Factor X and Prothrombin.[1] The APTT Lyophilized silica kit contains bovine cephalin and micronized silica to ensure a highly reproducible and stable product.[2]
Prolonged clotting times may be observed in the following situations: deficiency of Factor XII, XI, X, IX, VIII, V, II, or fibrinogen, liver diseases, Vitamin K deficiency, presence of heparin, lupus anticoagulant or other inhibitor.[3,4,5]

Composition

The **APTT Lyophilized Silica** kit consists of:

Cephalin (Cat. No. 0008468721): 5 x 9 mL vials of lyophilized bovine brain cephalin and micronized silica with stabilizers and preservative.

Calcium Chloride (Cat. No. 0019741900): 5 x 8 mL vials of calcium chloride (0.025 Mol/L) with preservative.

PRECAUTIONS AND WARNINGS:
Avoid contact with skin and eyes (S24/25). Do not empty into drains (S29).
Wear suitable protective clothing (S36).

Cephalin contains 200 ppm mercuric ions (from thimerosal) which may restrict its disposal. Refer to local environmental requirements for disposal.

Calcium Chloride contains sodium azide that may form explosive azides in metal plumbing. Use proper disposal procedures.

This product is For *in vitro* Diagnostic Use.

Preparation

Cephalin: Dissolve the contents of each vial with 9 mL of NCCLS Type II water or equivalent.[5] Replace the stopper and shake vigorously (approx. 15 seconds).
Make sure of the complete reconstitution of the product.
Keep the reagent at 15-25°C for 30 minutes and invert to mix before use.

Calcium Chloride: The reagent is ready for use.

Reagent storage and stability

Unopened reagents are stable until the expiration date shown on the vial, when stored at 2-8°C.

Cephalin - Stability after reconstitution: 7 days at 2-8°C in the original vial, 8 hours at 15°C on the ACL® Systems under continuous stirring, 8 hours at 15°C on the ACL Futura® and ACL Advance Systems under continuous stirring or 32 hours at 15°C on the ACL Futura and ACL Advance Systems when reagent is placed in a non-stirring position between runs and vigorously shaken before use.

Calcium Chloride: Opened reagent is stable 30 days at 2-8°C in the original vial.

Notes:

In order to assure optimal performance for both cephalin and $CaCl_2$ reagents, the indications reported below should be carefully followed:[2]

- always store vials of cephalin and $CaCl_2$ reagents at 2-8 °C when not in use
- shake cephalin vigorously immediately prior to use, to ensure homogeneity.

CAUTION: FREEZING OF THE REAGENT WILL ADVERSELY AFFECT PRODUCT PERFORMANCE.

Instrument/test procedures

Refer to the appropriate IL instrument's Operator's Manual and/or Application Manual for the complete assay procedure instructions.

Specimen collection and preparation

Nine parts of freshly drawn venous blood are collected into one part trisodium citrate. Refer to NCCLS Document H21-A3 for further instructions on specimen collection, handling and storage.[6]

Additional reagent and control plasmas

The following are not supplied with the kit and must be purchased separately.

	Cat. No.
Calibration plasma	0008467300
Normal Control	0020003110
Low Abnormal Control	0020003210
High Abnormal Control	0020003310
Factor diluent	0009757600

Quality control

Normal and abnormal controls are recommended for a complete quality control program.[6,9]

Normal control, Low Abnormal Control and High Abnormal Control are designed for this program. Each laboratory should establish its own mean and standard deviation and should establish a quality control program to monitor laboratory testing. Controls should be analyzed at least once every 8 hour shift in accordance with good laboratory practice. Refer to the instrument's Operator's Manual for additional information.
Refer to Westgard *et al* for identification and resolution of out-of-control situations.[10]

Results

APTT results may be reported in seconds and/or ratios.
Refer to the instrument's Operator's Manual for additional information.

Limitations/interfering substances

APTT results may be affected by many commonly administered drugs and further studies should be made to determine the source of unexpected abnormal results.
APTT results on IL Coagulation System are not affected by hemoglobin up to 100 mg/dL, triglycerides up to 700 mg/dL and bilirubin up to 15 mg/dL.

Expected values

A normal range study was performed using APTT Lyophilized Silica reagent.

System	N	Range (unit)
ACL Family	63	24.9 - 36.8 (seconds)
ACL Futura/ACL Advance	63	24.6 - 36.0 (seconds)

These results were obtained using a specific lot of reagent.

Due to many variables which affect clotting times, each laboratory should establish its own normal range.

Performance characteristics

Precision:

Within run and total (run to run and day to day) precision was assessed over multiple runs using both normal and abnormal samples.

ACL Family	Mean (APTT seconds)	CV % (Within run)	CV % (Total)
Normal Control	29.8	0.87	1.68
Low Abnormal Control	52.3	0.86	1.72
High Abnormal Control	82.0	1.62	3.02

ACL Futura/ACL Advance	Mean (APTT seconds)	CV % (Within run)	CV % (Total)
Normal Control	28.2	1.45	2.83
Low Abnormal Control	51.2	1.62	5.59
High Abnormal Control	61.2	2.34	5.74

Correlation:

System	slope	intercept	r	Reference method
ACL Family	0.902	6.386	0.946	Silica based APTT on ACL
ACL Futura/ACL Advance	0.970	0.642	0.990	APTT Lyophilized Silica on ACL

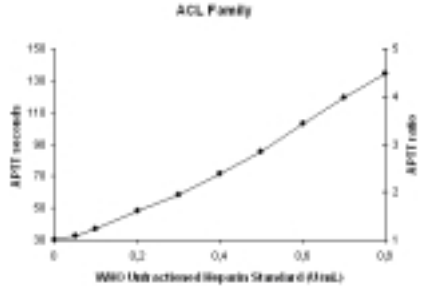
These precision and correlation results were obtained using specific lots of reagents and controls.

Heparin Therapy[11]

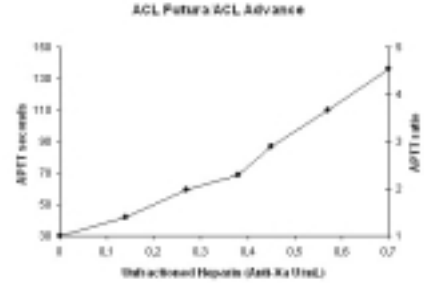
Therapeutic range: 0.2-0.4 U/mL

Heparin Dose-Response curve examples

The curve below is only an example obtained on the ACL System using one lot of APTT Lyophilized Silica reagent and one Normal Plasma Pool spiked with graduated quantities of WHO Unfractioned Heparin Standard.



The curve below is only an example obtained on the ACL Futura/ACL Advance System, using one lot of APTT Lyophilized Silica reagent and plasma samples from patients undergoing heparin therapy (Unfractioned heparin), to show the correspondence, for each level of heparin, between the heparin anti Xa activity and the relevant APTT response.



Due to many variables (i.e. different source of heparin) which may affect the clotting times, each laboratory should establish its own heparin therapeutic range.[12]

For further indications on therapeutic ranges and duration of treatment make reference to local guidelines.

Intrinsic Factor Sensitivity

Studies have shown APTT Lyophilized Silica to be sensitive to decreased concentration of intrinsic factors resulting in an abnormal APTT value when factors VIII, IX, XI and XII levels were in the 30-40% range.

Tests on the IL Coagulation Systems

APTT Lyophilized Silica 720 tests per kit (approx.)

Bibliography / Literatur / Bibliografía / Bibliographie / Bibliografia /Bibliografia / Litteratur / Litteraturförteckning / Βιβλιογραφία

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Symbols used / Verwendete Symbole / Símbolos utilizados / Symboles utilisés / Simboli impiegati / Símbolos utilizados / Anvendte symboler / Använda Symboler / Χρησιμοποιηθέντα σύμβολα

IVD	LOT				CONTROL				
In vitro diagnostic medical device	Batch code	Use by	Temperature limitation	Consult instructions for use	Control	Biological risks	Manufacturer	Authorised representative
In-vitro Diagnostikum	Chargen-Bezeichnung	Verwendbar bis	Festgelegte Temperatur	Beilage beachten	Kontrollen	Biologisches Risiko	Hergestellt von	Bevollmächtigter
De uso diagnóstico *in vitro*	Identificación número de lote	Caducidad	Temperatura de Almacenamiento	Consultar la metódica	Control	Riesgo biológico	Fabricado por	Representante autorizado
Dispositif mèdical de diagnostic *in vitro*	Désignation du lot	Utilisable jusqu'à	Températures limites de conservation	Lire le mode d'emploi	Contrôle	Risque biologique	Fabricant	Mandataire
Per uso diagnostico *in vitro*	Numero del lotto	Da utilizzare prima del	Limiti di temperatura	Vedere istruzioni per l'uso	Controllo	Rischio biologico	Prodotto da	Rappresentanza autorizzata
Dispositivo médico para utilização em diagnóstico *in vitro*	Número de lote	Data límite de utilização	Límite de temperatura	Consultar as instruções de utilização	Controlo	Risco biológico	Fabricado por	Representante autorizado
"in vitro" diagnostisk udstyr	Batch nr.	Anvendelse	Temperatur begrænsninger	Se vejledning for anvendelse	Kontrol	Miljø oplysninger	Producent	Leverandør
In vitro diagnostisk medicinsk produkt	Tillverkningskod	Användning	Temperatur gräns	Ta del av instruktionen före användning	Kontroll	Biologiska risker	Tillverkare	Auktoriserad representant
Προϊόν για διαγνωστική χρήση *In vitro*	Αρ. Παρτίδας	Χρήση έως	Περιορισμοί θερμοκρασίας	Συμβουλευτήτε τις οδηγίες χρήσης	Υλικό ποιοτικού ελέγχου	Βιολογικοί κίνδυνοι	Κατασκευαστής	Εξουσιοδοτημένος αντιπρόσωπος