HemosIL®

Providing the Right Solutions for Your APTT Testing

Sensitivities for
Heparin, Intrinsic Factors and Lupus Anticoagulants
To Meet Your Lab's Requirements

Werfen Group | Instrumentation Laboratory

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Introduction

The Activated Partial Thromboplastin Time (APTT) is an important assay for screening deficiencies and inhibitors of the intrinsic pathway of the coagulation cascade. In an APTT reagent, negatively charged particles (e.g., silica or Ellagic acid) are mixed with specific phospholipids and buffers to make an environment within which intrinsic plasma proteins are easily activated.

After plasma and the APTT reagent incubate together, Calcium is added in the form of Calcium Chloride, ($CaCl_2$). This initiates several steps in the intrinsic pathway, leading to a fibrin clot. The time from addition of $CaCl_2$ until clot formation is the APTT result in seconds.

What Can Cause an Abnormal APTT?

One of the most important uses of an APTT reagent is to monitor the therapeutic coagulation inhibitors, like unfractionated heparin. Heparin assists antithrombin in its binding and inhibition of several coagulation factors. Antithrombin binds various active coagulation serine proteases (i.e., Factor Xa, Factor IIa [thrombin], Factor IXa) resulting in the slowing of clotting and prolongation of the APTT.

Different APTT reagents vary significantly in their sensitivity to unfractionated heparin.[1] A consensus has developed that the appropriate level of prophylactic heparin is 0.2 - 0.4 U/mL by protamine sulfate titration.[2] The appropriate response to these levels of heparin for APTT is considered to be between 1.5 - 2.5 times longer than the mid-point of the normal range.[3,4]

Significant deficiencies of procoagulant factors of the intrinsic pathway (XII, XI, IX, or VIII), those of the common pathway or inhibition of the reactions of these factors, can cause prolongation of the APTT. Reference ranges of the factors vary from approximately 50 - 150% of normal activity.[5]

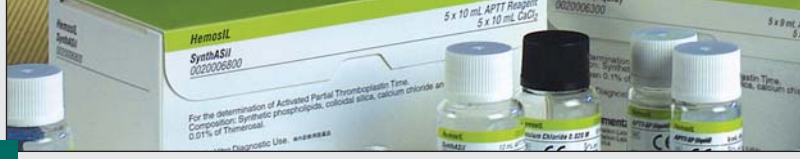
Inihibitors affecting APTT include immuno-globulins that bind intrinsic or common pathway factors. One particular heterogenous group of immunoglobulins, collectively referred to as Lupus Anticoagulants, results in a variety of physiological manifestations and diagnostic indications. The APTTs of Lupus patients can vary considerably. Although the APTT is typically prolonged with Lupus, no APTT reagent has been shown to produce an abnormal result for all cases of Lupus.[6]

While deficiencies of fibrinogen and Vitamin K, as well as liver disease and oral anticoagulants, can cause prolonged APTT results, the situations in which the APTT is most importantly used are:

- Unfractionated Heparin Monitoring
- Screening for Coagulation factor deficiencies and their inhibitors
- Screening for Lupus Anticoagulants

Raising the Standard for APTT Testing

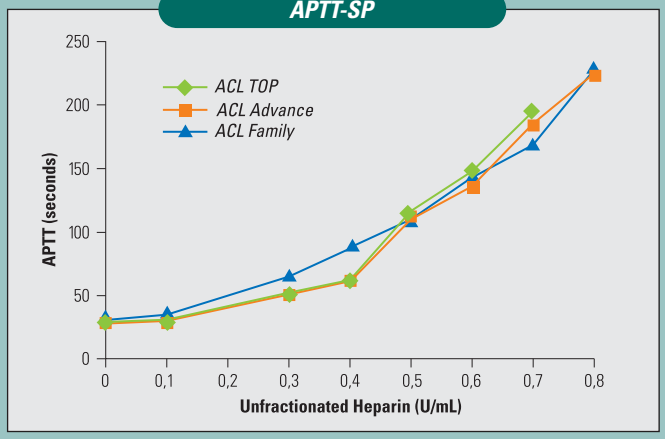
IL provides a choice of solutions to satisfy an array of APTT testing requirements, from state-of-the-art synthetic micro-silica and ellagic acid technology to the classic silica formulation.



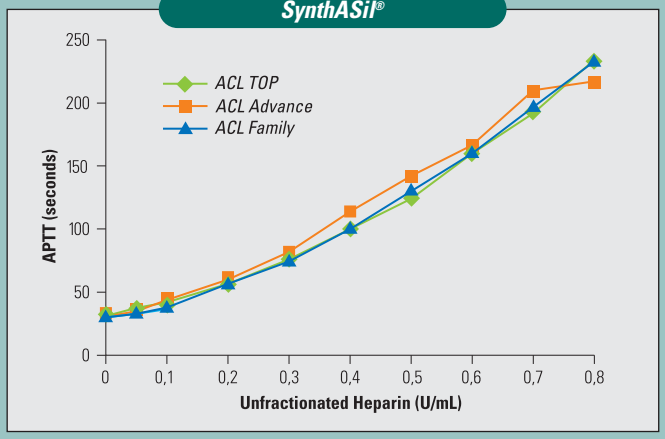
Solutions

Improved Patient Care	Value	Ease of Use
Provides consistent therapeutic ranges for improved heparin dosing and monitoring	*Efficiently manages anticoagulated patients*	*Ensures precision of results and simplifies clinical interpretation through lot-to-lot consistency*
Provides consistent sensitivity to intrinsic factor levels and Lupus Anticoagulants	*Minimizes waste through reagent stability*	*Minimizes time-consuming parallel lot cross-over studies*
Decreases risk of hemorrhagic and thrombotic complications by maintaining patients in therapeutic ranges	*Standardizes performance for safer and more effective anticoagulant therapy*	*Liquid ready-to-use (except APTT S Lyo) and packaged with corresponding $CaCl_2$*

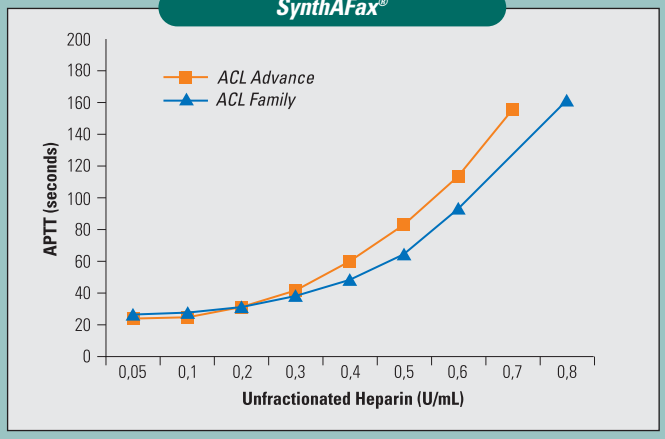
APTT-SP



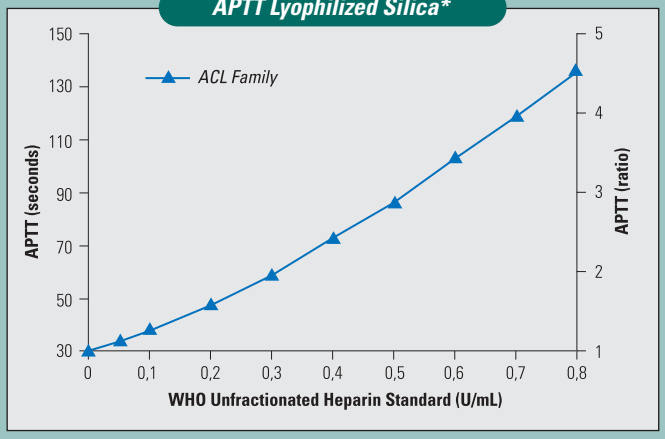
SynthASil®



SynthAFax®



APTT Lyophilized Silica*



Instrumentation Laboratory is dedicated to providing unique solutions for today's modern hemostasis laboratories. We are committed to the highest quality products, new technologies through extensive ongoing research efforts, advanced system design and extensive service and support. The HemosIL product line provides solutions for improved laboratory productivity and enhanced patient care.

* Not available in all countries.

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HemosIL Family of APTT reagents

APTT Reagent	APTT-SP	SynthASil	SynthAFax	APTT Lyo Silica***
Part Number and Size	0020006300 APTT reag. 5 x 9 mL 0.025M $CaCl_2$ 5 x 8 mL	0020006800 APTT reag. 5 x 10 mL 0.020M $CaCl_2$ 5 x 10 mL	0020007400 APTT reag. 5 x 10 mL 0.020M $CaCl_2$ 5 x 10 mL	0008468710 Cephalin 5 x 9 mL 0.025M $CaCl_2$ 5 x 8 mL
Liquid or Lyophilized	Liquid	Liquid	Liquid	Lyophilized
Activator	Silica	Colloidal Silica	Ellagic Acid	Micronized Silica
Phospholipds	Synthetic	Synthetic	Synthethic	Bovine brain cephalin
Reconstituted Stability at 2-8°C	APTT reagent 30 days in original vial $CaCl_2$ 30 days in original vial	APTT reagent 30 days in original vial $CaCl_2$ 30 days in original vial	APTT reagent 30 days in original vial $CaCl_2$ 30 days in original vial	APTT reagent 7 days in original vial $CaCl_2$ 30 days in original vial
Normal Range * **	24.4 - 35.0 seconds	25.4 - 38.4 seconds	19.7 - 27.6 seconds	24.9 - 36.8 seconds
Heparin Sensitivity	+++	+++	++	+++
Factor Sensitivity	+++	+++	++	++
Lupus Sensitivity	+++	++	+	+++

** Due to many factors which can affect clotting times, each laboratory should establish its own reference range. ** Obtained on the ACL Family of instruments. *** Not available in the all countries.*

Instrument Applications

	APTT-SP	SynthASil	SynthAFax	APTT Lyo Silica***
ACL TOP®	✓	✓	-	-
ACL Advance™	✓	✓	✓	✓
ACL ELITE/ELITE PRO - ACL 8/9/10000	✓	✓	✓	✓
ACL™ 100 - 7000	✓	✓	✓	✓

References

1. Kitchen S, Preston F E. "The Theraperutic Range for Heparin Therapy: Relationship Between Six Activated Thromboplastin Time Reagents and Two Assays." Thromb. Haemost, 1996; 5: 734-9.
2. Hirsh, J. "Heparin." N. Eng. J. Med. 1991; 324: 1565-74.
3. Basu D, Gallus A, Hirsh J, Cade J. "A Prospective Study of the Value of Monitoring Heparin Treatment with the Activated \ Partial Thromboplastin Time." N Engl J Med, 1972; 287: 324-7.
4. Hull, RD, Raskob GE, Pineo GF, Green D, Trowbridge AA, Elliott CG, Lerner RG, Hall J, Sparling T, Bretnell HR, Norton J, Carter CJ, Brant R, "Subcutaneous Low Molecular Weight Heparin Compared with Continuous Intravenous Heparin in the Treatment of Proximal-Vein Thrombosis." N Engl J Med, 1992; 326:975-82.
5. Data on file, Instrumentation Laboratory.
6. Triplett AD. "Laboratory Diagnosis of Lupus Anticoagulants." Sem. Thromb.Haemost. 1990; 16:183-192.

Werfen Group IVD

Worldwide Locations

Corporate Headquarters
Barcelona, Spain
Tel. +34-93-4010101
www.chwerfen.com

Instrumentation Laboratory Headquarters
Lexington, MA
Tel. +1-781-861-0710
www.ilus.com

US, Canada, Latin America

IL USA
Lexington, MA
Tel. +1-781-861-0710
www.ilus.com

IL Canada
Ontario, L4B 2N1
Tel. +1-800-522-2025x6115

IL Mexico
Col. Granada
Tel. +52-55-5262-1760
www.il-mexico.com.mx

Izasa Uruguay
Montevideo
Tel. +59-82-4818133

Pacific

Werfen Medical China
Shanghai
Tel. +86-21-32100745

Werfen Hong Kong
Hong Kong
Tel. +852-27927773

IL Japan
Minato-ku, Tokyo
Tel. +81-3-3437-6350

Werfen Medical Korea
Seo Cho-ku
Tel. +82-2-571-9246
www.werfenmedical.com

Europe, Middle East, Africa

Werfen Austria
Vienna
Tel. +43-1-2565800-0

IL Belgium
Zaventem
Tel. +32-2-7252052
www.il-be.com

Comesa Czech
Prague
Tel. +420-2-7816047

IL France
Paris
Tel. +33-1-53338600
www.il-france.fr

IL Germany
Munich
Tel. +49-89-909070
www.il-ger.de

IL Holland
Breda
Tel. +31-76-5480100
www.il-nl.com

Comesa Hungary
Budapest
Tel. +36-1-4392910 or 11

IL Italy
Milan
Tel. +39-02-25221
www.il-italia.it

Comesa Lithuania
Kaunas
Tel. +370-37-313157

Comesa Poland
Warsaw
Tel. +48-22-3361800

Izasa Portugal
Carnaxide
Tel. +351-21-4247300
www.izasa.com

Comesa Russia
Moscow
Tel. +7-495-9823723

Izasa Spain
Barcelona
Tel. +34-93-4010101
www.izasa.com

IL UK
Warrington, Cheshire
Tel. +44-1925-81-0141
www.il-uk.com

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