

CRYOcheck™ **IVD**

LUPUS POSITIVE CONTROL

Intended Use

CRYOcheck Lupus Positive control is prepared from human plasma and is recommended for use as a positive control in assays for lupus anticoagulant.

Summary and Principle

An association between circulating anticoagulants and systemic lupus erythematosus (SLE) was first described in 1952¹. In 1972 the term “lupus anticoagulant” (LA) was used to describe these non-specific, circulating inhibitors². The designation LA is still used today although it is now evident the majority of these patients do not suffer from SLE³. The presence of LA has been increasingly associated with a variety of disorders such as unexplained thrombosis and recurrent fetal loss^{4,5}.

LA are immunoglobulins, usually of the IgG, IgM or IgA classes, which are directed against anionic phospholipids or phospholipid-plasma protein complexes causing interference with *in vitro* phospholipid dependent coagulation tests. LA are clinically distinct members of a broader group of antiphospholipid antibodies (APA) characterized by antigenic protein targets such as β_2 glycoprotein 1 and prothrombin.

APA include LA as well as anticardiolipin, antiphosphatidylserine, and antiphosphatidylethanolamine antibodies^{6,7,8}.

The SSC Subcommittee has specified diagnostic criteria for the detection of LA⁹.

Reagents

CRYOcheck Lupus Positive control contains citrated human plasma collected from donors that have tested positive in accordance with the revised criteria of the SSC Subcommittee for the Standardization of Lupus Anticoagulants⁹. Source plasmas are processed in a manner that yields platelet-poor plasmas. Plasma is then buffered, aliquoted and rapidly frozen.



All blood products should be treated as potentially infectious. Source material from which this product was derived was found to be negative when tested in accordance with current required tests for transfusion-transmitted diseases. No known test methods can offer assurance that products derived from human blood will not transmit infectious agents. Accordingly, these human blood-based products should be handled and discarded as recommended for any potentially infectious human specimen¹⁰.

Storage, Preparation and Handling

When stored at -40 to -80 °C, CRYOcheck Lupus Positive control is stable to the end of the month indicated on the product packaging.

Thaw each vial at 37 °C (± 1 °C) in a waterbath. **The use of a dry bath or heating block for thawing is not recommended.** Thawing times are important and should be strictly adhered to. The use of a timer is recommended. Refer to the Thawing Table for recommended thawing times based on aliquot size. Allow thawed plasma to acclimate to room temperature (18 to 25 °C) and invert gently prior to use.

Thawing Table	
Aliquot Size	37 °C (± 1 °C) Waterbath
0.5 mL	3 minutes
1.0 mL	4 minutes

CRYOcheck Lupus Positive control may be used for up to eight hours after thawing, if capped in the original vial and maintained at 2 to 8 °C. Allow refrigerated plasma to acclimate to room temperature (18 to 25 °C) and invert gently prior to use. **Thawed material should be discarded after eight hours and should not be refrozen.**

Availability

Product	Catalog #	Format
CRYOcheck Lupus Positive Control	CCLP-05	25 vials x 0.5 mL
	CCLP-10	25 vials x 1.0 mL

Instruments

Each lab should prepare the local instrument in accordance with the manufacturer's instructions for use.

Procedure

After thawing and preparing CRYOcheck Lupus Positive control, use in accordance with established laboratory procedures for the quality control of assays for LA.

Materials Provided

- CRYOcheck Lupus Positive Control

Materials Required but not Provided

- Waterbath capable of maintaining 37 °C (± 1 °C)
- Assay reagents
- Coagulation instrument or assay system
- Sample cups
- Plastic disposable pipettes
- Volumetric pipettes
- Timer

Results and Interpretation

Control results should fall within the laboratory's established QC ranges provided the integrity of the test system has not been compromised.

Quality Control

Each laboratory should establish its own quality control (QC) ranges using acceptable statistical methods. These Qc ranges may then be used to monitor and validate the integrity of the test system¹¹. For all coagulation tests, the laboratory must include at least two levels of control for every eight hours of operation and any time a change in reagents occurs¹².

Limitations of the Procedure

When proper control values are not obtained, assessment of each component of the test system including reagents, control plasmas, instrumentation and operator technique must be undertaken in order to ascertain that all other components are functioning properly.

Expected Values

Quality control testing yielded the following results with a representative lot of *CRYOcheck* Lupus Positive control. results may vary depending on instrument, method and technique used.

Lupus Anticoagulant Assays	result	Interpretation
APTT (Lupus Sensitive)	80.9 sec	Positive
APTT (1:1 Normal Mix)	60.0 sec	Positive
APTT (1:1 Saline Mix)	75.8 sec	Positive
Kaolin Clotting Time (KCT)	216 KCT units	Positive
dilute Russell's Viper Venom Time (dRVVT)	1.9 ratio	Positive
Hexagonal Lupus Anticoagulant	32.2 sec	Positive
Platelet NeutralizationProcedure (PNP)	8.3 sec	Positive

Performance Characteristics

When used in accordance with established testing procedures for LA⁹, *CRYOcheck* Lupus Positive control demonstrates the following characteristics:











- *CRYOcheck* Lupus Positive control shows prolongation in phospholipid-dependent clotting tests.
- The clotting time of a mixture of *CRYOcheck* Lupus Positive control and pooled normal plasma is significantly longer (≥ 3 SD) than that of pooled normal plasma and non-LA patient plasma.
- *CRYOcheck* Lupus Positive control clotting times are corrected by the addition of lysed, washed platelets, or phospholipid liposomes containing phosphatidylserine or hexagonal phase phospholipids.
- *CRYOcheck* Lupus Positive control is non-specific for any individual clotting factor.


Each laboratory should establish its own diagnostic criteria for LA assays. *CRYOcheck* Lupus Positive control is subject to the limitations of the assay system in use.

Bibliography

1. Conley CL, Hartmann RC. A hemorrhagic disorder caused by circulating anticoagulant in patients with disseminated lupus erythematosus. *J clin Invest* 1952; 31:621-622.
2. Feinstein DI, Rapaport SI. Acquired inhibitors of blood coagulation. *Progress in hemostasis and thrombosis* 1972; 1:75-95.
3. Schleider MA, Nachman RI, Jaffe EA, Coleman M. A clinical study of the lupus anticoagulant. *Blood* 1976; 48:499-509.
4. Bowie EJW, Thompson JH, Jr., Pascuzzi CA, OWEN CA, Jr. Thrombosis in systemic lupus erythematosus despite circulating anticoagulants. *J Lab clin Med* 1963; 62:416-430.
5. Nilsson IM, Astedt B, Hedner U, Berezin D. Intrauterine death and circulating anticoagulant, "Antithromboplastin". *Acta Med Scand* 1975; 197:153-159.
6. Thiagarajan P, Shapiro SS, DeMarco L. Monoclonal immunoglobulin M lambda coagulation inhibitor with phospholipid specificity: Mechanism of a lupus anticoagulant. *J clin Invest* 1980; 66(3):397-405.
7. Triplett DA. Coagulation assays for the lupus anticoagulant: Review and critique of current methodology. *Stroke* 1992; 23(1):1-11-I-14.
8. Permpikul P, Rao LVM, Rapaport SI. Functional and binding studies of the roles of prothrombin and β_2 glycoprotein 1 in the expression of lupus anticoagulant activity. *Blood* 1994; 83(10):2878-2892.
9. Pengo V, Tripodi A, Reber G, Rand JH, Ortel TL, Galli M, De Groot PG; Update of the guidelines for lupus anticoagulant detection. Subcommittee on Lupus Anticoagulant / Antiphospholipid Antibody of the Scientific and Standardisation committee of the International Society on Thrombosis and Haemostasis. *J Thromb Haemost.* 2009; 7(10):1737-1740.
10. Biosafety in Microbiological and Biomedical Laboratories 6th ed. Centers for Disease Control and Prevention / National Institutes of Health, 2020.
11. Cembrowski GS, Carey RN. Laboratory quality management. Chicago: ASCP Press; 1989. p. 166-171.
12. CLIA 2004 – Code of Federal Regulations, 42CFR493.1269, 2004.

Symbols Used


	In vitro diagnostic medical device		Biological risks
	Batch code		Manufacturer
	Catalogue number		Authorized representative in the European Community / European Union
	Use by date		For prescription use only
	Temperature limit		Consult electronic instructions for use

 European Authorized Representative (Regulatory affairs only)
Emergo Europe—Westervoortsedijk 60, 6827 AT Arnhem, The Netherlands



UKRP United Kingdom Responsible Person
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