PrecisionBioLogic

CRYO*check*™ IVD

HEMOSTASIS CONTROL PLASMAS

APCR POSITIVE CONTROL

Intended Use

CRYO*check* APCR Positive Control is recommended for use as a positive control in the clot-based assessment of activated protein C resistance (APCR) in citrated human plasma.

Summary and Principle

Activated protein C (APC) is a serine protease with potent anticoagulant properties. During normal hemostasis, APC hinders clot formation through a mechanism of proteolytic inactivation of factors Va and VIIIa. A genetic single point mutation in the APC binding domain of the factor V gene, replacing Arg506 with Gln, was demonstrated to be both inherited and associated with familial thrombophilia[1-3]. The resulting resistance of factor Va to activated protein C (APCR), often referred to as the factor V_{Leiden} mutation, is now recognized as a commonly inherited risk factor for venous thrombosis.

Clot-based assays have been described which screen for the presence of APCR using citrated human plasma[4-6]. It is widely recommended, however, that individuals suspected of expressing this mutation on the basis of clotting assay results, undergo genetic testing. This will confirm the presence of the mutation at the molecular level and further define whether the patient is heterozygous, homozygous or normal[7].

Reagents

CRYO*check* APCR Positive Control is citrated human plasma collected from donor(s) that have tested positive for APCR by clot-based screening assays. The plasma is then buffered, aliquoted and rapidly frozen. Each donor used in the preparation of this product has been genetically tested using polymerase chain reaction (PCR) based techniques to confirm the presence of the heterozygous form of the factor V_{Leiden} mutation.

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 specimen[8].

Storage, Preparation and Handling

When stored at -40 to -80°C, CRYO*check* APCR 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

CRYO*check* APCR 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
APCR Positive Control	APCR-05	25 vials x 0.5 mL

Instruments

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

Procedure

After thawing and preparing CRYO*check* APCR Positive Control, use in accordance with established laboratory procedures for the quality control of clot-based assays for activated protein C resistance.

Materials Provided

- CRYO*check* APCR Positive Control

Materials Required but not Provided

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

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 quality control ranges may then be used to monitor and validate the integrity of the test system[9]. 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 occurs[10].

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

The following ratios were observed with three lots of CRYO*check* APCR Positive Control using Instrumentation Laboratory IL Test APC Resistance V on an Organon Teknika MDA 180.

ACPR Ratio	
Lot A	1.8
Lot B	1.7
Lot C	1.6

Actual APC ratios recovered with CRYO*check* APCR Positive Control may vary according to technique, instrument and reagent system used. It is recommended each laboratory establish its own mean values and tolerance limits for quality control purposes.

Performance Characteristics

The following percent coefficients of variation (%CV) were observed with three lots of CRYO*check* APCR Positive Control using Instrumentation Laboratory IL Test APC Resistance V on an Organon Teknika MDA 180.

Coefficient of Variation (%) n= 10	
Lot A	1.29
Lot B	2.79
Lot C	1.21

Each laboratory should establish its own acceptable limits of performance for quality control samples.

Bibliography

1. Dählback B, Hildebrand B. Inherited resistance to activated protein C is corrected by anticoagulant cofactor activity found to be a property of factor V. Proc Natl Acad Sci 1994; 91(4):1396-1400.
2. Greengard JS, Sun X, Xu X, Fernandez JA, Griffin JH, Evatt B. Activated protein C resistance caused by Arg506Gln mutation in Factor Va. Lancet 1994; 343(8909):1361-1362.
3. Sun X, Evatt B, Griffin JH. Blood coagulation factor Va abnormality associated with resistance to activated protein C in venous thrombophilia. Blood 1994; 83(11): 3120-3125.
4. de Ronde H, Bertina RM. Laboratory diagnosis of APC-resistance: A critical evaluation of the test and the development of diagnostic criteria. Thromb Haemost 1994; 72(6):880-886.
5. Rosen S, Johansson K, Lindberg K, Dählback B. Multicenter evaluation of a kit for activated protein C resistance on various coagulation instruments using plasmas from healthy individuals. Thromb Haemost 1994; 72(2):255-260.
6. Sochynsky CL, Joyner A, Ortel TI. A method for testing APC resistance in thrombophilic patients. Am Clin Lab 1994; 13(7):26-27.
7. Dählback B. APC-resistance as a pathogenic factor of venous thromboembolism. Clin Hem Rev 1995; 9(6):11-12.
8. Biosafety in Microbiological and Biomedical Laboratories 6th ed. Centers for Disease Control and Prevention / National Institutes of Health, 2020.
9. Cembrowski GS, Carey RN. Laboratory quality management. Chicago: ASCP Press; 1989. p. 166-171.
10. CLIA 2004 – Code of Federal regulations, 42CFR493.1269, 2004.

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Symbols Used

IVD	In vitro diagnostic medical device		Biological risks
LOT	Batch code		Manufacturer
REF	Catalogue number	EC REP	Authorized representative in the European Community / European Union
	Use by Date	**Rx ONLY**	For prescription use only
	Temperature limit		Consult electronic instructions for use

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

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