BIOLABO REAGENTS
www.biolabo.fr
MANUFACTURER:
BIOLABO SAS,
Les Hautes Rives,
02160, Maizy, France

Factor XII Deficient Plasma

Immuno-depleted plasma for the determination of Factor XII activity in citrated human plasma

REF 13312 **R1** 6 x 1 mL

CE

IVD

Made In France

I: corresponds to significant modifications

TECHNICAL SUPPORT AND ORDERS
Tel: (33) 03 23 25 15 50
Fax : (33) 03 23 256 256
support@biolabo.fr
Latest revision: www.biolabo.fr

INTENDED USE

I This reagent is designated for professional use in laboratory (automated or semi-automated method). It allows the quantitative determination of Factor XII activity in citrated human plasma.
This test is realized with reagents BIOLABO as follows:

REF 13660 and 13670: BIO-SIL (APTT Silica)
REF 13560 and 13570: BIO-CK (APTT Kaolin)
REF 13565 : $CaCl_2$ Solution 0.025 M
REF 13883: Owren Köller to dilute reference, control and patient's plasmas.

GENERALITIES (2) (3) (4) (5)

Factor XII is involved at different stages:
- In the endogenous coagulation pathway
- In relation with kallikreins in case of inflammation
- In fibrinolysis

There are pathological changes in the F.XII in the following cases:
- In congenital deficits (autosomal recessive), the rate of Factor XII varies from 15% to 80% in heterozygotes and less than 1% in Homozygotes.
- Factor XII deficiency is not accompanied by hemorrhagic syndromes, which suggests that there is another mechanism substituting to the activation of factor XII. It has not been demonstrated that this deficit increases risks of thrombosis.

PRINCIPLE (1)

The assay consists in the measurement of the clotting time, in the presence of cephalin and activator, of a system in which all the factors are present in excess except of factor XII which is derived from the sample being tested.

REAGENTS

R1 **F-XII** Deficient Plasma

Human Origin

Freeze dried citrated plasma without Factor XII (removed by selective immune adsorption).

SAFETY CAUTIONS

- Material Safety Data Sheet is available upon request.
- Each donor unit used to manufacture this product was tested and found non-reactive for HbsAg, antibody to Hepatitis C and antibody to HIV-1/HIV-2.
- However, no test method can offer complete assurance that infectious agents are absent. All specimens or reagents from biological origin should be handled as potentially infectious, in accordance with good laboratory practices using appropriate precautions.
- Waste disposal: Respect legislation in force in the country.

I 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.

REAGENTS PREPARATION

- Open the vial carefully and add exactly 1 mL of demineralised water**.**
- Recap and let stand for 15 minutes at room temperature.
- Before use, gently agitate to avoid the formation of foam.

STABILITY AND STORAGE

Stored away from light, well caped in the original vial at 2-8°C, when stored and used as described, reagents are stable:

Unopened:
- Until expiry date stated on the label of the kit.

Once opened:
- R1 must be reconstituted immediately.

I Once reconstituted, plasma is stable: 8 hours at 2-25°C.

SPECIMEN COLLECTION AND HANDLING (6) (7)

Citrated Plasma: Mix freshly drawn blood (9 Volumes) with buffered tri-sodium citrate solution 3.2% (1 volume).
Centrifuge for 10 min at 3000 g and extract supernatant.

Storage in plastic tube: 4h at 2-25°C

If quickly frozen: 15 days at -20°C, 1 month at -80°C (Thaw frozen plasmas at 37°C until complete thawing)

LIMITES (8) (9)

Anticoagulants present in the specimen to be tested may interfere with the factor XII activity in the specimen.

The presence of Lupus anticoagulants may lead to an under-estimation of Factor XII activity in the specimen.

For a more comprehensive review of factors affecting this assay refer to the publication of Young D.S.

MATERIAL REQUIRED BUT NOT PROVIDED

1. Basic medical analysis laboratory equipment.
2. Automated or semi-automated coagulation analyzer

Manufacturer	Expiry date	In vitro diagnostic	Storage temperature	Dematerialized water	Biological risk
Product Reference	See Insert	Batch number	Store away from light	Sufficient for	Dilute with

CALIBRATION

- REF 13970: BIO CAL, reference plasma for calibration of coagulation tests

Calibration frequency depends on proper instrument functions and on the preservation of reagent.

QUALITY CONTROL

- REF 13971: COATROL1 Level 1
- REF 13972: COATROL 2 Level 2
- External quality control program.

It is recommended to control in the following cases:

- At least once a run
- At least once within 24 hours
- When changing vial of reagent
- After maintenance operations on the instrument

If control is out of range, apply following actions:

1. Prepare a fresh control serum and repeat the test
2. If control is still out of range, use a new vial of fresh calibrator
3. If control is still out of range, use a new vial of reagent and reassay

If control is still out of range, please contact BIOLABO technical support or your local Agent.

REFERENCE INTERVALS (10) (11) (12)

Plasma (adult)	Usually 60-150%

Newborn: factor XII is lower (approx. 50% of the adult values).

After strenuous physical exercises, Factor XII can rise to 200-300%.

Each laboratory should establish its own normal ranges for the population that it serves.

PERFORMANCES

On automatic analyser SOLEA 100 at 37°C:

Precision:

Intra-Assay N = 20	level 1	level 2
Mean %	143	84
S.D. %	6.7	5.0
C.V. %	4.0	5.9

Inter-Assay N = 20	level 1	level 2
Mean %	104	54
S.D. %	7.2	6.4
C.V. %	7.0	11.7

Detection limit: 4% of Factor XII

Measuring Range: from 25% (QL) to 125%

Interferences APTT Kaolin (sec.):

Turbidity	No interference up to 0.543 abs
Bilirubin	Positive interference from 143 µmol/L
Hemoglobin	No interference up to 261 µmol/L

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

Onboard stability: Deficient plasma is stable 4 hours

Calibration Stability: Re-calibrate each day

Make a new calibration when changing reagent batch, if quality control results are found out of the established range and after maintenance operations

PROCEDURE

Manual procedure on semi-automate BIO SOLEA 2, BIO SOLEA 4:

Prepare dilutions 1/10, 1/20, 1/40, 1/80 of REF 13970 BIO-CAL Reference Plasma in Owren Köller buffer

Pre-incubate PT Reagent at least 15 min at 37°C and mix gently.

Measure and record the clotting time for each dilution as follows:

Reference plasma diluted 1/10 to 1/80	0,1 mL
Deficient plasma	0,1 mL
APTT Reagent :	0,1mL
Incubate 3 minutes at 37°C.	
$CaCl_2$ 0,025 M :	0,1mL
The automatic countdown timer will start immediately after $CaCl_2$ addition and stop when the clot is formed.	

Do the same for controls and specimens to be tested (pre-diluted 1/10 in Owren Köller buffer):

Controls and specimens (diluted 1/10)	0,1 mL
Deficient Plasma	0,1 mL
APTT Reagent :	0,1mL
Incubate 3 minutes at 37°C.	
$CaCl_2$ 0,025 M :	0,1mL
The automatic countdown timer will start immediately after $CaCl_2$ addition and stop when the clot is formed.	

Automated procedure : Full detailed application available on request

- Performances and stability data have been validated on SOLEA 100 and Thrombolyzer Compact X (available on request).
- With manual procedure and on other automated coagulation analyzer, performances and stability data must be validated by user.
- Other validated applications or proposal are available on request.

CALCULATION

Manual procedure:

Plot a Standard Curve using results obtained with dilutions 1/10 to 1/80 of reference plasma

Concentration % = f (Clotting Time)

Read the concentration of controls and samples reporting clotting time on the graph.

Automated and semi-automated procedure:

Patients results (seconds) will be automatically converted in % of Deficient Factor according to calibration curve.

REFERENCES

*(1) GRIFFIN J.H., COCHRANE C.G. : « Human Factor XII (Hageman factor) dans « Methods in enzymology », L. Lorand, New York : academeic Press, **45**, 56-65, 1976*

*(2) SCHMAIER A.H., MACCRAE K.R. : «The plasma kallicrein, kinine system : its evolution from contact activation ». Journal of Thrombosis and haemostasis, **5**, 2323-2329, 2007*

*(3) SAMPOL J., ARNOUX D., BOUTIERE B.: "Manuel d'hemostase" Paris: Editions scientifiques et médicales ELSEVIER, **48** , 361-362, 1995.*

*(4) BLAT Y., SEIFFERT D. : « A renaisssance for the contact system in blood coagulation ? »Thromb. Haemos., **99,** 457-460, 2008*

*(5) GIROLAMI A., RUZZON E., LOMBARDI A.M., CABRIO L., RANDI M.L. : « Thrombosis-free surgical procedures in severe (homozigote) factor XII deficiency : report of four additional cases and literature review ». Clin. Appl. Thrombosis/Haemostasis, **10**, 4, 351-355, 2004*

*(6) WOODHAMS B., GIRARDOT O., BLANCO M.J., COLESSE G., GOURMELIN Y.: "Stability of coagulation proteins in frozen plasma" Blood Coag. Fibrinolysis, **12**, 229-236, 2001*

(7) CLSI Document H21-A5: "Collection, transport, and processing of blood specimens for testing plasma-based coagulation assays and molecular haemostasis assys; approved guideline". Fifth edition, 28, 5, 2008

*(8) BRANDTJ.T., TRIPLETT D.A., ROCK W.A., BOVILL E.G., ARKIR C.F. : « Effect of lupus anticoagulants on the activated partial thromboplastin time ». Arch. Pathol. Lab. Med., **115**, 109-114, 1991*

(9) YOUNG D.S., Effect of Drugs on Clinical laboratory Tests, 4th Ed. (1995) p.3-254 à 3-257

(10) CAEN J., LARRIEU M-J., SAMMAMA M. : « L'hémostase, méthode d'exploration et diagnostic prue ». Paris : L'expansion scientitifique, 1975

*(11) ANDREW M., PAES B., MILNER R., JOHNSTON M., MITCHELL L., TOLLEFSEN D.M., POWERS P. : « Development of the human cogulation system in the full—term infant ». Blood, **70**, 1, 165-172, 1987*

*(12) IATRIDIS S.G., FERGUSON J.H. : « Effect of physical exercise in blood clotting and fibrinolysis ». J. Appl. Physiol., **18**, 337-344, 1963*