Test Definition: 9INHE

Factor IX Inhibitor Evaluation, Plasma

Overview

Useful For

Detection and titering of coagulation inhibitor to the specific factor requested, primarily factor IX in patients with hemophilia B

This test is **not useful** for the detection of a lupus-like circulating anticoagulant inhibitor, a nonspecific circulating anticoagulant, or other inhibitors that are not specific for coagulation factors.

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
9INHT	FIX Inhib Profile Tech Interp	No	Yes
F_9	Coag Factor IX Assay, P	Yes	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
9AINH	FIX Inhib Profile Prof Interp	No	No
9BETH	FIX Bethesda Units, P	No	No
F9_IS	Factor IX Inhib Scrn	No	No

Testing Algorithm

Testing begins with the coagulation factor IX activity assay with dilutions to evaluate assay inhibition; if the factor IX activity assay is normal or increased, then a technical interpretation will be provided.

If the factor IX activity assay is decreased, then an inhibitor screen to look for specific factor IX inhibition will be performed at an additional charge and a professional interpretation will be provided. If specific inhibition is apparent, the titer of the inhibitor will be determined.

Special Instructions

- Coagulation Guidelines for Specimen Handling and Processing

Method Name

F_9, 9BETH, F9_IS: Optical Clot-Based
9INHT: Technical Interpretation
9AINH: Medical Interpretation

NY State Available

Yes

Specimen

Specimen Type
Plasma Na Cit

Ordering Guidance
This test is for factor IX inhibitors only. If the patient is known to have hemophilia B, this is the correct test to order. If the presence or type of inhibitor is unknown, first order APROL / Prolonged Clot Time Profile, Plasma. When screening studies are needed for patients with known hemophilia A, order 8INHE / Factor VIII Inhibitor Evaluation, Plasma.

Shipping Instructions
Send all vials in the same shipping container.

Specimen Required
Specimen Type: Platelet-poor plasma
Patient Preparation:
1. Patient **should not** be receiving anticoagulant treatment (eg, warfarin, heparin). If not possible for medical reasons, note on request.
 a. If medically feasible, for 4 to 6 hours before specimen collection, **do not** administer intravenous heparin.
 b. If medically feasible, for 10 to 14 days before specimen collection, **do not** administer subcutaneous heparin or warfarin**.**
2. Patient **should not** be receiving fibrinolytic agents (streptokinase, urokinase, tissue plasminogen activator [tPA]).
3. It is recommended that specimens be collected pretransfusion. If patient has been transfused, **a specimen should not be collected for 48 hours.**
Collection Container/Tube: Light-blue top (3.2% sodium citrate)
Submission Container/Tube: 13-mm x 75-mm, 5-mL, plastic vial (polypropylene preferred)
Specimen Volume: 3 mL Platelet-poor plasma in 3 plastic vials, each containing 1 mL
Collection Instructions:
1. Specimen must be collected prior to factor replacement therapy.
2. For complete instructions, see Coagulation Guidelines for Specimen Handling and Processing.
3. Centrifuge, transfer all plasma into a plastic vial, and centrifuge plasma again.
4. Aliquot plasma (1-2 mL per aliquot) into 3 separate plastic vials, leaving 0.25 mL in the bottom of centrifuged vial.
5. Immediately freeze plasma (no longer than 4 hours after collection) at -20 degrees C or, ideally, at -40 degrees C or below.
Additional Information:
1. A double-centrifuged specimen is critical for accurate results as platelet contamination may cause spurious results.
2. Each coagulation assay requested should have its own vial.

Forms
If not ordering electronically, complete, print, and send a Coagulation Test Request (T753) with the specimen.

Specimen Minimum Volume
Platelet-poor plasma: 2 Plastic vials, each containing 1 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma Na Cit	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Factor IX inhibitors arise in patients with severe hemophilia B after factor IX transfusion. Patients with factor IX inhibitors may also develop anaphylactic reactions in response to factor IX infusions. Acquired factor IX inhibitors, occurring in previously healthy people, are exceedingly rare.

Reference Values

FACTOR IX ACTIVITY ASSAY
Adults: 65-140%
Normal, full-term infants or healthy premature infants may have decreased levels (> or =20%) that may not reach adult levels for 180 days or more postnatal.*
*See Pediatric Hemostasis References section in Coagulation Guidelines for Specimen Handling and Processing.

FACTOR IX INHIBITOR SCREEN:
Negative

GENERAL FACTOR BETHESDA UNITS:
< or =0.4 Bethesda Units

Interpretation

Normally, there is no inhibitor (ie, negative result).

If the screening assays indicate the presence of an inhibitor, it will be quantitated and reported in Bethesda (or equivalent) units.

Cautions

Occasionally, a potent lupus-like anticoagulant may cause false-positive testing for a specific factor inhibitor (eg, factor VIII or IX).

Clinical Reference

1. Hoffman R, Benz Jr EJ, Silberstein LE, et al, eds. Hematology: Basic Principles and Practice. 7th ed. Elsevier; 2018
2. Chitlur M, Warrier I, Rajpurkar M, et al. Inhibitors in factor IX deficiency a report of the ISTH-SSC international FIX inhibitor registry (1997-2006). Haemophilia. 2009;15(5):1027-1031. doi:10.1111/j.1365-2516.2009.02039.x

Performance

Method Description

The factor IX assay is performed on the Instrumentation Laboratory ACL TOP using the activated partial thromboplastin time (aPTT) method and a factor-deficient substrate. Patient plasma is combined and incubated with a factor IX-deficient substrate (normal plasma depleted of factor IX by immunoadsorption) and an aPTT reagent. After a specified incubation time, calcium is added to trigger the coagulation process in the mixture. Then the time to clot formation is measured optically at a wavelength of 671 nm.(Owen CA Jr, Bowie EJW, Thompson JH Jr. Diagnosis of Bleeding Disorders. 2nd ed. Little, Brown and Company; 1975; Cielsa B. Defects of plasma clotting factors. In: Hematology in Practice. 3rd ed. FA Davis; 2019:chap 17)

The factor IX inhibitor screen consists of measuring the difference in factor IX activity (partial thromboplastin time assay) before and after incubation of a mixture of normal plasma and patient's plasma for 1 hour at 37 degrees C. For optimal sensitivity, the factor IX value of the normal plasma is adjusted to approximately 20%, because the factor IX assay is more sensitive in this area of the curve. In addition, an excess of patient's plasma will make the test more sensitive to small amounts of inhibitors.(Owen CA Jr, Bowie EJW, Thompson JH Jr. The Diagnosis of Bleeding Disorders. 2nd ed. Little, Brown, and Company; 1975:143-145; Cielsa B. Defects of plasma clotting factors. In: Hematology in Practice. 3rd ed. FA Davis; 2019:chap 17)

If the inhibitor screen is positive for an inhibitor of factor IX, the inhibitor will be quantitated by the Bethesda assay. In the Bethesda procedure, inhibitors are quantified by mixing equal volumes of serially diluted plasma with normal plasma. This mixture is incubated 2 hours at 37 degrees C, and its factor IX activity is measured and compared to a control run at the same time. The difference between the factor IX activity of the patient's incubation mixture and that of the control is used to calculate the titer. The residual factor IX activity is converted to Bethesda units: 50% residual factor IX is equal to 1 Bethesda unit. Assays using the same basic principle as the Bethesda assay are used to quantitate the inhibitors of other coagulation factors.(Kasper CK, Aledort LM, Counts RB, et al. A more uniform measurement of factor VIII inhibitors. Thromb Diath Haemorrh. 1975;34:869-872; Cielsa B. Defects of plasma clotting factors. In: Hematology in Practice. 3rd ed. FA Davis; 2019:chap 17)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

1 to 3 days

Specimen Retention Time

7 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test has been modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

85390
85250
85335 (if appropriate)
85335 (if appropriate)
85390 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
9INHE	Factor IX Inhib Profile, P	96459-3

Result ID	Test Result Name	Result LOINC® Value
F_9	Coag Factor IX Assay, P	3187-2
9INHT	FIX Inhib Profile Tech Interp	69049-5