

## Overview

### Useful For

Evaluation of patients with incident or recurrent venous thromboembolism (VTE)

Evaluation of individuals with a family history of VTE

### Special Instructions

- [Coagulation Guidelines for Specimen Handling and Processing](#)

### Method Name

Optical Clot-Based

### NY State Available

Yes

## Specimen

### Specimen Type

Plasma Na Cit

### Advisory Information

Although this assay can be performed in the absence of other coagulation tests and clinical information, it is most reliably performed as part of a consultative coagulation test panel with interpretive reporting (including appropriate testing of the same specimen to evaluate for the presence or absence of coagulation abnormalities or conditions that may affect interpretation of the APC resistance assay). This test is included among a panel of tests designated AATHR / Thrombophilia Profile.

### Necessary Information

If a priority specimen, mark request form, give reason, and request a call-back.

### Specimen Required

See [Coagulation Guidelines for Specimen Handling and Processing](#) in Special Instructions.

**Specimen Type:** Platelet-poor plasma

**Collection Container/Tube:** Light-blue top (citrate)

**Submission Container/Tube:** Polypropylene vial

**Specimen Volume:** 1 mL

### Collection Instructions:

1. Centrifuge specimen, remove plasma
2. Centrifuge plasma again; remove plasma aliquot without disturbing bottom 0.5 mL
3. Freeze plasma immediately (no longer than 4 hours after collection) at -20 degrees C, or, ideally < or =-40

degrees C

**Additional Information:**

1. Double-centrifuged specimen is critical for accurate results as platelet contamination may cause spurious results.
2. If priority specimen, mark request form, give reason, and request a call-back.
3. 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**

0.5 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 and Interpretive**
**Clinical Information**

Protein C, a part of the natural anticoagulant system, is a vitamin K-dependent protein zymogen (molecular weight=62,000 da) that is synthesized in the liver and circulates at a plasma concentration of approximately 5 mcg/mL. Protein C is activated to activated protein C (APC) via proteolytic cleavage by thrombin bound to thrombomodulin, an endothelial cell surface membrane protein. APC downregulates the procoagulant system by proteolytically inactivating procoagulant factors Va and VIIIa. Protein S, another vitamin K-dependent coagulation protein, catalyzes APC inactivation of factors Va and VIIIa. APC interacts with and proteolyzes factors V/Va and VIII/VIIIa at specific APC binding and cleavage sites, respectively. Resistance to activated protein C (APC resistance) is a term used to describe abnormal resistance of human plasma to the anticoagulant effects of human APC. APC resistance is characterized by a reduced anticoagulant response of patient plasma after adding a standard amount of APC. For this assay, the activated partial thromboplastin time clotting test fails to prolong significantly after the addition of APC.

The vast majority of individuals with familial APC resistance have a specific point mutation in the procoagulant factor V gene (1691G-A, factor V Leiden) encoding for a glutamine (Q) substitution for arginine (R)-506 in the heavy chain of factor V (factor V R506Q). This amino acid change alters an APC cleavage site on factor V such that factor V/Va is partially resistant to inactivation by APC. The carrier frequency for the factor V Leiden mutation varies depending on the population. Approximately 5% of asymptomatic white Americans of non-Hispanic ancestry are heterozygous carriers, while the carrier frequency among African Americans, Asian Americans, and Native Americans is less than

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1%, and the carrier frequency for Hispanics is intermediate (2.5%). The carrier frequency can be especially high (up to 14%) among whites of Northern European or Scandinavian ancestry. Homozygosity for factor V Leiden is much less common, but may confer a substantially increased risk for thrombosis. The degree of abnormality of the APC-resistance assay correlates with heterozygosity or homozygosity for the factor V Leiden mutation; homozygous carriers have a very low APC-resistance ratio (eg, 1.1-1.4), while the ratio for heterozygous carriers is usually 1.5 to 1.8.

## Reference Values

### APCRV RATIO

> or =2.3

Pediatric reference range has neither been established nor is available in scientific literature. The adult reference range likely would be applicable to children older than 6 months.

## Interpretation

An activated protein C (APC) resistance ratio of less than 2.3 suggests abnormal resistance to APC of hereditary origin.

If the APC resistance test is abnormal, DNA-based testing for the factor V Leiden mutation (F5DNA / Factor V Leiden [R506Q] Mutation, Blood) may be helpful in confirming or excluding hereditary APC resistance.

## Cautions

This assay is highly sensitive and specific for inherited activated protein C (APC) resistance, most commonly due to the factor V Leiden mutation, but it will not detect patients with acquired APC resistance. Persons with acquired APC resistance are at similar risk for venous thromboembolism.

Preanalytical conditions of the patient and the blood specimen are extremely important for reliable performance and interpretation of testing for APC resistance. Plasmas demonstrating prolongation of clotting times (prothrombin time, activated partial thromboplastin time) for reasons other than anticoagulant effects (eg, lupuslike anticoagulants or specific coagulation factor inhibitors) generally cannot be reliably tested for the presence or absence of APC resistance. Proper preparation of the blood (plasma) specimen is extremely important to help insure accuracy of results and interpretation.

The activated protein C resistance ratio (APCRV) assay has greater than 99% sensitivity for detecting the presence of a factor V Leiden mutation. Discrepant results of plasma-based APCRV and DNA-based factor V Leiden testing may occur in recipients of liver or allogeneic hematopoietic stem cell transplants; or due to anticoagulant effects such as excess heparin; direct thrombin inhibitors argatroban (Acova), bivalirudin (Angiomax), or dabigatran (Pradaxa); or direct factor Xa inhibitors rivaroxaban (Xarelto), apixaban (Eliquis), and edoxaban (Savaysa); or a sample mix-up. Clinical correlation is suggested. If clinically indicated, consider follow-up repeat APCRV testing or direct DNA-based testing for the factor V Leiden (R506Q) mutation (F5DNA / Factor V Leiden [R506Q] Mutation, Blood).

## Clinical Reference

1. Nichols WL, Heit JA: Activated protein C resistance and thrombosis. *Mayo Clin Proc* 1996;71:897-898
2. Dahlback B: Resistance to activated protein C as risk factor for thrombosis: molecular mechanisms, laboratory investigation, and clinical management. *Semin Hematol* 1997;34(3):217-234
3. Rodeghiero F, Tosetto A: Activated protein C resistance and Factor V Leiden mutation are independent risk factors for venous thromboembolism. *Ann Intern Med* 1999;130:643-650
4. Grody WW, Griffin JH, Taylor AK, et al: American College of Medical Genetics consensus statement on factor V

Leiden mutation testing. Genet Med 2001;3:139-148

5. Press RD, Bauer KA, Kujovich JL, Heit JA: Clinical utility of factor V Leiden (R506Q) testing for the diagnosis and management of thromboembolic disorders. Arch Pathol Lab Med 2002;126:1304-1318

## Performance

### Method Description

This assay is performed using the HemosIL Factor V Leiden (APC Resistance V) Kit on the Instrumentation Laboratory ACL TOP instrument. The method uses a modified activated partial thromboplastin time (APTT) test to detect activated protein C (APC) resistance. The plasma specimen is prediluted in factor V-deficient plasma. Then the APTT test is performed by incubating patient plasma with a standardized amount of platelet-like phospholipids and activator of the contact factors of the intrinsic coagulation pathway, followed by recalcification of plasma and measurement of clotting time. The ratio of the APTT test with and without added APC is reported as the APC resistance (or sensitivity) ratio. (Package insert: HemosIL Factor V Leiden [APC Resistance V]. Instrumentation Laboratory Company, Bedford, MA, Rev 10/2012)

### PDF Report

No

### Day(s) and Time(s) Test Performed

Monday through Friday

### Analytic Time

1 day

### Maximum Laboratory Time

3 days

### Specimen Retention Time

7 days

### Performing Laboratory Location

Rochester

## Fees and 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 Regional Manager. For assistance, contact [Customer Service](#).

### Test Classification

This test has been cleared, approved or is exempt by the U.S. Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

### CPT Code Information

85307

**LOINC® Information**

Test ID	Test Order Name	Order LOINC Value
APCR <sub>V</sub>	Activated Protein Resistance V, P	13590-5

Result ID	Test Result Name	Result LOINC Value
APCR	APCR <sub>V</sub> Ratio	13590-5
INT55	Interpretation	48591-2