

## Overview

### Useful For

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

Evaluation of individuals with a family history of VTE

### Testing Algorithm

If the assay ratio is abnormal, then factor V Leiden variant analysis will be performed at an additional charge.

When the activated protein C resistance V is abnormal or indeterminate and the factor V Leiden variant assay is performed, a summary interpretation will be provided.

### Special Instructions

- [Coagulation Guidelines for Specimen Handling and Processing](#)
- [Informed Consent for Genetic Testing](#)
- [Coagulation Patient Information](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)

### Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
APCRV	Activated Protein Resistance V, P	Yes	Yes

### Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
F5DNA	Factor V Leiden (R506Q) Mutation, B	Yes	No
F5DNI	APCRV/F5DNA Summary Interpretation	No	No

### Method Name

Optical Clot-Based

### NY State Available

Yes

---

**Specimen****Specimen Type**

Plasma Na Cit

Whole blood

**Necessary Information**

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

**Specimen Required****Blood and plasma are required.****Specimen Type:** Whole blood**Container/Tube:****Preferred:** Lavender top (EDTA)**Acceptable:** Yellow top (ACD) or light-blue top (3.2% sodium citrate)**Specimen Volume:** 3 mL**Collection Instructions:**

1. Invert several times to mix blood.
2. Send specimen in original tube. **Do not** aliquot.

**Specimen Type:** Platelet-poor plasma**Patient Preparation:** Fasting preferred**Collection Container/Tube:** Light-blue top (3.2% sodium citrate)**Submission Container/Tube:** Polypropylene vial**Specimen Volume:** 1 mL**Collection Instructions:**

1. For complete instructions, see [Coagulation Guidelines for Specimen Handling and Processing](#) in Special Instructions.
2. Within 4 hours of collection, centrifuge, transfer all plasma into a plastic vial, and centrifuge plasma again.

3. Aliquot plasma into separate plastic vial leaving 0.25 mL in the bottom of centrifuged vial.

4. Freeze plasma aliquot immediately 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. Each coagulation assay requested should have its own vial.

**Forms**

[1. New York Clients-Informed consent is required.](#) Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

[-Informed Consent for Genetic Testing \(T576\)](#)

[-Informed Consent for Genetic Testing-Spanish \(T826\)](#)

2. [Coagulation Patient Information \(T675\)](#) in Special Instructions

3. If not ordering electronically, complete, print, and send a [Coagulation Test Request \(T753\)](#) with the specimen.

**Reject Due To**

- Gross hemolysis    Reject
- Gross lipemia      Reject
- Gross icterus        Reject

**Specimen Minimum Volume**

Plasma: 0.5 mL

Whole Blood: 3 mL

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Plasma Na Cit	Frozen (preferred)	14 days	
Whole blood	Ambient (preferred)	14 days	
	Frozen	14 days	
	Refrigerated	14 days	

**Clinical & 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 fails to prolong significantly after the addition of APC.

The vast majority of individuals with familial APC resistance have a specific alteration in the procoagulant factor V gene (*F5*) encoding for a p.Arg534Gln substitution in the heavy chain of factor V (formerly R506Q). This glutamine to arginine 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 variant 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 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 variant; 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

&gt; 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 below 2.3 suggests abnormal resistance to APC of hereditary origin.

If the screening APC resistance test is abnormal, DNA-based testing for the factor V Leiden variant (p.Arg534Gln, formerly R506Q) is performed to confirm or exclude 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 variant but 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. Plasma specimens demonstrating prolongation of clotting times (prothrombin time, activated partial thromboplastin time) for reasons other than anticoagulant effects (eg, lupus-like anticoagulants or specific coagulation factor inhibitors) generally cannot be reliably tested for the presence or absence of APC resistance. Proper preparation of the plasma specimen is extremely important to help ensure accuracy of results and interpretation.

This assay has greater than 99% sensitivity for detecting the presence of the factor V Leiden variant. Discrepant results of plasma-based activated protein C resistance ratio (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. Suggest clinical correlation. If DNA-based testing for the factor V Leiden variant is clinically indicated, call 800-533-1710.

Although the APC-resistance 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, Plasma and Whole 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. doi: 10.7326/0003-4819-130-8-199904200-00004.
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. doi: 10.1097/00125817-200103000-00009.
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. doi: 10.5858/2002-126-1304-CUOFVL.
6. Yohe S, Olson J: Thrombophilia: Assays and interpretation. In: Kottke-Marchant K, ed: *Laboratory Hematology*

---

Practice. Wiley Blackwell Publishing; 2012:492-508

## 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 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; Rev 11/2017)

### PDF Report

No

### Specimen Retention Time

Plasma: 7 days: Whole blood: 2 weeks

### Performing Laboratory Location

Rochester

## Fees & Codes

### Test Classification

See Individual Test IDs

### CPT Code Information

85307

### LOINC® Information

Test ID	Test Order Name	Order LOINC Value
APCRR	APCRV, w/Reflex, P	13590-5

Result ID	Reporting Name	LOINC®
-----------	----------------	--------

---

APCR	APCRV Ratio	13590-5
INT55	Interpretation	48591-2