

## Overview

### Useful For

Confirmation of a diagnosis of very long chain acyl-CoA dehydrogenase (VLCAD) deficiency

Carrier screening in cases where there is a family history of VLCAD deficiency, but an affected individual is not available for testing or disease-causing mutations have not been identified

### Special Instructions

- [Molecular Genetics: Biochemical Disorders Patient Information](#)
- [Informed Consent for Genetic Testing](#)
- [Blood Spot Collection Card-Spanish Instructions](#)
- [Blood Spot Collection Card-Chinese Instructions](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)
- [Blood Spot Collection Instructions](#)

### Method Name

Polymerase Chain Reaction (PCR)/DNA Sequencing Analysis

### NY State Available

Yes

## Specimen

### Specimen Type

Varies

### Shipping Instructions

Specimen preferred to arrive within 96 hours of draw.

### Specimen Required

**Patient Preparation:** A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

**Submit only 1 of the following specimens:**

**Preferred:**

**Specimen Type:** Whole blood

**Container/Tube:** Lavender top (EDTA) or yellow top (ACD)

**Specimen Volume:** 3 mL

**Collection Instructions:**

1. Invert several times to mix blood.
2. Send specimen in original tube.

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**Specimen Stability Information:** Ambient (preferred)/Refrigerated

**Specimen Type:** Blood spot

**Supplies:** Card - Blood Spot Collection (Filter Paper) (T493)

**Container/Tube:**

**Preferred:** Collection card (Whatman Protein Saver 903 Paper)

**Acceptable:** Ahlstrom 226 filter paper, or Blood Spot Collection Card (T493)

**Specimen Volume:** 2 to 5 Blood Spots on collection card (Whatman Protein Saver 903 Paper; Ahlstrom 226 filter paper; or Blood Spot Collection Card)

**Collection Instructions:**

1. An alternative blood collection option for a patient >1 year of age is finger stick.
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry

**Specimen Stability Information:** Ambient (preferred)/Refrigerated

**Additional Information:**

1. For collection instructions, see [Blood Spot Collection Instructions](#) in Special Instructions.
2. For collection instructions in Spanish, see [Blood Spot Collection Card-Spanish Instructions](#) (T777) in Special Instructions.
3. For collection instructions in Chinese, see [Blood Spot Collection Card-Chinese Instructions](#) (T800) in Special Instructions.

**Specimen Type:** Cultured fibroblasts

**Container/Tube:** T-75 or T-25 flask

**Specimen Volume:** 1 Full T-75 or 2 full T-25 flasks

**Specimen Stability Information:** Ambient (preferred)/Refrigerated <24 hours

**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. [Molecular Genetics: Biochemical Disorders Patient Information](#) (T527) in Special Instructions

3. If not ordering electronically, complete, print, and send an [Inborn Errors of Metabolism Test Request](#) (T798) with the specimen.

### Specimen Minimum Volume

Blood: 1 mL

Blood Spots: 5 punches, 3-mm diameter

### Reject Due To

All specimens will be evaluated by Mayo Clinic Laboratories for test suitability.

### Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

## Clinical and Interpretive

### Clinical Information

Very long chain acyl-CoA dehydrogenase (VLCAD) deficiency is an autosomal recessive disorder of mitochondrial fatty acid beta-oxidation. Mitochondrial beta-oxidation plays a major role in energy production and VLCAD catalyzes the first step in the breakdown of fatty acids that are 14 to 20 carbons long.

VLCAD deficiency has a reported incidence of approximately 1 in 30,000 births and has a variable age of onset that is generally classified into 3 categories. Individuals with the early-onset type present with cardiomyopathy, hypotonia, and hepatomegaly in the first months of life; sudden death is also frequent. Individuals with the early-childhood onset type typically present with hypoketotic hypoglycemia and hepatomegaly without cardiomyopathy. Individuals with the late-onset type of VLCAD deficiency generally present after childhood with intermittent rhabdomyolysis and muscle dysfunction that often manifests as muscle cramps and exercise intolerance.

Review of clinical features and biochemical analysis via plasma acylcarnitines, plasma fatty acid profile, urine organic acids, and fibroblast fatty acid oxidation probe studies are recommended as laboratory evaluations for VLCAD deficiency. Plasma and urine biochemical testing are not reliable for identifying all individuals with VLCAD deficiency or confirming carrier status, as biochemical findings may normalize during periods of good metabolic control. It is uncertain whether skin fibroblast analysis can identify carriers of VLCAD deficiency. The diagnosis is confirmed by molecular testing.

Mutations in the *ACADVL* gene are responsible for VLCAD deficiency. Most mutations are family specific with the exception of the *V283A* mutation (also reported in the literature as *V243A*). This mutation is estimated to account for 20% of pathogenic alleles in patients identified by newborn screening. When this test is ordered, results of biochemical assays should be included with the specimen as they are necessary for accurate interpretation of the VLCAD sequence analysis.

### Reference Values

An interpretive report will be provided.

## Interpretation

All detected alterations are evaluated according to American College of Medical Genetics recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

## Cautions

A small percentage of individuals who are carriers or have a diagnosis of very long chain acyl-CoA dehydrogenase (VLCAD) deficiency may have a mutation that is not identified by this method (eg, large genomic deletions, promoter mutations). The absence of a mutation, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of VLCAD deficiency. For carrier testing, it is important to first document the presence of an *ACADVL* gene mutation in an affected family member.

In some cases, DNA alterations of undetermined significance may be identified.

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete.

## Clinical Reference

1. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med* 2015 May;17(5):405-424
2. Andresen BS, Olpin S, Poorthuis BJ, et al: Clear correlation of genotype with disease phenotype in very-long-chain acyl-CoA dehydrogenase deficiency. *Am J Hum Genet* 1999;64:479-494
3. Liebig M, Schymik I, Mueller M, et al: Neonatal screening for very long-chain acyl-CoA dehydrogenase deficiency: enzymatic and molecular evaluation of neonates with elevated C14:1-carnitine levels. *Pediatrics* 2006;118:1065-1069

## Performance

### Method Description

Bidirectional sequence analysis is performed to test for the presence of a mutation in all coding regions and intron/exon boundaries of the *ACADVL* gene.(Unpublished Mayo method)

### PDF Report

No

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

Performed weekly; Varies

### Analytic Time

14 days

### Maximum Laboratory Time

20 days

**Specimen Retention Time**

Whole blood-2 weeks (if available) Extracted DNA-3 months

**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 was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

**CPT Code Information**

81406-ACADV (acyl-CoA dehydrogenase, very long chain) (eg, very long chain acyl-coenzyme A dehydrogenase deficiency), full gene sequence

**LOINC® Information**

Test ID	Test Order Name	Order LOINC Value
VLCZ	VLCAD Deficiency Full Gene Analysis	73735-3

Result ID	Test Result Name	Result LOINC Value
54041	Result Summary	50397-9
54042	Result	82939-0
54043	Interpretation	69047-9
54044	Additional Information	48767-8
54045	Specimen	31208-2
54046	Source	31208-2
54047	Released By	18771-6