

## Overview

### Useful For

Confirmation of diagnosis of medium-chain acyl-CoA dehydrogenase (MCAD) deficiency (as a follow-up to biochemical analyses)

Screening of at-risk carriers of MCAD deficiency when an affected relative has not had molecular testing

Diagnosis of MCAD deficiency in autopsy specimens

### Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No

### Testing Algorithm

For skin biopsy or cultured fibroblast specimens, fibroblast culture testing will be performed at an additional charge. If viable cells are not obtained, the client will be notified.

### 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 \(PCR\) Amplification/DNA Sequencing](#)

### NY State Available

Yes

## Specimen

### Specimen Type

Varies

## Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

## Specimen Required

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

### Submit only 1 of the following specimens:

#### Preferred:

**Specimen Type:** Whole blood

#### Container/Tube:

**Preferred:** Lavender top (EDTA) or yellow top (ACD)

**Acceptable:** Any anticoagulant

**Specimen Volume:** 3 mL

#### Collection Instructions:

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

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

**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)

**Additional Information:** A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks is required to culture fibroblasts before genetic testing can occur.

**Specimen Type:** Skin biopsy

**Container/Tube:** Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin. Tubes can be supplied upon request (Eagle's minimum essential medium with 1% penicillin and streptomycin [T115]).

**Specimen Volume:** 4-mm punch

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

**Additional Information:** A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks is required to culture fibroblasts before genetic testing can occur.

**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

**Specimen Volume:** 2 to 5 Blood spots

#### Collection Instructions:

1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions,

see [How to Collect Dried Blood Spot Samples](#).

2. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 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. Due to lower concentration of DNA yielded from blood spot, it is possible that additional specimen may be required to complete testing.
2. For collection instructions, see [Blood Spot Collection Instructions](#)
3. For collection instructions in Spanish, see [Blood Spot Collection Card-Spanish Instructions](#) (T777)
4. For collection instructions in Chinese, see [Blood Spot Collection Card-Chinese Instructions](#) (T800)

**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:
  - [Informed Consent for Genetic Testing](#) (T576)
  - [Informed Consent for Genetic Testing-Spanish](#) (T826)
2. [Molecular Genetics: Biochemical Disorders Patient Information](#) (T527)
3. If not ordering electronically, complete, print, and send a [Biochemical Genetics Test Request](#) (T798) with the specimen.

**Specimen Minimum Volume**

Blood: 1 mL  
 Blood Spots: 5 punches, 3-mm diameter  
 All other specimen types: See Specimen Required

**Reject Due To**

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

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

**Clinical & Interpretive**

**Clinical Information**

Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency is an autosomal recessive inherited defect in the mitochondrial oxidation of fatty acids. The mitochondrial beta-oxidation pathway plays a major role in energy production, especially during periods of fasting and physical exertion. MCAD deficiency is prevalent among individuals of northern European origin, affecting 1 in 4900 to 1 in 17,000 individuals, with a carrier frequency estimated as high as 1 in 40 for some populations.

Phenotypic expression of MCAD deficiency is episodic in nature (ie, asymptomatic between attacks). Symptoms are typically precipitated by any stress (eg, fever, infection, vaccination) and mostly occur during the first 2 years of life, although some cases have been diagnosed in adulthood. Characteristic features of MCAD deficiency include: Reye-like syndrome (an acquired encephalopathy characterized by recurrent vomiting, agitation, and lethargy), fasting intolerance with vomiting, recurrent episodes of hypoglycemic coma, hypoketotic dicarboxylic aciduria, low plasma and tissue levels of carnitine, hepatic failure with fat infiltration (fatty liver), encephalopathy, and rapidly progressive deterioration leading to death. MCAD deficiency has also been associated with sudden infant death or sudden unexpected death syndrome.

Review of clinical features and biochemical analysis via plasma acylcarnitines (ACRN / Acylcarnitines, Quantitative, Plasma), fatty acid profile (FAO / Fatty Acid Oxidation Probe Assay, Fibroblast Culture), urine organic acids (OAU / Organic Acids Screen, Random, Urine), and urine acylglycines (ACYLG / Acylglycines, Quantitative, Urine) are always recommended as the initial evaluation for MCAD. If previously performed, the results of these biochemical assays should be included with the specimen as they are necessary for accurate interpretation of the MCAD sequence analysis.

The MCAD gene (*ACADM*) maps to 1p31 and has 12 exons, spanning 44 kb of DNA. Most variants are family-specific with the exception of the recurrent A->G transition at nucleotide 985 (985A->G). Among MCAD-deficient patients, approximately 52% are homozygous for the 985A->G pathogenic variant. The majority of the remaining patients are compound heterozygous for the 985A->G pathogenic variant and a different pathogenic variant.

## Reference Values

An interpretive report will be provided.

## Interpretation

All detected alterations are evaluated according to American College of Medical Genetics recommendations.<sup>(1)</sup> 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 medium-chain acyl-CoA dehydrogenase (MCAD) deficiency may have a variant that is not identified by this method (eg, large genomic deletions, promoter variants). The absence of a variant, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of MCAD. For carrier testing, it is important to first document the presence of an *ACADM* gene variant in an affected family member.

In some cases, DNA variants 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;17(5):405-424

2. Grosse SD, Khoury MJ, Greene CL, et al. The epidemiology of medium chain acyl-CoA dehydrogenase deficiency: An update. Genet Med. 2006;8(4):205-212

2. Ziadeh R, Hoffman EP, Finegold DM, et al. Medium chain acyl-CoA dehydrogenase deficiency in Pennsylvania: neonatal screening shows high incidence and unexpected mutation frequency. Pediatr Res. 1995;37(5):675-678

3. Roe CR, Coates PM: Mitochondrial fatty acid oxidation. In Scriver CR, Beaudet AL, Sly WS, eds. The Metabolic and Molecular Bases of Inherited Disease. Vol 1. 7th ed. McGraw-Hill Book Company, 1995:1501-1533

## Performance

### Method Description

Bidirectional sequence analysis is performed to test for the presence of a sequence variant in all coding regions and intron/exon boundaries of the medium-chain acyl-CoA dehydrogenase (MCAD) gene (*ACADM*). (Highsmith WE: Unpublished Mayo information)

### PDF Report

No

### Day(s) Performed

Varies

### Report Available

14 to 20 days

### Specimen Retention Time

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

### Performing Laboratory Location

Rochester

## 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 was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

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**CPT Code Information**

81479-Unlisted molecular pathology procedure  
88233-Tissue culture, skin or solid tissue biopsy (if appropriate)  
88240-Cryopreservation (if appropriate)

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
MCADZ	MCAD Deficiency, Full Gene Analysis	95773-8

Result ID	Test Result Name	Result LOINC® Value
53971	Result Summary	50397-9
53972	Result	82939-0
53973	Interpretation	69047-9
53974	Additional Information	48767-8
53975	Specimen	31208-2
53976	Source	31208-2
53977	Released By	18771-6