

Overview

Useful For

Providing a genetic evaluation for patients with a personal or family history of congenital heart disease

Establishing a diagnosis of a genetic condition associated with congenital heart disease

Reflex Tests

| Test Id | Reporting Name | Available Separately | Always Performed |
|---------|---------------------------------------|----------------------|------------------|
| CULFB | Fibroblast Culture for Genetic Test | Yes | No |
| CULAF | Amniotic Fluid Culture/Genetic Test | Yes | No |
| MATCC | Maternal Cell Contamination, B | Yes | No |
| _STR1 | Comp Analysis using STR (Bill only) | No, (Bill only) | No |
| _STR2 | Add'l comp analysis w/STR (Bill Only) | No, (Bill only) | No |

Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in 44 genes associated with isolated and syndromic congenital heart disease: *ACTB, ACTG1, BRAF, CBL, CHD7, CITED2, ELN, FOXF1, FOXH1, GATA4, GATA5, GATA6, GDF1, HRAS, JAG1, KRAS, LZTR1, MAP2K1, MAP2K2, MRAS, MYH11, NKX2-5, NKX2-6, NODAL, NOTCH1, NOTCH2, NR2F2, NRAS, PLD1, PPP1CB, PTPN11, RAF1, RIT1, RRAS2, SHOC2, SMAD6, SOS1, SOS2, TAB2, TBX1, TBX20, TBX5, TFAP2B, and ZIC3*. See [Targeted Genes and Methodology Details for Congenital Heart Disease Gene Panel](#) and Method Description for additional details.

Identification of a disease-causing variant may assist with diagnosis, prognosis, clinical management, familial screening, and genetic counseling for congenital heart disease.

[Prior Authorization](#) is available for this assay.

Testing Algorithm

For prenatal specimens only:

- If amniotic fluid (nonconfluent cultured cells) is received, amniotic fluid culture will be added at an additional charge.
- If chorionic villus specimen (nonconfluent cultured cells) is received, fibroblast culture will be added at an additional charge.

For any prenatal specimen that is received, maternal cell contamination testing will be performed at an additional charge.

Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)
- [Congenital Heart Disease Genetic Testing Patient Information](#)
- [Targeted Genes and Methodology Details for Congenital Heart Disease Gene Panel](#)
- [Congenital Heart Disease Gene Panel \(CHDGG\) Prior Authorization Ordering Instructions](#)

Method Name

Sequence Capture and Targeted Next-Generation Sequencing followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

Chromosomal microarray is often used as a first-tier test in the setting of congenital heart disease. If chromosomal microarray testing is desired, order either CMACB / Chromosomal Microarray, Congenital, Blood or CMAP / Chromosomal Microarray, Prenatal, Amniotic Fluid/Chorionic Villus Sampling.

Customization of this panel and single gene analysis for any gene present on this panel are available. For more information see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies.

Targeted testing for familial variants (also called site-specific or known mutations testing) is available for the genes on this panel. See FMTT / Familial Variant, Targeted Testing, Varies. To obtain more information about this testing option, call 800-533-1710.

Additional Testing Requirements

All prenatal specimens must be accompanied by a maternal blood specimen; order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen as this must be a different order number than the prenatal specimen.

Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

Necessary Information

[Prior Authorization](#) is available, **but not required**, for this test. If proceeding with the prior authorization process, submit the required form with the specimen.

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:

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

Due to its complexity, consultation with the laboratory is required for all prenatal testing; call 800-533-1710 to speak to a genetic counselor.

Specimen Type: Amniotic fluid

Container/Tube: Amniotic fluid container

Specimen Volume: 20 mL

Specimen Stability Information: Refrigerated (preferred)/Ambient

Additional information:

1. If amniotic fluid or nonconfluent cultures are received, CULAF / Culture for Genetic Testing, Amniotic Fluid will be added at an additional charge.
2. **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Specimen Type: Chorionic villi

Container/Tube: 15-mL tube containing 15 mL of transport media

Specimen Volume: 20 mg

Specimen Stability Information: Refrigerated

Additional Information:

1. If nonconfluent cultures are received, CULFB / Fibroblast Culture for Biochemical or Molecular Testing will be added at an additional charge.
2. **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Acceptable:

Specimen Type: Confluent cultured cells

Container/Tube: T-25 flask

Specimen Volume: 2 Flasks

Collection Instructions: Submit confluent cultured cells from another laboratory.

Specimen Stability Information: Ambient (preferred)/Refrigerated

Additional Information: **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

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. [Congenital Heart Disease Genetic Testing Patient Information](#)

3. [Congenital Heart Disease Gene Panel \(CHDGG\) Prior Authorization Ordering Instructions](#)

4. If not ordering electronically, complete, print, and send a [Cardiovascular Test Request \(T724\)](#) with the specimen.

Specimen Minimum Volume

Blood: 1 mL; 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

Congenital heart disease/defects (CHD/CHD) is a general term used to describe one or more problems with the heart's structure that exist at birth. CHD represent the most common birth defects in humans, with approximately 1% of births affected. CHD may involve one or more structures of the heart, including chambers, valves, arteries and veins, and may be isolated (nonsyndromic) or part of a systemic condition involving additional congenital anomalies (syndromic).

In the absence of an identifiable environmental or teratogenic cause, most CHD are considered multifactorial and do not have a genetic cause identified. However, it is estimated that a genetic etiology can be determined in around 20% to 30% of CHD cases, with increased likelihood of diagnostic findings in individuals with extracardiac anomalies and/or dysmorphic features. When an underlying genetic cause is detected, it is most often due to chromosomal copy-number variants, followed by aneuploidy, then single-gene variants.(1) For this reason, chromosomal microarray analysis is often used as the first-tier test for individuals with CHD, followed by single- or multi-gene panel analysis, depending on the cardiac lesion, presence or absence of extra-cardiac features, and family history.

This panel includes genes associated with both isolated CHD as well as syndromic conditions commonly involving CHD, such as Noonan syndrome and related disorders, CHARGE syndrome (coloboma, heart defects, atresia choanae [also known as choanal atresia], growth retardation, genital abnormalities, and ear abnormalities), Holt-Oram syndrome, and Alagille syndrome.

Confirmation of the genetic cause of CHD may inform further screening or surveillance strategies, as well as genetic counseling for the family.

Reference Values

An interpretive report will be provided

Interpretation

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.⁽²⁾ Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

Clinical Correlations:

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

If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.

To discuss the availability of additional testing options or for assistance in the interpretation of these results, contact the Mayo Clinic Laboratories genetic counselors at 800-533-1710.

Technical Limitations:

Next-generation sequencing may not detect all types of genomic variants. In rare cases, false-negative or false-positive results may occur. The depth of coverage may be variable for some target regions; assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine content, and repetitive sequences. Confirmation of select reportable variants will be performed by alternate methodologies based on internal laboratory criteria.

This test is validated to detect 95% of deletions up to 75 base pairs (bp) and insertions up to 47 bp. Deletions-insertions (delins) of 40 or more bp, including mobile element insertions, may be less reliably detected than smaller delins.

Deletion/Duplication Analysis:

This analysis targets single and multi-exon deletions/duplications; however, in some instances single exon resolution cannot be achieved due to isolated reduction in sequence coverage or inherent genomic complexity. Balanced structural rearrangements (such as translocations and inversions) may not be detected.

This test is not designed to detect low levels of mosaicism or to differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.

Genes may be added or removed based on updated clinical relevance. Refer to the [Targeted Genes and Methodology Details for Congenital Heart Disease Gene Panel](#) for the most up to date list of genes included in this test. For detailed

information regarding gene specific performance and technical limitations, see Method Description or contact a laboratory genetic counselor.

If the patient has had an allogeneic hematopoietic stem cell transplant or a recent blood transfusion, results may be inaccurate due to the presence of donor DNA. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

Reclassification of Variants:

At this time, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages healthcare providers to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time.

Variant Evaluation:

Evaluation and categorization of variants are performed using published American College of Medical Genetics and Genomics and the Association for Molecular Pathology recommendations as a guideline.(2) Other gene-specific guidelines may also be considered. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Variants classified as benign or likely benign are not reported.

Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and periodic updates to these tools may cause predictions to change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgment.

Rarely, incidental or secondary findings may implicate another predisposition or presence of active disease. Incidental findings may include, but are not limited to, results related to the sex chromosomes. These findings will be carefully reviewed to determine whether they will be reported.

Clinical Reference

1. Ison HE, Griffin EL, Parrott A, et al: Genetic counseling for congenital heart disease-Practice resource of the National Society of Genetic Counselors. *J Genet Couns.* 2022 Feb;31(1):9-33
2. 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

Performance**Method Description**

Next-generation sequencing (NGS) and/or Sanger sequencing is performed to test for the presence of variants in coding regions and intron/exon boundaries of the genes analyzed, as well as some other regions that have known disease-causing variants. The human genome reference GRCh37/hg19 build was used for sequence read alignment. At least 99% of the bases are covered at a read depth over 30X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for deletions-insertions (delins) less than 40 base pairs (bp), above 95% for deletions up to 75 bp

and insertions up to 47 bp. NGS and/or a polymerase chain reaction-based quantitative method is performed to test for the presence of deletions and duplications in the genes analyzed.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. See [Targeted Genes and Methodology Details for Congenital Heart Disease Gene Panel](#) for details regarding the targeted genes analyzed for each test and specific gene regions not routinely covered. (Unpublished Mayo method)

Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

Genes analyzed: *ACTB, ACTG1, BRAF, CBL, CHD7, CITED2, ELN, FOXF1, FOXH1, GATA4, GATA5, GATA6, GDF1, HRAS, JAG1, KRAS, LZTR1, MAP2K1, MAP2K2, MRAS, MYH11, NKX2-5, NKX2-6, NODAL, NOTCH1, NOTCH2, NR2F2, NRAS, PLD1, PPP1CB, PTPN11, RAF1, RIT1, RRAS2, SHOC2, SMAD6, SOS1, SOS2, TAB2, TBX1, TBX20, TBX5, TFAP2B, and ZIC3*

PDF Report

Supplemental

Day(s) Performed

Varies

Report Available

28 to 42 days

Specimen Retention Time

Whole blood: 2 weeks (if available); Extracted DNA: 3 months; Cord blood, amniotic fluid, cultured amniocytes, chorionic villi, cultured chorionic villi: 1 month

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.

CPT Code Information

- 81404
- 81405 x 3
- 81406 x 6
- 81407 x 3
- 81408
- 81479
- 81479 (if appropriate for government payers)
- 81265-Maternal cell contamination (if appropriate)
- 88233-Tissue culture, skin, solid tissue biopsy (if appropriate)
- 88235-Amniotic Fluid culture (if appropriate)
- 88240-Cryopreservation (if appropriate)

Prior Authorization

Insurance preauthorization is available for this testing; forms are available.

Patient financial assistance may be available to those who qualify. Patients who receive a bill from Mayo Clinic Laboratories will receive information on eligibility and how to apply.

LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---------|-------------------------------------|--------------------|
| CHDGG | Congenital Heart Disease Gene Panel | 51966-0 |

| Result ID | Test Result Name | Result LOINC® Value |
|-----------|------------------------|---------------------|
| 617198 | Test Description | 62364-5 |
| 617199 | Specimen | 31208-2 |
| 617200 | Source | 31208-2 |
| 617201 | Result Summary | 50397-9 |
| 617202 | Result | 82939-0 |
| 617203 | Interpretation | 69047-9 |
| 617204 | Additional Results | 82939-0 |
| 617205 | Resources | 99622-3 |
| 617206 | Additional Information | 48767-8 |
| 617207 | Method | 85069-3 |
| 617208 | Genes Analyzed | 48018-6 |
| 617209 | Disclaimer | 62364-5 |
| 617210 | Released By | 18771-6 |