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MAYO CLINIC LABORATORIES

# Test Definition: CFTRN

Cystic Fibrosis Transmembrane Conductance Regulator, CFTR, Full Gene Analysis, Varies

## Overview

### Useful For

Carrier screening for cystic fibrosis

Follow-up testing to identify variants in individuals with a clinical diagnosis of cystic fibrosis (CF)

Identifying genetic variants in individuals with atypical presentations of CF (eg, congenital bilateral absence of the vas deferens or pancreatitis)

Identifying genetic variants in individuals where detection rates by targeted variant analysis are low or unknown for their ancestral background

Identifying patients who may respond to cystic fibrosis transmembrane conductance regulator (*CFTR*) potentiator therapy

### Reflex Tests

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

### Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in the *CFTR* gene associated with cystic fibrosis (CF).

Identification of a disease-causing variant may assist with diagnosis, prognosis, clinical management, recurrence risk assessment, familial screening, and genetic counseling for CF.

### Testing Algorithm

**Prenatal specimens:**

If an amniotic fluid specimen or cultured amniocytes are received, an amniotic fluid culture will be performed at an additional charge.

If a chorionic villi specimen or cultured chorionic villi are received, a fibroblast culture will be performed at an additional

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

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

**Cord blood:**
For cord blood specimens that have an accompanying maternal blood specimen, maternal cell contamination studies will be performed at an additional charge.

### Special Instructions

- Molecular Genetics: Congenital Inherited Diseases Patient Information
- Informed Consent for Genetic Testing
- Informed Consent for Genetic Testing (Spanish)

### Method Name

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

### NY State Available

Yes

## Specimen

### Specimen Type

Varies

### Ordering Guidance

This gene is available to be added to a custom panel. For more information see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies. To modify this panel via CGPH, use the Inborn Errors of Immunity/Bone Marrow Failure/Telomeropathy/Pulmonary Fibrosis/Very Early Onset IBD/Pancreatitis disease state for step 1 on the Custom Gene Ordering Tool.

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

### Specimen Required

**Patient Preparation:** A previous hematopoietic stem cell transplant from an allogenic donor will interfere with testing. For information about testing patients who have received a hematopoietic stem cell 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:** Green top (sodium heparin)
**Specimen Volume:** 3 mL
**Collection Instructions**:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
3. Whole blood collected postnatal from an umbilical cord is also acceptable. See Additional Information
**Specimen Stability Information:** Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days
**Additional Information:**
1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA are met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
3. For postnatal umbilical cord whole blood specimens, maternal cell contamination studies are recommended to ensure test results reflect that of the patient tested. A maternal blood specimen is required to complete maternal cell contamination studies. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the cord blood and maternal blood specimens under separate order numbers.

**Specimen Type**: Saliva
**Patient Preparation:** Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.
**Supplies:**
DNA Saliva Kit High Yield (T1007)
Saliva Swab Collection Kit (T786)
**Container/Tube:**
**Preferred**: High-yield DNA saliva kit
**Acceptable**: Saliva swab
**Specimen Volume**: 1 Tube if using T1007 or 2 swabs if using T786
**Collection Instructions:** Collect and send specimen per kit instructions.
**Specimen Stability Information:** Ambient (preferred) 30 days/Refrigerated 30 days
**Additional Information:** Saliva specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from saliva, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

**Specimen Type**: Blood spot
**Supplies**: Card-Blood Spot Collection (Filter Paper) (T493)
**Container/Tube**:
**Preferred**: Collection card (Whatman Protein Saver 903 Paper)
**Acceptable**: PerkinElmer 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 a Dried Blood Spot Sample.
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. Blood spot specimens are acceptable but not recommended. Multiple extractions will be required to obtain sufficient yield for supplemental analysis, and there is significant risk for test failure due to insufficient DNA.
2. Due to lower concentration of DNA yielded from blood spot, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.
3. For collection instructions, see Blood Spot Collection Instructions
4. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777)
5. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800)

**Specimen Type:** Skin biopsy
**Supplies:** Fibroblast Biopsy Transport Media (T115)
**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.
**Specimen Volume:** 4-mm Punch
**Specimen Stability Information:** Ambient (preferred) <24 hours/Refrigerated <24 hours
**Additional Information:**
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

**Specimen Type**: Cultured fibroblasts
**Source**: Skin or tissue
**Container/Tube**: T-25 flask
**Specimen Volume**: 2 Flasks
**Collection Instructions**: Submit confluent cultured fibroblast cells from a skin or tissue biopsy. Cultured cells from a prenatal specimen will not be accepted.
**Specimen Stability Information**: Ambient (preferred) <24 hours/Refrigerated <24 hours
**Additional Information**:
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

**Specimen Type**: Extracted DNA
**Container/Tube**:
**Preferred**: Screw Cap Micro Tube, 2 mL with skirted conical base
**Acceptable**: Matrix tube, 1 mL
**Collection Instructions**:
1. The preferred volume is at least 100 mcL at a concentration of 75 ng/mcL.
2. Include concentration and volume on tube.
**Specimen Stability Information**: Frozen (preferred) 1 year/Ambient/Refrigerated
**Additional Information**: DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

**Prenatal Specimens**
**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**: Ambient (preferred) <24 hours/Refrigerated <24 hours
**Additional Information**: Specimen will only be tested after culture.
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULAF / Culture for Genetic Testing, Amniotic Fluid. An additional 2 to 3 weeks are required to culture amniotic fluid before genetic testing can occur.
3. **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**: Confluent cultured amniocytes
This does not include cultured chorionic villi.
**Container/Tube**: T-25 flask
**Specimen Volume**: 2 Full flasks
**Collection Instructions**: Submit confluent cultured amniocytes from another laboratory.
**Specimen Stability Information**: Ambient (preferred) <24 hours/Refrigerated <24 hours
**Additional Information**:
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing.
3. **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**: Ambient (preferred) <24 hours/Refrigerated <24 hours
**Additional Information**: Specimen will only be tested after culture.
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.
3. **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**: Cultured chorionic villi
**Container/Tube**: T-25 flasks
**Specimen Volume**: 2 Full flasks
**Collection Instructions**: Submit confluent cultured cells from another laboratory.
**Specimen Stability Information**: Ambient (preferred) <24 hours/Refrigerated <24 hours
**Additional Information**:
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing.
3. **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. Molecular Genetics: Congenital Inherited Diseases Patient Information (T521)

## 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

Cystic fibrosis (CF), in the classic form, is a severe autosomal recessive disorder characterized by a varying degree of

chronic obstructive lung disease and pancreatic enzyme insufficiency.(1) Clinical diagnosis is generally made based on these features, combined with a positive sweat chloride test or positive nasal potential difference.(1) CF can also have an atypical presentation (*CFTR*-related disorder [CFRD] or *CFTR*-related metabolic syndrome [CRMS]) and may manifest solely as congenital absence of the vas deferens or chronic idiopathic pancreatitis.(2) Several states have implemented newborn screening for CF, which identifies potentially affected individuals by measuring immunoreactive trypsinogen in a dried blood specimen collected on filter paper.(3)

To date, over 2000 variants have been described within the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene that can cause CF.(3) The most common variant, deltaF508, accounts for approximately 67% of the variants worldwide and approximately 70% to 75% in the North American White population.(4) Most of the remaining variants are rare, although some show a relatively higher prevalence in certain ancestries or in some atypical presentations of CF, such as CFRD or CRMS.

If a clinical diagnosis of CF has been made or is suspected, full gene analysis of the *CFTR* gene may be utilized to genetically confirm the diagnosis. Full gene and deletion/duplication analysis of the *CFTR* gene can identify over 98% of the sequence variants in the coding region and splice junctions.

Of note, *CFTR* potentiator therapies may improve clinical outcomes for patients with a clinical diagnosis of CF and at least one copy of a select subset of variants.(3)

### Reference Values

An interpretive report will be provided

### Interpretation

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.(5) 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 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 (GC) 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.

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.

Deletion/duplication events that extend past the genes included on the panel may occur. In these instances, genes included in the ordered test are provided on the report and interpreted, and genomic breakpoints are reported if they are confirmed. However, copy number variants for genes not listed in the Method Description are typically not reported or interpreted for haploinsufficiency/triplosensitivity. CMACB / Chromosomal Microarray, Congenital, Blood; WESPR / Panel to Whole Exome Sequencing Reflex Test, Varies; or WGSDX / Whole Genome Sequencing for Hereditary Disorders, Varies is recommended for a full interpretation of deletions/duplications predicted to extend past the genes included on the panel.

This test is not designed to detect low levels of mosaicism or to differentiate between somatic mutations 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.

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 non-leukocyte-reduced 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**:**
Currently, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages health care professionals to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time. Due to broadening genetic knowledge, it is possible that the laboratory may discover new information of relevance to the patient. Should that occur, the laboratory may issue an amended report.

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.(5) 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. These findings will be carefully reviewed to determine whether they will be reported.

### Clinical Reference

1. Savant A, Lyman B, Bojanowski C, et al. Cystic fibrosis. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 1993-2025. Updated August 8, 2024. Accessed December 22, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK1250/
2. Bombieri C, Claustres M, De Boeck K, et al. Recommendations for the classification of diseases as CFTR-related disorders. J Cyst Fibros. 2011;10 Suppl 2:S86-S102
3. Link SL, Nayak RP. Review of rapid advances in cystic fibrosis. Mo Med. 2020;117(6):548-554
4. Bobadilla JL, Macek M Jr, Fine JP, Farrell PM. Cystic fibrosis: a worldwide analysis of CFTR mutations--correlation with incidence data and application to screening. Hum Mutat. 2002;19(6):575-606
5. Richards S, Aziz N, Bale S, et al. ACMG Laboratory Quality Assurance Committee: 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

## Performance

### Method Description

Next-generation sequencing (NGS) and/or Sanger sequencing are performed to test for the presence of variants in coding regions and intron/exon boundaries of the *CFTR* gene, 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), and 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 *CFTR* gene.

There may be regions of *CFTR* 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.(Unpublished Mayo method)

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

Reference transcript numbers may be updated due to transcript re-versioning. Always refer to the final patient report for gene transcript information referenced at the time of testing.

| Gene symbol | Reference transcript | Additional evaluations | Technical limitations |
|---|---|---|---|
| *CFTR* | NM_000492.4 | Poly T tract<br>TG repeat region for 5T alleles only<br>deletion/duplication analysis<br>c.870-1113_870-1110del<br>c.1393-18G>A<br>c.1585-9T>A<br>c.1585-8G>A<br>c.1585-9412A>G<br>c.1680-886A>G<br>c.1680-883A>G<br>c.1680-877G>T<br>c.2909-15T>G<br>c.2989-313A>T<br>c.3140-26A>G<br>c.3140-16T>A<br>c.3469-1304C>G<br>c.3717+40A>G<br>c.3718-2477C>T<br>c.3874-4522A>G | Copy number variation analysis in exon 13 is not performed |

### PDF Report
No

### Day(s) Performed
Varies

### Report Available
21 to 28 days

### Specimen Retention Time
Whole blood: 25 days (if available); Extracted DNA: 3 months, Saliva: 30 days (if available); Blood Spots: 1 year (if available)

### Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

## 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

81223
88233- Tissue culture, skin, solid tissue biopsy (if appropriate)
88240- Cryopreservation (if appropriate)

## LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| CFTRN | CFTR Gene, Full Gene Analysis | 90256-9 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 619775 | Test Description | 62364-5 |
| 619776 | Specimen | 31208-2 |
| 619777 | Source | 31208-2 |
| 619778 | Result Summary | 50397-9 |
| 619779 | Result | 82939-0 |
| 619780 | Interpretation | 69047-9 |
| 619781 | Additional Results | 82939-0 |
| 619782 | Resources | 99622-3 |
| 619783 | Additional Information | 48767-8 |
| 619784 | Method | 85069-3 |
| 619785 | Genes Analyzed | 82939-0 |
| 619786 | Disclaimer | 62364-5 |
| 619787 | Released By | 18771-6 |