

## Overview

### Useful For

Providing a genetic evaluation for patients with a personal or family history suggestive of primary ciliary dyskinesia

Establishing a diagnosis of primary ciliary dyskinesia

### Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in 40 genes associated with primary ciliary dyskinesia (PCD): *CCDC103*, *CCDC114 (ODAD1)*, *CCDC151 (ODAD3)*, *CCDC39*, *CCDC40*, *CCDC65*, *CCNO*, *CFAP298*, *CFAP300*, *DNAAF1*, *DNAAF2*, *DNAAF3*, *DNAAF4*, *DNAAF5*, *DNAH1*, *DNAH11*, *DNAH5*, *DNAH8*, *DNAH9*, *DNAI1*, *DNAI2*, *DNAJB13*, *DNAL1*, *DRC1*, *FOXJ1*, *GAS8*, *LRRC6 (DNAAF11)*, *MCIDAS*, *ODAD2(ARMC4)*, *OFD1*, *PIH1D3 (DNAAF6)*, *RPGR*, *RSPH1*, *RSPH3*, *RSPH4A*, *RSPH9*, *SPAG1*, *TTC25 (ODAD4)*, and *ZMYND10*. See [Targeted Genes and Methodology Details for Primary Ciliary Dyskinesia 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 PCD.

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

### Special Instructions

- [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](#)
- [Primary Ciliary Dyskinesia Genetic Testing Patient Information](#)
- [Targeted Genes and Methodology Details for Primary Ciliary Dyskinesia Gene Panel](#)
- [Primary Ciliary Dyskinesia Gene Panel \(PCDGG\) 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

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**Ordering Guidance**

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 Mutation, Targeted Testing, Varies](#). To obtain more information about this testing option, call 800-533-1710.

**Shipping Instructions**

Specimen preferred to arrive within 96 hours of collection.

**Necessary Information**

[Prior Authorization](#) is available for this test. **Submit the required form with the specimen.**

**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.

**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

**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. [Primary Ciliary Dyskinesia Genetic Testing Patient Information](#)

3. [Primary Ciliary Dyskinesia Gene Panel \(PCDGG\) Prior Authorization Ordering Instructions](#)

**Specimen Minimum Volume**

[1 mL](#)

**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		

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## Clinical & Interpretive

### Clinical Information

Primary ciliary dyskinesia (PCD) is a condition characterized by motile ciliary dysfunction due to structural or biogenesis defects of the cilia.(1,2) The primary clinical manifestation of PCD is chronic upper and lower respiratory disease (including neonatal respiratory distress, chronic cough, chronic nasal congestion, chronic pansinusitis, recurrent pulmonary infections, and bronchiectasis) leading to respiratory failure.(1-3) Other common features of PCD include laterality (situs) defects and infertility.(1-3) When laterality defects are present in addition to respiratory manifestations, the condition may be described as Kartagener syndrome.(4)

Diagnostic workup for suspected PCD can include ciliary ultrastructure analysis via transmission electron microscopy, high-speed video microscopy with ciliary beat pattern analysis, nasal nitric oxide level measurement, immunofluorescence imaging of axonemal proteins, and molecular genetic testing.(1,2) Genetic testing can be diagnostic when other analyses have normal or ambiguous results.(2)

The prevalence of PCD is not established and estimates of prevalence have ranged from 1:2200 to 1:40,000 births.(4) In individuals with well-supported PCD diagnoses via clinical and ciliary analyses, it is estimate that a genetic etiology can be identified in up to 80% of cases.(3) In most cases, PCD follows an autosomal recessive pattern of inheritance. Rarely, PCD can follow an autosomal dominant or X-linked pattern of inheritance.

### 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 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 Primary Ciliary Dyskinesia Gene Panel](#) or 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.<sup>(5)</sup> 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. Shapiro AJ, Davis SD, Polineni D, et al. Diagnosis of primary ciliary dyskinesia. An official American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2018;197(12):e24-e39. doi: 10.1164/rccm.201805-0819ST
2. Shapiro AJ, Zariwala MA, Ferkol T, et al. Diagnosis, monitoring, and treatment of primary ciliary dyskinesia: PCD foundation consensus recommendations based on state of the art review. *Pediatr Pulmonol*. 2016;51(2):115-132. doi: 10.1002/ppul.23304
3. Zariwala MA, Knowles MR, Leigh MW. Primary ciliary dyskinesia. In: Adam MP, Ardinger HH, Pagon RA, et al., eds. *GeneReviews* [Internet]. University of Washington, Seattle; 2007. Updated December 5, 2019. Accessed August 1, 2022. Available at [www.ncbi.nlm.nih.gov/books/NBK1122/](http://www.ncbi.nlm.nih.gov/books/NBK1122/)
4. Mirra V, Werner C, Santamaria F. Primary ciliary dyskinesia: An update on clinical aspects, genetics, diagnosis, and future treatment strategies. *Front Pediatr*. 2017 Jun 9;5:135.. doi: 10.3389/fped.2017.00135
5. 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 are 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 [deletion-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 content, and repetitive sequences. See [Targeted Genes and Methodology Details for Primary Ciliary Dyskinesia 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: *CCDC103*, *CCDC114 (ODAD1)*, *CCDC151 (ODAD3)*, *CCDC39*, *CCDC40*, *CCDC65*, *CCNO*, *CFAP298*, *CFAP300*, *DNAAF1*, *DNAAF2*, *DNAAF3*, *DNAAF4*, *DNAAF5*, *DNAH1*, *DNAH11*, *DNAH5*, *DNAH8*, *DNAH9*, *DNAI1*, *DNAI2*, *DNAJB13*, *DNAL1*, *DRC1*, *FOXJ1*, *GAS8*, *LRR6 (DNAAF11)*, *MCIDAS*, *ODAD2 (ARMC4)*, *OFD1*, *PIH1D3 (DNAAF6)*, *RPGR*, *RSPH1*,

*RSPH3, RSPH4A, RSPH9, SPAG1, TTC25 (ODAD4), and ZMYND10*

## 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

## 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. This test has not been cleared or approved by the US Food and Drug Administration.

### CPT Code Information

81479

### LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PCDGG	Primary Ciliary Dyskinesia Panel	51966-0

Result ID	Test Result Name	Result LOINC® Value
617422	Test Description	62364-5
617423	Specimen	31208-2
617424	Source	31208-2
617425	Result Summary	50397-9
617426	Result	82939-0
617427	Interpretation	69047-9
617428	Additional Results	In Process

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617429	Resources	99622-3
617430	Additional Information	48767-8
617431	Method	85069-3
617432	Genes Analyzed	48018-6
617433	Disclaimer	62364-5
617434	Released By	18771-6