MAYO CLINIC LABORATORIES

# Test Definition: 2C19R

Cytochrome P450 2C19 Genotype, Varies

## Overview

### Useful For

Identifying patients who may be at risk for altered metabolism of cytochrome P450 2C19 (CYP2C19) substrate medications, including clopidogrel, citalopram, and voriconazole

### 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 |
| _STR1 | Comp Analysis using STR (Bill only) | No, (Bill only) | No |
| _STR2 | Add'l comp analysis w/STR (Bill Only) | No, (Bill only) | No |
| MATCC | Maternal Cell Contamination, B | Yes | No |

### Testing Algorithm

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

### Special Instructions

- Informed Consent for Genetic Testing
- Pharmacogenomic Association Tables
- Multiple Genotype Test List
- Informed Consent for Genetic Testing (Spanish)

### Method Name

Real-Time Polymerase Chain Reaction (PCR) with Allelic Discrimination Analysis

### NY State Available

Yes

## Specimen

### Specimen Type

Varies

## Ordering Guidance

Testing is available as the single gene assay (this test) and as a part of a psychotropic or focused pharmacogenomics panel.

If multiple pharmacogenomic genotype testing is needed, consider PGXQP / Focused Pharmacogenomics Panel, Varies.

If genotype testing for psychotropic medications is requested, order PSYQP / Psychotropic Pharmacogenomics Gene Panel, Varies.

## Specimen Required

Multiple genotype tests can be performed on a single specimen after a single extraction. See Multiple Genotype Test List for a list of tests that can be ordered together.

**Patient Preparation:** A previous hematopoietic stem cell or liver 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:** Lavender top (EDTA)
**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**: 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.

## 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. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
-Neurology Specialty Testing Client Test Request (T732)
-Therapeutics Test Request (T831)
-Cardiovascular Test Request (T724)

## Specimen Minimum Volume

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

Primary metabolism of many drugs is performed by the cytochrome P450 (CYP) enzymes, a group of oxidative/dealkylating enzymes localized in the microsomes of many tissues including the intestines and liver. One of these CYP enzymes, CYP2C19, participates in the metabolism of a wide variety of drugs, including the activation of the anticoagulant clopidogrel and the inactivation of citalopram.

CYP2C19 drug metabolism is variable among individuals. Some individuals have *CYP2C19* genetic variants that lead to severely diminished or absent CYP2C19 catalytic activity (ie, poor metabolizers). The frequency of *CYP2C19* variants (previously known as polymorphisms) varies by ancestry. *CYP2C19* variants that result in poor metabolizers are found with frequencies of 2% to 5% in populations of European descent, 4% in populations of African descent, 13% to 23% in populations of Asian descent, and 38% to 79% in Polynesian and Micronesian populations.

The following table displays the *CYP2C19* variants detected by this assay, the corresponding star allele, and the effect on CYP2C19 enzyme activity.

Table. Enzyme Activity of Individual Star Alleles

| ***CYP2C19* allele** | **cDNA nucleotide change (NM_000769.1)** | **Effect on enzyme activity** |
|---|---|---|
| **1* | None (wild type) | Normal (extensive) activity |
| **2* | c.681G>A | No activity |
| **3* | c.636G>A | No activity |
| **4* | c.1A>G | No activity |
| **5* | c.1297C>T | No activity |
| **6* | c.395G>A | No activity |
| **7* | c.819+2T>A | No activity |
| **8* | c.358T>C | No activity |
| **9* | c.431G>A | Decreased activity |
| **10* | c.680C>T | Decreased activity |
| **17* | c.-806C>T | Enhanced activity |
| **35* | c.332-23A>G in the absence of c.681G>A | No activity |

CYP2C19 drug metabolism is dependent on the specific genotype detected and also on the number and type of drugs administered to the patient. Phenotyping is derived from the Pharmacogene Variation Consortium website,(1) the Clinical Pharmacogenetics Implementation Consortium website,(2) published guidelines,(3-8) and an exhaustive review of the CYP2C19 literature.(9-10) Individuals without a detectable *CYP2C19* variant are designated as *CYP2C19*1/*1* with a corresponding normal metabolizer (historically referred to as "extensive metabolizer") predicted phenotype. If an individual is homozygous or compound heterozygous for alleles with no activity, the individual is predicted to be a poor metabolizer. If an individual is heterozygous for an allele with no activity, the individual is predicted to be an intermediate metabolizer. Individuals with the *CYP2C19*17* allele (in the absence of any inactive or decreased activity alleles) may have enhanced metabolism of drugs (ie, rapid or ultrarapid metabolizer). In some cases, a range of potential phenotypes may be given, depending on the combination of alleles identified.

Patients with altered CYP2C19 metabolism may benefit from dose alteration or selection of a comparable drug that is not primarily metabolized by CYP2C19. It is important to interpret the results of testing in the context of other

coadministered drugs.

### Reference Values

An interpretive report will be provided.

### Interpretation

An interpretive report will be provided.

The genotype, with associated star alleles, is assigned using standard allelic nomenclature as published by the Pharmacogene Variation (PharmVar) Consortium.(1)

For additional information regarding pharmacogenomic genes and their associated drugs, see Pharmacogenomic Associations Tables. This resource also includes information regarding enzyme inhibitors and inducers, as well as potential alternate drug choices.

Drug-drug interactions and drug-metabolite inhibition must be considered when treating intermediate metabolizers. It is important to interpret the results of testing and dose adjustments in the context of hepatic and renal function and patient age.

### Cautions

Rare variants may be present that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings (phenotype), additional testing should be considered.

Samples may contain donor DNA if obtained from patients who received non-leukocyte reduced blood transfusions or allogeneic hematopoietic stem cell transplantation. Results from samples obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received non-leukocyte reduced blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. For individuals who have received allogeneic hematopoietic stem cell transplantation, a pretransplant DNA specimen is recommended for testing.

*CYP2C19* genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's *CYP2C19* status.

This method may not detect all variants that result in altered CYP2C19 activity. Therefore, absence of a detectable variant does not rule out the possibility that a patient has altered CYP2C19 metabolism due to other *CYP2C19* variants that cannot be detected with this method. Furthermore, when 2 or more variants are identified, the cis-/trans-status (whether the variants are on the same or opposite chromosomes) is not always known.

This test is designed to detect only the variants specified above. Other variants in the primer binding regions can affect testing and, ultimately, the genotype and phenotype predictions made.

### Clinical Reference

1. PharmVar: Pharmacogene Variation Consortium. Updated October 28, 2025. Accessed November 20, 2025. Available at www.pharmvar.org/
2. Clinical Pharmacogenetics Implementation Consortium (CPIC). Accessed November 20, 2025. Available at https://cpicpgx.org/
3. Lee CR, Luzum JA, Sangkuhl K, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for *CYP2C19*

genotype and clopidogrel therapy: 2022 update. Clin Pharmacol Ther. 2022;112(5):959-967. doi:10.1002/cpt.2526
4. Lima JJ, Thomas CD, Barbarino J, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2C19 and proton pump inhibitor dosing. Clin Pharmacol Ther. 2021;109(6):1417-1423. doi:10.1002/cpt.2015
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6. Bousman CA, Stevenson JM, Ramsey LB, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A genotypes and serotonin reuptake inhibitor antidepressants. Clin Pharmacol Ther. 2023;114(1):51-68. doi:10.1002/cpt.2903
7. Hicks JK, Sangkuhl K, Swen JJ, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther. 2017;102(1):37-44. doi:10.1002/cpt.597
8. Pereira NL, Cresci S, Angiolillo DJ, et al. *CYP2C19* Genetic testing for oral P2Y12 inhibitor therapy: A scientific statement from the American Heart Association. Circulation. 2024;150(6):e129-e150. doi:10.1161/CIR.0000000000001257
9. Blaisdell J, Mohrenweiser H, Jackson J, et al. Identification and functional characterization of new potentially defective alleles of human CYP2C19. Pharmacogenetics. 2002;12(9):703-711. doi:10.1097/00008571-200212000-00004
10. Mega JL, Close SL, Wiviott SD, et al. Cytochrome p-450 polymorphisms and response to clopidogrel. N Engl J Med. 2009;360(4):354-362. doi:10.1056/NEJMoa0809171

## Performance

### Method Description
Genomic DNA is extracted from whole blood or saliva. Genotyping for *CYP2C19* alleles is performed using a polymerase chain reaction (PCR)-based 5'-nuclease assay. Fluorescently labeled detection probes anneal to the target DNA. PCR is used to amplify the DNA section that contains the variant. If the detection probe is an exact match to the target DNA, the 5'-nuclease polymerase degrades the probe, the reporter dye is released from the effects of the quencher dye, and a fluorescent signal is detected. Genotypes are assigned based on the allele-specific fluorescent signals that are detected.(Unpublished Mayo method)

### PDF Report
No

### Day(s) Performed
Varies

### Report Available
2 to 4 days

### Specimen Retention Time
Whole blood: 28 days (if available); Saliva: 30 days (if available); Extracted DNA: 3 months

### 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

81225

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| 2C19R | CYP2C19 Genotype, V | 57132-3 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 610089 | CYP2C19 Genotype | 57132-3 |
| 610090 | CYP2C19 Phenotype | 79714-2 |
| 610567 | CYP2C19 Activity Score | 104667-1 |
| 610091 | Interpretation | 69047-9 |
| 610092 | Additional Information | 48767-8 |
| 610093 | Method | 85069-3 |
| 610094 | Disclaimer | 62364-5 |
| 610095 | Reviewed by | 18771-6 |