

## Overview

### Useful For

Preemptive or reactive genotyping of patients for pharmacogenomic purposes

Providing an assessment for genes with strong drug-gene associations

### Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
2D61Z	CYP2D6 Full Gene Sequence	No, (Bill Only)	No
2D62Z	CYP2D6 GEN CYP2D6-2D7 Hybrid	No, (Bill Only)	No
2D63Z	CYP2D6 GEN CYP2D7-2D6 Hybrid	No, (Bill Only)	No
2D64Z	CYP2D6 Nonduplicated Gene	No, (Bill Only)	No
2D65Z	CYP2D6 5' Gene DUP/MLT	No, (Bill Only)	No
2D66Z	CYP2D6 3' Gene DUP/MLT	No, (Bill Only)	No

### Genetics Test Information

This test includes targeted testing to evaluate the following genes:

*CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, SLCO1B1, VKORC1, CYP4F2,* and rs12777823.

*CYP2D6* testing is done in 2 tiers when needed. Tier 1 uses a polymerase chain reaction (PCR)-based 5'-nuclease assay to determine the variants present. All samples also have copy number determined by PCR-based 5'-nuclease assay. Testing in tier 1 allows for the detection of all common *CYP2D6* variants (eg, \*2, \*3, \*4, \*5, \*6, \*7, \*8, \*9, \*10, \*17, \*29, \*35, \*41, \*59) and rarer alleles such as \*11, \*12, \*14, \*15, and \*114. Duplications and multiplications of alleles are also identified. Unitary and tandem *CYP2D7-2D6* (\*13) alleles and *CYP2D6-2D7* (eg, \*4N, \*36, and \*68) alleles can also be detected. Tier 2 testing involves sequencing using fluorescent dye-terminator chemistry and is only done if an ambiguous phenotype results from tier 1 testing. Approximately 3% of samples require tier 2 testing.

### Testing Algorithm

If a specimen requires follow-up for *CYP2D6*, then reflex testing will be performed as appropriate at an additional charge.

For more information see [CYP2D6 Comprehensive Cascade Testing Algorithm](#).

### Special Instructions

- [Informed Consent for Genetic Testing](#)
- [CYP2D6 Comprehensive Cascade Testing Algorithm](#)
- [Pharmacogenomic Association Tables](#)

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- [Informed Consent for Genetic Testing \(Spanish\)](#)

## Method Name

Real Time Polymerase Chain Reaction (RT-PCR) with Allelic Discrimination Analysis/PCR followed by DNA Sequencing, when appropriate

## NY State Available

Yes

## Specimen

### Specimen Type

Varies

### Specimen Required

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.**

**Specimen Stability Information:** Ambient (preferred) 9 days/Refrigerated 30 days

**Specimen Type:** Saliva

**Patient Preparation:** Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.

**Supplies:** Saliva Swab Collection Kit (T786)

**Specimen Volume:** 1 Swab

**Collection Instructions:** Collect and send specimen per kit instructions.

**Additional Information:** Due to lower concentration of DNA yielded from saliva, testing cannot proceed to reflex testing for 2D6 sequencing and will stop after initial testing is complete.

**Specimen Stability Information:** Ambient 30 days

**Specimen Type:** Extracted DNA

**Container/Tube:** 2-mL screw top tube

**Specimen Volume:** 100 µL (microliters)

**Collection Instructions:**

1. The preferred volume is 100 µL at a concentration of 50 ng/µL.
2. Provide concentration of DNA and volume on tube.

**Specimen Stability Information:** Frozen (preferred) 1 year/Ambient/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. 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)
- [Renal Diagnostics Test Request](#) (T830)

### Specimen Minimum Volume

Whole Blood: 1 mL

Saliva, extracted DNA: 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

This panel provides a comprehensive analysis for multiple genes with strong drug phenotype associations. Each sample is tested for specific variations with known functional impact. Pharmacogenomic data for the following specific variants are reviewed and reported (if present):

- CYP1A2 \*1F, \*1K, \*6, and \*7
- CYP2C9 \*2, \*3, \*4, \*5, \*6, \*8, \*9, \*11, \*12, \*13, \*14, \*15, \*16, \*17, \*18, \*25, \*26, \*28, \*30, \*33, and \*35
- CYP2C19 \*2, \*3, \*4, \*5, \*6, \*7, \*8, \*9, \*10, \*17, and \*35
- CYP2D6 \*2, \*3, \*4, \*4N, \*5, \*6, \*7, \*8, \*9, \*10, \*11, \*12, \*13, \*14A (now known as \*114), \*14B (now known as \*14), \*15, \*17, \*29, \*35, \*36, \*41, \*59, \*68, and CYP2D6 gene duplication; additional CYP2D6 variants may be detected through the reflex testing process
- CYP3A4 \*8, \*11, \*12, \*13, \*16, \*17, \*18, \*22, and \*26
- CYP3A5 \*3, \*6, \*7, \*8, and \*9
- CYP4F2 \*3
- rs12777823G>A
- SLCO1B1 rs4149056 (\*5)
- VKORC1 c. -1639G>A, c.85G>T, c.106G>T, c.121G>T, c.134T>C, c.172A>G, c.196G>A, c.358C>T, and c.383T>G

Based on the results of each assay, a genotype is assigned, and a phenotype is predicted for each gene. Assessment of multiple genes may assist the ordering clinician with personalized drug recommendations, avoidance of adverse drug reactions, and optimization of drug treatment.

## Reference Values

An interpretive report will be provided.

## Interpretation

An interpretive report will be provided, which focuses on only drugs and genes with published pharmacogenomic practice guidance by the Clinical Pharmacogenetics Implementation Consortium, other professional organizations or where strong FDA guidance has been issued in drug labels.

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.

## Cautions

Specimens may contain donor DNA if obtained from patients who received non-leukoreduced blood transfusions or allogeneic hematopoietic stem cell transplantation. Results from specimens obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received 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. Genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's genetic status for the genes on this panel.

This test is not designed to provide specific dosing recommendations and is to be used as an aid to clinical decision making only. Results should be used along with other clinical and laboratory data. Drug-label guidance should be used when dosing patients with medications regardless of the predicted phenotype.

For additional information, see the following tests:

- 1A2Q / Cytochrome P450 1A2 Genotype, Varies
- 2C9QT / Cytochrome P450 2C9 Genotype, Varies
- 2C19R / Cytochrome P450 2C19 Genotype, Varies
- 2D6Q / Cytochrome P450 2D6 Comprehensive Cascade, Varies
- 3A4Q / Cytochrome P450 3A4 Genotype, Varies
- 3A5Q / Cytochrome P450 3A5 Genotype, Varies
- SLC1Q / Solute Carrier Organic Anion Transporter Family Member 1B1 (*SLCO1B1*) Genotype, Statin, Varies
- WARSQ / Warfarin Response Genotype, Varies

## Clinical Reference

1. Ji Y, Skierka JM, Blommel JH, et al. Preemptive pharmacogenomic testing for precision medicine: A comprehensive analysis of five actionable pharmacogenomic genes using next-generation DNA sequencing and a customized CYP2D6 genotyping cascade. *J Mol Diagn*. 2016;18(3):438-445. doi:10.1016/j.jmoldx.2016.01.003
2. Samwald M, Xu H, Blagec K, et al. Incidence of exposure of patients in the United States to multiple drugs for which pharmacogenomic guidelines are available. *PLoS One*. 2016;11(10):e0164972. doi:10.1371/journal.pone.0164972
3. Clinical Pharmacogenetic Implementation Committee (CPIC): Genes-Drugs. CPIC; Accessed October 25, 2023. Available at <https://cpicpgx.org/genes-drugs/>
4. Pharmacogenomics Knowledgebase (PharmGKB). Accessed October 25, 2023. Available at [www.pharmgkb.org/](http://www.pharmgkb.org/)
5. Crews KR, Monte AA, Huddart R, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6, OPRM1, and COMT Genotypes and Select Opioid Therapy. *Clin Pharmacol Ther*. 2021;110(4):888-896. doi:

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10.1002/cpt.2149

## Performance

### Method Description

Genomic DNA is extracted from whole blood or saliva. Genotyping for each allele 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 section of DNA 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)

#### *CYP2D6* Copy Number Assay:

This assay utilizes a duplex real-time PCR, which includes 1 copy number probe and a reference assay per reaction. Each copy number probe detects the genomic sequence of interest and the reference assay detects a sequence that is known to be present in 2 copies in a diploid genome. Relative quantitation is used to determine the relative copy number of the target of interest in a genomic DNA (gDNA) sample normalized to 10 ng/mL for each probe. Each probe is normalized to the known copy number of the reference sequence, and compared to a calibrator sample with known copies of the target sequence included with each run. (Package insert: Taqman Copy Number Assays. Applied Biosystems; Revision D, 02/2019)

#### 2D6 Sequencing Assays (Tier 2, as needed):

The *CYP2D6* allele of interest is amplified by PCR. The PCR product is then purified and sequenced in both directions using fluorescent dye-terminator chemistry. Sequencing products are separated on an automated sequencer and trace files analyzed for variations in the exons and intron/exon boundaries of all 9 exons using mutation detection software and visual inspection. (Unpublished Mayo method)

### PDF Report

Supplemental RE

### Day(s) Performed

Monday through Friday

### Report Available

3 to 14 days

### Specimen Retention Time

Whole blood/Saliva: 2 weeks; Extracted DNA: 2 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.

### CPT Code Information

- 0029U
- 0071U (if appropriate)
- 0072U (if appropriate)
- 0073U (if appropriate)
- 0074U (if appropriate)
- 0075U (if appropriate)
- 0076U (if appropriate)

### LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PGXQP	Focused Pharmacogenomics Panel, V	82118-1

Result ID	Test Result Name	Result LOINC® Value
610185	CYP1A2 Genotype	72884-0
610186	CYP1A2 Phenotype	94254-0
610187	CYP2C19 Genotype	57132-3
610188	CYP2C19 Phenotype	79714-2
610570	CYP2C19 Activity Score	104667-1
610189	CYP2C9 Genotype	46724-1
610190	CYP2C9 Phenotype	79716-7
610571	CYP2C9 Activity Score	104668-9
610191	CYP2D6 Genotype	40425-1
610192	CYP2D6 Phenotype	79715-9
610572	CYP2D6 Activity Score	104669-7
610193	CYP3A4 Genotype	81139-8
610194	CYP3A4 Phenotype	81145-5
610195	CYP3A5 Genotype	81140-6
610196	CYP3A5 Phenotype	79717-5
610197	SLCO1B1 Genotype	93412-5
610198	SLCO1B1 Phenotype	79722-5
610199	Warfarin CYP2C9 Genotype	46724-1

610201	Warfarin VKORC1 Resistance Genotype	50722-8
610200	Warfarin VKORC1 Promoter Genotype	50722-8
614000	Warfarin CYP2C9 and VKORC1 Promoter Phenotype	54451-0
610202	Warfarin CYP4F2 *3 Genotype	93197-2
610203	Warfarin rs12777823 Genotype	93198-0
610204	Interpretation	69047-9
610205	Additional Information	48767-8
610207	Disclaimer	62364-5
610208	Reviewed by	18771-6
610206	Method	85069-3