

## Overview

### Useful For

Identifying individuals with genetic variants in *DPYD* who are at increased risk of toxicity when prescribed 5-fluorouracil (5-FU) or capecitabine chemotherapy treatment

### Genetics Test Information

[This is a pharmacogenomics test associated with 5-fluorouracil and capecitabine drug sensitivity. Biallelic variation in the \*DPYD\* gene is also associated with dihydropyrimidine dehydrogenase \(DPD\) deficiency.\(1\) Individuals who have variations identified in the \*DPYD\* may benefit from genetic consultation.](#)

### Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Pharmacogenomic Associations 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

### Advisory Information

This test does not detect or report variants other than the \*2A, \*7, \*8, \*9B, \*10, \*11, \*13, rs67376798, rs75017182, and rs115232898 alleles. Sequencing of the full gene is also available for detection of additional variants as well as the alleles listed: order DPYDG / Dihydropyrimidine Dehydrogenase, *DPYD* Full Gene Sequencing, Varies.

### Specimen Required

Multiple genotype tests can be performed on a single specimen after a single extraction. See [Multiple Genotype Test List](#) in Special Instructions for a list of tests that can be ordered together.

### 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.

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2. Send specimen in original tube.

**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:** DNA Saliva Collection Kit (T786)

**Container/Tube:** Saliva Swab Collection Kit

**Specimen Volume:** 1 swab

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

**Specimen Stability Information:** Ambient 30 days

**Specimen Type:** DNA

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

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

**Collection Instructions:**

1. The preferred volume is 100 mcL at a concentration of 50 ng/mcL.
2. Include concentration and volume on tube.

**Specimen Stability Information:** Frozen (preferred)/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 in Special Instructions:

[-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:

[-Pharmacogenomics Test Request](#) (T797)

[-Therapeutics Test Request](#) (T831)

## Specimen Minimum Volume

Blood: 0.4 mL

Saliva: 1 swab

## 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 and Interpretive

#### Clinical Information

5-Fluorouracil (5-FU) and its orally administered prodrug, capecitabine, are fluoropyrimidine-based chemotherapeutic agents that are widely used for the treatment of colorectal cancer and other solid tumors.

The dihydropyrimidine dehydrogenase (*DPYD*) gene encodes the rate-limiting enzyme for fluoropyrimidine catabolism and eliminates over 80% of administered 5-FU. Dihydropyrimidine dehydrogenase (DPYD) activity is subject to wide variability, mainly due to genetic variation. This results in a broad range of enzymatic deficiency from partial (3%-5% of population) to complete loss (0.2% of population) of enzyme activity.(2,3) Patients who are deficient in DPYD are at an increased risk for side effects and toxicity when undergoing 5-FU treatment.(4) In addition, pathogenic homozygous or compound heterozygous variants within *DPYD* are associated with dihydropyrimidine dehydrogenase (DPD) deficiency. DPD deficiency shows large phenotypic variability, ranging from no symptoms to a convulsive disorder with motor and mental retardation.

The following table displays the *DPYD* variants detected by this assay, the corresponding star allele, and the effect on DPYD enzyme activity. Other or novel variations, besides those listed here, may also impact fluoropyrimidine-related side effects and tumor response.

<i>DPYD</i> Allele	cDNA Nucleotide Change	Effect on Enzyme Activity
*1	None (wild type)	Normal activity
*2A	1905+1G->A	No activity
*7	299_302delTCAT	No activity
*8	703C->T	Probable reduced activity
*9B	2657G->A	Variant of unknown significance
*10	2983G->T	Probable reduced activity
*11	1003G->T	Probable reduced activity
*13	1679T->G	No activity
rs67376798	2846A->T	Reduced activity
rs75017182	1129-5923C->G	Reduced activity
rs115232898	557A->G	Probable reduced activity

#### Reference Values

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An interpretive report will be provided.

### Interpretation

An interpretive report will be provided.

For additional information regarding pharmacogenomic genes and their associated drugs, see [Pharmacogenomic Associations Tables](#) in Special Instructions. This resource also includes information regarding enzyme inhibitors and inducers, as well as potential alternate drug choices.

### Cautions

[Rare genetic variants may be present that could lead to false-negative or false-positive results. Other variants in the primer binding regions can affect the testing, and ultimately, the genotype assessment made.](#)

Samples may contain donor DNA if obtained from patients who received heterologous blood transfusions or allogeneic blood or marrow transplantation. Results from samples 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 blood or marrow transplantation, a pretransplant DNA specimen is recommended for testing.

Dihydropyrimidine dehydrogenase (*DPYD*) genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's *DPYD* status.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Large deletions or rearrangements are not detected by this assay, and these may affect *DPYD* protein expression and their impact on fluoropyrimidine related side effects and tumor response.

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

### Clinical Reference

1. Online Mendelian Inheritance in Man: Dihydropyrimidine dehydrogenase deficiency. #274270. Updated 4/18/2012. Available at <http://omim.org/>
2. Caudle KE, Thorn CF, Klein TE, et al: Clinical Pharmacogenetics Implementation Consortium guidelines for dihydropyrimidine dehydrogenase genotype and fluoropyrimidine dosing. *Clin Pharmacol Ther* 2013;94(6):640-645
3. Morel A, Boisdron-Celle M, Fey L, et al: Clinical relevance of different dihydropyrimidine dehydrogenase gene single nucleotide polymorphisms on 5-fluorouracil tolerance. *Mol Cancer Ther* 2006 Nov;5(11):2895-2904
4. FDA Table of Pharmacogenomic Biomarkers in Drug Labeling. Accessed June 2017. Available at [www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm](http://www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm)
5. Offer SM, Fossum CC, Wegner NJ, et al: Comparative functional analysis of *DPYD* variants of potential clinical relevance to dihydropyrimidine dehydrogenase activity. *Cancer Res* 2014;74(9):2545-2554

### Performance

### Method Description

Genomic DNA is extracted from whole blood or saliva. Genotyping for *DPYD* alleles is performed using a 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. (User Guide: TaqMan SNP Genotyping Assay, Applied Biosystems, Revision A.0 January 2014)

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Monday through Friday; 8 a.m.

**Analytic Time**

3 days (Not reported on Saturday or Sunday)

**Maximum Laboratory Time**

10 days

**Specimen Retention Time**

Whole blood/Saliva swab: 2 weeks; Extracted DNA: 2 months

**Performing Laboratory Location**

Rochester

**Fees and 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 Regional Manager. 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 U.S. Food and Drug Administration.

**CPT Code Information**

81232

**LOINC® Information**

Test ID	Test Order Name	Order LOINC Value
DPYDV	DPYD Genotype	93199-8

Result ID	Test Result Name	Result LOINC Value
BA0148	DPYD Predicted Toxicity Risk	83009-1
BA0149	DPYD Result Details	45284-7
BA0153	Interpretation	69047-9
BA0154	Additional Information	48767-8



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Result ID	Test Result Name	Result LOINC Value
BA0209	Method	49549-9
BA0210	Disclaimer	62364-5
BA0155	Reviewed by	18771-6