Patient ID	Patient Name		Birth Date	Sex	Age
SA00179773	DPYDZ, ABNORMAL		1990-10-30	M	35
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00179773	SA00179773	CLIENT,CLIENT			
Account Information		**Collected**			
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DPYD Full Gene Sequencing, V

DPYD Total Activity Score

MCR

0

DPYD Phenotype

MCR

Poor metabolizer

Result Details

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The following PATHOGENIC variants were detected:

Gene (Transcript): DPYD (NM_000110.4)
Variant name: *2A
Zygosity: heterozygous
gDNA change: chr1(GRCh37):g.97915614C>T
cDNA change: c.1905+1G>A
Amino Acid change: p.?
Activity Score: 0
Functional Status: No Function

Gene (Transcript): DPYD (NM_000110.4)
Variant name: rs146170505
Zygosity: heterozygous
gDNA change: chr1(GRCh37):g.98164926C>A
cDNA change: c.661G>T
Amino Acid change: p.Glu221* (p.E221*)
Activity Score: 0
Functional Status: No Function

Interpretation

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This individual has no functional DPYD alleles (activity score of 0) due to multiple variants with no function. Based on this activity score, this individual is expected to be a poor metabolizer and is at increased risk for severe or fatal drug toxicity when treated with fluoropyrimidines at a standard dose.

The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline recommends avoiding use of fluoropyrimidines for this patient (1,2).

The two variants detected are presumed to be in trans (on opposite alleles), therefore, this result may be consistent with this individual having a diagnosis of autosomal recessive DPD deficiency. However, whether the variants identified are in cis (on the same allele) or in trans (on opposite alleles) cannot be definitively determined with the methodology used for this test. If the variants are in cis, the impact on the activity score may differ from the predicted activity score provided. Additionally, if the variants are in cis, this individual would be a carrier rather than affected. A genetic consultation may be of benefit.

Note: in an individual with no reportable variants the expected combined activity score is 2.

REFERENCES:

1. Amstutz U, Henricks LM, Offer SM, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Dihydropyrimidine Dehydrogenase Genotype and Fluoropyrimidine Dosing: 2017 Update. Clin Pharmacol Ther. 2018;103(2):210–216. doi:10.1002/cpt.911 (PMID 29152729)
2. CPIC Guideline for Fluoropyrimidines and DPYD: https://cpicpgx.org/guidelines/guideline-for-fluoropyrimidin es-and-dpyd/

Method

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Next-generation sequencing (NGS) and/or Sanger sequencing is performed to test for the presence of variants in coding regions and intron/exon boundaries (± 30 bp) of the DPYD gene, as well as the c.1129–5923C>G variant. 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 20X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for deletions/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 (PCR)-based quantitative method is performed to test for the presence of deletions and duplications in the DPYD gene.

Variant curation is performed using the ACMG/AMP recommendations with modifications and professional judgment. In addition, variants are assigned a function and activity score based on literature review together with information provided by the Clinical Pharmacogenetics Implementation Consortium (CPIC). The activity score is generated by adding the scores from

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MCR	Mayo Clinic Laboratories - Rochester Main Campus	200 First Street SW, Rochester, MN 55905	Nikola Baumann Ph.D.	24D0404292

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individual variant alleles, with 0 assigned for no function, 0.5 for decreased function, and 1 for normal function alleles. The expected activity score for a normal metabolizer is 2.

The medication-specific interpretation is provided based on the FDA label and CPIC guideline, and should be used together with professional judgment and patient-specific knowledge of additional variables that impact pharmacologic treatment.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis because of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences.

The reference transcript for the DPYD gene is NM_000110.4. Reference transcript numbers may be updated due to transcript re-versioning. Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

The following additional noncoding variant is being analyzed by this test: c.1129–5923C>G (HapB3, rs75017182).

Disclaimer

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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.

DPYD genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's dihydropyrimidine dehydrogenase (DPD) status. Similarly, samples may contain donor DNA if obtained from patients who received an allogeneic hematopoietic stem cell transplantation or non-leukocyte reduced blood transfusions. 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.

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 and activity score.

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.

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.

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.

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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.

Reviewed By MCR

Ann Marie Moyer, M.D., Ph.D.

Received: 09 Apr 2026 15:05 **Reported:** 09 Apr 2026 17:04

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