

**CYTOCHROME P450 2D6 (CYP2D6) COMPREHENSIVE CASCADE,  
 BLOOD**  
**Test ID: 2D6CB**

**USEFUL FOR:**

- Providing information relevant to tamoxifen, psychotropic medications (including fluoxetine, nortriptyline, paroxetine, and pimozide), codeine, and tramadol, as well as other medications metabolized by CYP2D6
- Determining the exact genotype when other methods fail to generate this information or if genotype-phenotype discord is encountered clinically
- Identifying exact genotyping when required (e.g., drug trials, research protocols)
- Identifying novel mutations that may interfere with drug metabolism

**GENETICS INFORMATION:** Approximately 94-96% of individuals will have results after tier one testing has been performed, and will not need additional testing through tier two or three. Based on tier one test sensitivity and CYP2D6 polymorphism carrier frequencies, persons of Caucasian descent have a 4-6% risk of having an undetected variation which would impact the predicted phenotype (this risk may be higher or lower in other ethnic groups). In these cases, testing will be continued through the tiers until the comprehensive genotype is determined. Testing through tier 3 will allow for the detection of all common variants (e.g., \*2, \*3, \*4, \*5, \*6, \*9, \*10, \*17, \*19, \*29, \*35, \*41, \*1XN, \*2XN, \*4XN) but also rarer alleles such as \*11, \*14, \*12, and \*15. Unitary and tandem CYP2D7-2D6 (\*13) alleles and CYP2D6-2D7 (e.g., \*4N and \*36) alleles can also be detected. Furthermore, the actual alleles that are duplicated or multiplied can be determined in most cases.

**TESTING ALGORITHM:** Cytochrome P450 2D6 (*CYP2D6*) Comprehensive Cascade, Blood, will always include *CYP2D6* genotype testing via Luminex (tier one). Tier two reflex testing will be performed as appropriate and will include *CYP2D6* Copy Number Variation, B. If additional testing is needed, any or all of the following tier three testing will be performed: *CYP2D6* Full Gene Sequencing, B; *CYP2D6-2D7* Gene Sequencing, B; *CYP2D7-2D6* Gene Sequencing, B; *CYP2D6* Duplication Sequence A, B; *CYP2D6* Duplication Sequence B, B; and *CYP2D6* Duplication Sequence C, B.

**TIER TWO REFLEX TESTS:**

Test ID	Reporting Name	Available Separately	Always Performed
2D6CN	<i>CYP2D6</i> Copy Number Variation, B	No	No

**TIER THREE REFLEX TESTS:**

Test ID	Reporting Name	Available Separately	Always Performed
2D6FG	<i>CYP2D6</i> Full Gene Sequencing, B	No	No
2D6N	<i>CYP2D6-2D7</i> Gene Sequencing, B	No	No
2D6R	<i>CYP2D7-2D6</i> Gene Sequencing, B	No	No
2D6DA	<i>CYP2D6</i> Duplication Sequence A, B	No	No
2D6DB	<i>CYP2D6</i> Duplication Sequence B, B	No	No
2D6DC	<i>CYP2D6</i> Duplication Sequence C, B	No	No

**METHODOLOGY:**

Tier 1: Polymerase Chain Reaction (PCR) with Allele-Specific Primer Extension (ASPE)

Tier 2: Real-Time Quantitative Polymerase Chain Reaction (PCR)

Tier 3: Polymerase Chain Reaction (PCR) Followed by DNA Sequence Analysis

**REFERENCE VALUES:** A comprehensive interpretive report will be provided.

**SPECIMEN REQUIREMENTS:** Multiple whole blood EDTA genotype tests can be performed on a single specimen after a single extraction. See Multiple Whole Blood EDTA Genotype Tests in Special Instructions within the on-line test catalog for a list of tests that can be ordered together.

**Container/Tube:** Lavender top (EDTA)

**Specimen Volume:** 3 mL

**Collection Instructions:** Send specimen in original tube

**Minimum Volume:** 1.0 ml

**ADDITIONAL INFORMATION:**

1. This assay will provide information relevant to tamoxifen, psychotropic medications (including fluoxetine, nortriptyline, paroxetine, and pimozide), codeine, and tramadol, as well as other medications metabolized by CYP2D6.

2. Bone marrow and liver transplants will interfere with testing. Call Mayo Medical Laboratories at 800-533-1710 or 507-266-5700 for instructions.

3. Transfusions will interfere with testing for up to 4 to 6 weeks. DNA obtained from white cells may not provide useful information for patients who received a recent transfusion of blood that was not leukocyte-reduced. Wait 4 to 6 weeks until transfused cells have left the patient's circulation before drawing the patient's blood specimen for genotype testing.

4. Cytochrome P450 Patient Education Brochure (Supply T526) is available upon request.

**FORMS:** **New York Clients-Informed consent is required.** Please document on the request form or electronic order that a copy is on file. An Informed Consent for Genetic Testing (Supply T576) is available as needed.

**SPECIMEN STABILITY INFORMATION:**

Specimen Type	Temperature	Time
Whole Blood EDTA	Refrigerated (preferred)	
	Ambient	

**CAUTIONS:**

•Direct DNA testing will not detect all the known mutations that result in a decreased or inactive CYP2D6 gene. Absence of a detectable gene mutation or polymorphism does not rule out the possibility that a patient has an ultrarapid, intermediate, or poor metabolizer phenotype.

•Other polymorphisms in the primer binding regions can affect the testing, and ultimately, the genotyping assessments made.

•Genotyping patients using DNA obtained from leukocytes may not provide useful information in patients who have had a bone marrow or liver transplant or a recent transfusion. To obtain an accurate genotype on a bone marrow transplant recipient, a saliva sample should be provided (2D6O, Cytochrome P450 2D6 Genotype, Saliva). Note that saliva samples cannot be used for the CYP2D6 Comprehensive Cascade due to performance characteristics of DNA extracted from saliva. If the patient has been

transfused, wait 4 to 6 weeks until transfused cells have left the circulation or provide a saliva sample.

- Liver donor blood must be provided to obtain a relevant genotype for patients who have received a liver transplant.
- A complicating factor in correlating CYP2D6 genotype with phenotype is that many drugs or their metabolites are inhibitors of CYP2D6 catalytic activity. Serotonin-specific reuptake inhibitors (SSRIs), as well as some tricyclic antidepressants (TCAs) and other drugs, may reduce CYP2D6 catalytic activity. Patients with an ultrarapid, extensive, or intermediate metabolizer genotype may have CYP2D6 enzyme activity inhibited by a variety of medications or their metabolites. Among the strongest inhibitors of CYP2D6 are bupropion, cinacalcet, fluoxetine, paroxetine, quinidine, duloxetine, sertraline, terbinafine, amiodarone, and cimetidine, although other drugs are also inhibitors. Consequently, an individual may require a decreased drug dose than predicted by genotyping alone. It is important to interpret the results of testing in the context of other co-administered drugs.
- CYP2D6 alleles with "reduced function" may metabolize different drugs at different rates, ranging from near normal to poor, but the literature on this is incomplete at this time.
- 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.
- This test is not for use in assessing for autoimmune hepatitis. Autoantibodies for CYP2D6 enzyme are found in many cases of autoimmune hepatitis. Order LKM Liver/Kidney Microsome Type 1 Antibodies, Serum, for autoimmune hepatitis assessment.

**CPT CODE:**

2D6CB: 81226: CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism), gene analysis, common variants (e.g., \*2, \*3, \*4, \*5, \*6, \*9, \*10, \*17, \*19, \*29, \*35, \*41, \*1XN, \*2XN, \*4XN)

2D6CN: 81479: Unlisted molecular pathology procedure

2D6FG: 81479: Unlisted molecular pathology procedure

2D6N: 81479: Unlisted molecular pathology procedure

2D6R: 81479: Unlisted molecular pathology procedure

2D6DA: 81479: Unlisted molecular pathology procedure

2D6DB: 81479: Unlisted molecular pathology procedure

2D6DC: 81479: Unlisted molecular pathology procedure

**DAY(S) SET UP:** Monday and Thursday

**ANALYTIC TIME:** 8 days

QUESTIONS: Contact your Mayo Medical Laboratories' Regional Manager or Shirley Pokorski, MML Laboratory Technologist Resource Coordinator  
Telephone: 800-533-1710