



## Quick Facts

- ▶ **Order Code: CYP2D6**
- ▶ **CYP2D6 is a highly polymorphic liver enzyme that metabolizes many commonly prescribed drugs.**
- ▶ **Some genetic variants in the *CYP2D6* gene can significantly alter its enzymatic function.**
- ▶ **Altered enzyme function can affect drug efficacy and can induce adverse drug reactions.**
- ▶ **About 5-10% of Caucasians have no CYP2D6 enzyme activity due to mutations in the gene.**
- ▶ **This assay can detect the majority of mutations responsible for the loss of enzyme activity.**

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## Cytochrome P450 2D6 Genotyping

### CLINICAL APPLICATION

Cytochrome P450 2D6 (*CYP2D6*) genotyping is useful for identifying individuals with altered *CYP2D6* enzyme activity, which increases the risk for reduced drug response and adverse drug reactions. In Caucasians, about 5% to 10% of the population has no *CYP2D6* enzyme activity (also known as poor metabolizers). These individuals are unlikely to achieve a therapeutic response when using drugs like Tamoxifen and Opioids; and may often experience drug-induced adverse reactions with some antidepressants or antipsychotics.

The FDA recommended adding a warning label to the package insert of Tamoxifen and Strattera, which require *CYP2D6* for their metabolism. This label warns of the implications of treating poor *CYP2D6* metabolizers with these drugs.

### CLINICAL BACKGROUND

*CYP2D6* is a highly polymorphic liver enzyme involved in the metabolism of many therapeutic drugs, including some antidepressants, antipsychotics, antiarrhythmics, antiemetics, b-adrenoceptor antagonists (b-blockers), opioids, and selective estrogen receptor modulators (Tamoxifen).

Genetic variation in the *CYP2D6* gene is common in most ethnic groups and can affect enzyme function and therapeutic response to the drugs it metabolizes. Certain variants completely abolish the enzymatic function of *CYP2D6*; other variants partially disrupt its activity. Therefore, four distinct groups of metabolizer (poor, intermediate, extensive, and ultrarapid) have been defined based on the combination of different alleles of the *CYP2D6* gene.

Genotyping of the *CYP2D6* gene is the most straightforward approach to identifying individuals who may experience adverse drug reactions with conventional doses of certain medications.

### TECHNICAL INFORMATION

This assay detects 17 small nucleotide variants found within the *CYP2D6* gene, along with gene rearrangements associated with deletion and duplication genotypes.

This mutation panel identifies about 95% of variants responsible for poor metabolism and has an analytical sensitivity and specificity close to 100%.

Mutation specific regions are PCR amplified from extracted genomic DNA for an allele specific primer extension (ASPE) reaction. Amplicon from the ASPE reaction are then hybridized into a liquid bead array to determine the patient's genotype.

## TEST INFORMATION

CYTOCHROME P450 2D6 GENOTYPING	
<b>DESCRIPTION</b>	Cytochrome P450 2D6 Genotyping
<b>METHOD</b>	PCR, ALLELE SPECIFIC PRIMER EXTENSION, AND DETECTION BY LIQUID BEAD ARRAY.
<b>ORDER CODE</b>	CYP2D6
<b>CPT CODE</b>	83891, 83900, 83901X6, 83914X17, 83912, 83892
<b>SPECIMEN REQUIREMENTS</b>	Whole blood (1 mL minimum, 3 mL preferred) in EDTA, sodium citrate, or ACD tube.
<b>RANGES</b>	NORMAL, POOR METABOLIZER

### Selected References

1. Cascorbi I. Pharmacogenetic of cytochrome P4502D6: genetic background and clinical implication. Eur J Clin Invest. 2003;33(Suppl.2):17-22
2. Ingelman-Sundberg M. Genetic polymorphisms of cytochrome P450 2D6 (CYP2D6): clinical consequences, evolutionary aspects and functional diversity. Pharmacogenomics J. 2005;5:6-13
3. Neafsey P, Ginsberg G, Hattis D, and Sonawane B. Genetic polymorphism in cytochrome P450 2D6 (CYP2D6): Population distribution of CYP2D6 activity. J Toxicol Environ Health B Crit Rev. 2009;12:334-361
4. Zhou S. Polymorphism of human cytochrome P450 2D6 and its clinical significance, part I. Clin Pharmacokinet. 2009;48(11):689-723

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