

**Specimen ID:** 247-988-9017-0  
**Control ID:**
**Acct #:** 90000999      **Phone:** (336) 436-8645      **Rte:** 00  
 LabCorp Test Master  
 Test Account  
 5450 Millstream Road  
 MCLEANSVILLE NC 27301

**SAMPLE REPORT, 511905**
**Patient Details**
**DOB:** 01/01/1980  
**Age(y/m/d):** 039/08/03  
**Gender:** M      **SSN:**  
**Patient ID:**
**Specimen Details**
**Date collected:** 09/04/2019 0000 Local  
**Date received:** 09/04/2019  
**Date entered:** 09/04/2019  
**Date reported:** 09/06/2019 0000 ET

**Physician Details**
**Ordering:**  
**Referring:**  
**ID:**  
**NPI:**
**Ordered Items**

Cytochrome P450 2D6/2C19

TESTS	RESULT	FLAG	UNITS	REFERENCE	INTERVAL	LAB
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**Cytochrome P450 2D6/2C19**

2D6 Genotype:	*2/*41					01
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Interpretation:						01
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Cytochrome P4502D6 (CYP2D6) is a member of the cytochrome P450 superfamily. CYP2D6 is involved in the metabolism of more than 65 commonly used drugs including beta-blockers, antipsychotics, anti-depressants, analgesics, and antiarrhythmics (Shimada, Yamazaki et al. 1994; Wilkinson 2005). The CYP2D6 gene is highly polymorphic. Many alleles of 2D6 encode enzymes that have reduced no function compared to the wild-type enzyme. Individuals can also have gene rearrangements with more than two copies of the CYP2D6 gene (gene duplication) or absence of both copies (gene deletion). Depending on the combination of alleles in an individual, drug-metabolizing phenotypes associated with the CYP2D6 enzyme can vary.

Drug-metabolizing phenotypes have been classified into groups, from the lowest level of metabolism to the highest level of metabolism: poor metabolizers (PMs), intermediate metabolizers (IMs), normal metabolizers (NMs), rapid metabolizers (RM), and ultra-rapid extensive metabolizers (UMs) (Caudle, et al. 2016). The combination of alleles contributes to the individual's phenotype.

For CYP2D6, categories of alleles include: normal function (\*1, \*2, \*35), reduced function (\*9, \*10, \*17, \*29 and \*41), non-functional (\*3, \*4, \*5, \*6, \*7, \*8, \*11 and \*15), and increased function resulting from gene duplication (Gaedigk, et al. 2017, <https://cpicpgx.org/>). The combination of inherited alleles is a diplotype. There is no standard approach to convert diplotypes into predicted phenotype (Gaedigk, et al. 2017) and more importantly predictions may not absolutely correlate to the observed phenotype. However, the Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines describe a frequently referenced model for assigning activity scores to diplotypes and subsequently predict a phenotypic metabolic classification (<https://cpicpgx.org/>). The CYP2D6 phenotype also depends on environmental factors in addition to the CYP2D6 genotype. These factors include the individual's age, size and gender, renal and liver function, disease status, and lifestyle factors such as smoking, some foods, and alcohol consumption (Meyer 2000). The co-administration of drugs metabolized by the CYP2D6, or

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other drugs that can act as inducers or inhibitors of CYP2D6 also affect the drug metabolizing phenotype. Variations in CYP2D6 enzyme activity can lead to a variety of problems in clinical practice. PMS develop a higher serum concentration of drug, which may lead to increased risk of concentration-dependent side effects. They may also experience drug toxicity or other adverse drug reactions, or prolonged therapeutic effect because of impaired clearance of drug. If a drug is administered as a pro-drug that requires biotransformation to an active form, PMS may experience inadequate therapeutic effect if the drug does not reach the therapeutic dose. IMs may experience some of these same problems to a lesser extent. For UMs, rapid metabolism of the drug may lead to inadequate drug efficacy and therapeutic failure, because the drug may not reach the therapeutic serum concentration. For pro-drugs, UMs may be at higher risk of adverse drug reactions and side effects.

**CYP2D6 Information:**

01

**Methodology/Intended Use/Indications for Use:**

This assay utilizes the Luminex xTAG(R) CYP2D6 Kit v3 US-IVD. The xTAG(R) CYP2D6 Kit v3 is a device used to simultaneously detect and identify a panel of nucleotide variants found within the highly polymorphic CYP2D6 gene located on chromosome 22 from genomic DNA extracted from EDTA and citrate anticoagulated whole blood samples. This kit can also identify gene rearrangements associated with the deletion (\*5) and duplication genotypes. The xTAG(R) CYP2D6 Kit v3 is a qualitative genotyping assay which can be used as an aid to clinicians in determining therapeutic strategy for therapeutics that are metabolized by the CYP2D6 gene product. This kit is not indicated for stand-alone diagnostic purposes. This test is not intended to be used to predict drug response or non-response.

The xTAG(R) CYP2D6 Kit v3 incorporates multiplex Polymerase Chain Reaction (PCR) and multiplex Allele Specific Primer Extension (ASPE) with Luminex's proprietary Universal Tag sorting system on the Luminex(R) 100/200(TM)xMAP(R) platform.

Alleles detected by the xTAG(R) CYP2D6 Kit v3: \*1, \*2, \*3, \*4, \*5, \*6, \*7, \*8, \*9, \*10, \*11, \*15, \*17, \*29, \*35, \*41, and DUP (duplication).

The \*1 allele is the most common allele in all ethnicities. Only alleles listed above will be identified by this product. Other CYP2D6 alleles, which are rare, or were unknown at the time of release of this product, will not be identified by this product. These other CYP2D6 alleles may result in either a \*1 call, a no-call, or a genetically related allele included in this kit.

**References:**

1. Shimada, T., H. Yamazaki, et al. (1994). "Interindividual variations in human liver cytochrome P-450 enzymes involved in the oxidation of drugs, carcinogens and toxic chemicals: studies with liver microsomes of 30 Japanese and 30 Caucasians." *J Pharmacol Exp Ther* 270(1): 414-423.
2. Wilkinson, G.R. (2005). "Drug metabolism and variability among patients in drug response." *N Engl J Med* 352(21): 2211-2221.
3. Caudle, K.E., H.M. Dunnenberger, et al. (2016). "Standardizing

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terms for clinical pharmacogenetic test results: consensus terms from the Clinical Pharmacogenetics Implementation Consortium (CPIC). " Genetics in Medicine. Advance Online Publication. doi:10.1038/gim.2016.87.

4. Gaedigk, A., K.Sangkuhl, et al. (2017). "Prediction of CYP2D6 phenotype from genotype across world populations." Genetics in Medicine. Advance Online Publication. doi:10.1038/gim.2016.80.

5. Meyer, U.A. (2000). "Pharmacogenetics and adverse drug reactions." Lancet 256(9242): 1667-71.

6. Package Insert: Luminex xTAG(R) CYP2D6 Kit v3 US-IVD. MLD-030-KPI-001 Rev G 2/2018.

**Director Review:**

Weidong Huang, MD, PhD

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 Director  
 Monogram Biosciences

2C19 Genotype: \*2/\*3

01

 2C19 Metabolic Activity:  
 Poor Metabolizer

01

**Interpretation:**

01

Cytochrome P4502C19 (CYP2C19) is a member of the cytochrome P450 superfamily. CYP2C19 is involved in the metabolism of drugs including clopidogrel, anticonvulsants, diazepam, omeprazole, tricyclic antidepressants and proton pump inhibitors. The CYP2C19 Cytochrome P4502C19 (CYP2C19) is a member of the cytochrome P450 superfamily. CYP2C19 is involved in the metabolism of drugs compared to wild-type. Depending on the combination of alleles in an individual, drug-metabolizing phenotypes associated with the CYP2C19 enzyme can vary.

Drug-metabolizing phenotypes can be classified according to the level of metabolism: poor metabolizers (PMs), intermediate metabolizers (IMs), extensive metabolizers (EMs), and ultrarapid metabolizers (UMs). An individual's phenotype depends on the combination of alleles they have. PMs have little to no CYP2C19 enzyme activity and have two non-functional alleles. EMs are defined as having normal enzyme activity, and are homozygous wild-type for the \*1 functional allele. UMs have increased enzyme activity resulting from two gain-of-function alleles or one functional allele and one gain-of-function allele. The \*17 allele is the only UM allele identified thus far for CYP2C19. IMs have intermediate enzyme activity resulting from one functional allele and one loss-of-function allele. The consequence of a \*17 allele with a loss of function allele may be in between the EM and IM phenotypes and may possibly be substrate dependent.

Variations in CYP2C19 enzyme activity can lead to variety of clinical implications. PMs have reduced enzyme activity and may require alternative therapeutic treatment or adjustment of standard dosage regime to reduce the risk of concentration-dependent side effects, overdose drug toxicity or prolonged therapeutic effect as a result of impaired clearance of drug. If a drug is administered as a prodrug that requires activation by CYP2C19 enzyme, PMs may experience inadequate therapeutic effect if the drug does not reach the therapeutic dose. EMs in general

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have normal enzyme activity and can be administered CYP2C19-metabolized drugs using standard dosing. EMs who are heterozygous for a variant allele with a non-functional allele may have a modest decrease in enzyme activity. For UMs, rapid metabolism of the drug may lead to inadequate drug efficacy and therapeutic failure, because the drug may not reach the therapeutic serum concentration. For prodrugs like clopidogrel, UMs may be at risk of elevated exposure to active drug metabolites leading to adverse drug reactions (Xie, et al. 2011). The physiological effect of CYP2C19 phenotype depends on individual clinical profile. The co-administration of drugs metabolized by CYP2C19, or other drugs that can act as inducers or inhibitors of CYP2C19, also affects the drug metabolizing phenotype. Other factors include the individual's age, weight, gender, renal and liver function, disease status, and lifestyle factors such as smoking, diet and alcohol consumption (Meyer 2000). It is important to interpret genotyping test results in the context of an individual's profile.

CYP2C19 Information:

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Methodology / Intended Use / Indications for Use:

This assay utilizes the Luminex xTAG(R) CYP2C19 Kit v3 US-IVD. The xTAG(R) CYP2C19 Kit v3 is an in vitro diagnostic test used to simultaneously detect and identify a panel of nucleotide variants found within the highly polymorphic CYP450 2C19 gene, located on chromosome 10q24, from genomic DNA extracted from EDTA or citrate anticoagulated whole blood samples. The xTAG(R) CYP2C19 Kit v3 is a qualitative genotyping assay which can be used as an aid to clinicians in determining therapeutic strategy for the therapeutics that are metabolized by the CYP2C19 gene product, specifically \*2, \*3 and \*17. The kit is not indicated for stand-alone diagnostic purposes. This test is not intended to be used to predict drug response or non-response.

The xTAG(R) CYP2C19 Kit v3 incorporates multiplex Polymerase Chain Reaction (PCR) and multiplex Allele Specific Primer Extension (ASPE) with a proprietary universal array sorting system on the Luminex platform.

Alleles detected by xTAG(R) CYP2C19 Kit v3: \*1,\*2,\*3,\*17.

The wild-type (WT) allele, CYP2C19\*1, is the most common variant. Only alleles listed above will be identified by this product. Other CYP2C19 alleles, which are rare, or were unknown at the time of release of this product, will not be identified by this product. These other alleles may result in either a \*1 call, a no-call, or a call of a genetically related allele included in this kit.

References:

1. Xie, et al. (2011). "Individual variability in the disposition of and response to clopidogrel: pharmacogenomics and beyond." *Pharmacol Ther* 129(3): 267-89.
2. Meyer, U. A. (2000). "Pharmacogenetics and adverse drug reactions." *Lancet* 356(9242): 1667-71.
3. Package Insert: Luminex xTAG(R) CYP2C19 Kit v3 US-IVD. MLD-046-KPI-001 Rev E 2/2018.

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Director Monogram Biosciences	Weidong Huang, MD, PhD					01

01	L9	Monogram Biosciences Inc 345 Oyster Point Blvd, S San Francisco, CA 94080-1913	Dir: Weidong Huang, MD
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For inquiries, the physician may contact **Branch: 800-222-7566 Lab: 336-436-2762**