



(818) 789-1033
http://www.firmalab.com

Laboratory Director: Marvin Pietruszka, MD, JD
Clinical Consultant: Daniel Darvish, MD
21053 Devonshire St. #106, Chatsworth, CA 91311

Dr. Richard Roe
12345 Main Street
Anytown, USA

Phone: 555-555-5555
Fax: 555-555-5556

Patient Name

John Doe

DOB	Gender	Ethnicity
01/01/1975	M	Caucasian

Test Ordered	Test Result	Expected (Negative) Value
CYP2C19 Genotype	Intermediate Metabolizer	Extensive Metabolizer
<p>Result Note: CYP2C19 *2 heterozygous variation [c.681G>A, g.19154G>A, Splicing Defect].</p> <p>Result Interpretation: CYP2C19 Intermediate Metabolizer (IM). This result is consistent with lower than expected enzyme activity. IM patients are at increased risk of drug induced adverse events or side effects due to slower drug elimination of active drugs, or slower activation of prodrugs. Clopidogrel antiplatelet agent (prodrug) may be suboptimally activated, leading to increased risk of cardiovascular events compared to CYP2C19 Extensive Metabolizers, consider prasugrel or other alternative therapy (if no contraindication). Prasugrel is not, or to a much smaller extent, metabolized by CYP2C19 but is associated with an increased bleeding risk compared to clopidogrel. Common medications metabolized by CYP2C19 and additional information are attached. See additional information attached.</p>		
CYP2D6 Genotype	Ultrarapid Metabolizer	Extensive Metabolizer
<p>Result Note: Three variations found: 1.Ultrarapid Metabolizer, CYP2D6*2 more than one copy of variant in chromosome found. 2.CYP2D6*10 homozygous variation [100C>T, p.P34S]. 3.CYP2D6*4 heterozygous variation [1846G>A aka 1934G>A; splicing defect].</p> <p>CYP2D6 resulting Activity Score is estimated to be equal or more than 1, interpreted within the range of Extensive to Ultrarapid metabolizer. Activity Score calculation is based on publication by Crews, et, al., Clin Pharmacol Ther. 2012 Feb; 91(2): 321-326.</p> <p>Tramadol recommendation: For CYP2D6 ultrarapid metabolizers, it is recommended to begin dosing at 70% of recommended dose, and monitor for adverse events. Alternatively, consider using an alternative to tramadol (not oxycodone or codeine).</p> <p>Result Interpretation: CYP2D6 Ultrarapid Metabolizer (UM): This result is consistent with higher than expected enzyme activity. UM patients are at increased risk of drug induced adverse events or side effects due to more rapid activation of prodrugs which may be life-threatening (e.g. codeine or tramadol), or suboptimal effect or duration of active drugs that is eliminated/inactivated by CYP2D6. This variation has been described in Northern Africans 10-16%, Asians 0-2%, and Caucasians 1-5%. Common medications metabolized by CYP2D6 and additional information are attached. See additional information attached.</p>		
CYP2C9 Genotype	Extensive Metabolizer	Extensive Metabolizer
<p>Result Interpretation: CYP2C9 Extensive Metabolizer (EM): This result is consistent with the normal enzyme activity. Generally, standard dosing of CYP2C9 metabolized medications can be used if no other factors are expected to alter metabolism. Common medications metabolized by CYP2C9 and additional information are attached. See additional information attached.</p>		

Electronically signed by: Daniel Darvish, MD, on 12/08/2016 14:49
Report Type: Complete

Specimen ID	Specimen Type	Collection Date Time	Date Received	Report Date
1256	Buccal Swab	11/30/2010 15:15	12/01/2010 09:45	12/08/2010 13:56

The laboratory is accredited by College of American Pathologists (CAP), and regulated under the Clinical Laboratory Improvement Amendments 1988 (CLIA) as qualified to perform high complexity clinical testing.

CYP2C19

The CYP2C19 gene encodes for the metabolic enzyme of Cytochrome P450, family 2, subfamily C, polypeptide 19. Below tables include some of the clinically relevant examples of substrates, inhibitors, and inducers of CYP2C19.

SUBSTRATES

Antidepressants: amitriptyline citalopram clomipramine fluvoxamine fluoxetine imipramine moclobemide sertraline venlafaxine	Antiepileptics: diazepam mephenytoin nordazepam phenobarbitone phenytoin primidone S-mephenytoin	Proton-pump inhibitors: lansoprazole omeprazole pantoprazole rabeprazole (E3810) esomeprazole
Others: carisoprodol (Soma) ** clopidogrel (Plavix) ** cyclophosphamide hexobarbital indomethacin	R-mephobarbital nelfinavir nilutamide progesterone	proguanil propranolol teniposide R-warfarin

** **Prodrug** that is converted to active form or active intermediate

INHIBITORS & DEGREE OF INHIBITION

fluvoxamine +++	indomethacin ++	probenicid ++
ketoconazole +++	lansoprazole ++	ticlopidine ++
cimetidine ++	omeprazole ++	

+++ **Strong** inhibitor may cause more than 80% decrease in metabolism.

++ **Moderate** inhibitor may cause 50-80% decrease in metabolism.

+ **Weak** inhibitor may cause 20-50% decrease in metabolism.

INDUCERS

carbamazepine	prednisone	artemisinin
norethindrone	rifampin	

For a more comprehensive list of drug substrate, inducers, and inhibitors, please consult your local pharmacist.

Ultra-rapid or poor metabolizers may benefit from change to other comparable drugs and/or increasing/decreasing doses of current drugs. Carriers of variant alleles exhibit a reduced capacity to produce the active metabolite of **clopidogrel**, and are at increased risk of adverse cardiovascular events, consider **prasugrel** as alternative.

Prodrugs are usually converted to active form by the enzyme, and ultra-rapid metabolizer may be higher at risk of overdose/toxicity.

Inhibitors and inducers should also be considered in determining appropriate treatment course and monitoring response. Inhibitors can decrease the enzyme metabolic rate, and inducers can increase it.

Although DNA testing is highly accurate, it may not predict the effective overall metabolic rate of a patient. Other factors that can alter the rate of metabolism include liver and kidney function, drug-drug and drug-food interactions, smoking, age, gender, race, and/or variations in other genes. The genetic test results can provide adjunctive information to support a more effective and safer treatment decision.

METHOD OF ANALYSIS: DNA is isolated from the *sample* and tested for the variations listed above. Specific regions of the gene are analyzed by Sanger based sequencing. Borderline results are confirmed by repeat sequencing. The assay will test only the variations ordered, alleles *1-8, and 17. This assay was developed and its performance characteristic determined by FirmaLab. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA), or the FDA has determined that such clearance of approval is not needed. The laboratory is accredited by College of American Pathologists (CAP), and regulated by the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity molecular testing.

References

- Kassimis G, et al. *Curr Pharm Des.* 2013;19(13):2489-95.
- Furuta T, et al. *Mol Diagn Ther.* 2012 Aug 1;16(4):223-34.
- Scott SA, et al. *Clin Pharmacol Ther.* 2011 Aug;90(2):328-32
- Camilleri E, et al. *Curr Cardiol Rep.* 2011 Aug;13(4):296-302.
- Li-Wan-Po A, et al. *Br J Clin Pharmacol.* 2010 Mar;69(3):222-30
- Samer DF, et al. *Mol Diagn Ther.* 2013 June; 17(3): 165-184.

CYP2D6

The CYP2D6 gene encodes for the metabolic enzyme of Cytochrome P450, family 2, subfamily D, polypeptide 6. Below tables include some of the clinically relevant examples of substrates, inhibitors, and inducers of CYP2D6.

SUBSTRATES

Antidepressants: amitriptyline clomipramine desipramine duloxetine fluoxetine fluvoxamine imipramine doxepine minaprine nortriptyline praxetine venlafaxine	Cardiac & Antihypertensives: alprenolol carvedilol bufuralol debrisoquine diltiazem disopyramide encainide flecainide s-metoprolol mexiletine propafenone metoprolol propranolol timolol	
	Opioids: codeine ** methadone	Chemotherapeutics: tamoxifen **
Antipsychotics: aripiprazole chlorpromazine haloperidol perphenazine risperidone t-thioridazine zuclopenthixol clozapine olanzapine	Other Examples: amphetamine atomoxetine chlorpheniramine dexfenfluramine dextromethorphan felbamate hydrocodone** lidocaine mephobarbital metoclopramide methoxyamphetamine ondansetron oxycodone ** perhexilene phenacetin phenfromin sparteine tramadol**	

** Prodrug that is converted to active form or active intermediate

INHIBITORS & DEGREE OF INHIBITION

cimetidine +++	celecoxib ++	metoclopramide ++
cocaine +++	citalopram ++	methadone ++
fluoxetine +++	clomipramine ++	moclobemide ++
paroxetine +++	desethylamiodarone ++	ritonavir ++
perphenazine +++	desmethylcitalopram ++	sertraline ++
quinidine +++	duloxetine ++	tripelennamide ++
tegaserod +++	escitalopram ++	bupropion +
amiodarone ++	halofantrine ++	chlorpromazine +
biperiden ++	levomepromazine ++	chlorpheniramine +

+++ **Strong** inhibitor may cause more than 80% decrease in metabolism.

++ **Moderate** inhibitor may cause 50-80% decrease in metabolism.

+ **Weak** inhibitor may cause 20-50% decrease in metabolism.

INDUCERS

dexamethasone	rifampin
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For a more comprehensive list of drug substrate, inducers, and inhibitors, please consult your local pharmacist.

Ultra-rapid (UM) and poor metabolizers (PM) may benefit from change to other comparable drugs and/or adjusting doses of current drugs.

Prodrugs are usually converted to active form by the enzyme, and ultra-rapid metabolizers (UM) are at higher risk of overdose/toxicity. In UM, cases of life-threatening toxicity have been reported with the prodrugs **tramadol** and **codeine**.

Inhibitors and inducers should also be considered in determining appropriate treatment course and monitoring response. Inhibitors can decrease the metabolic rate, and inducers can increase it.

Although DNA testing is highly accurate, it may not predict the effective overall metabolic rate of a patient. Other factors that can alter the rate of metabolism include liver/kidney dysfunction, smoking, drug/diet interactions, age, gender, race, and/or variations in other genes. The genetic test results can provide adjunctive information in the support of more effective and safer treatment decisions.

METHOD OF ANALYSIS: DNA is isolated from the *sample* and tested for the variations listed above. Specific regions of the gene are analyzed by Sanger based sequencing. Borderline results are confirmed by repeat sequencing. The assay will test only the variations ordered, alleles *1-12, 14, 15, 17, 41, and gene duplication. This assay was developed and its performance characteristic determined by FirmaLab. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA), or the FDA has determined that such clearance of approval is not needed. The laboratory is accredited by College of American Pathologists (CAP), and regulated by the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity molecular testing.

References

- Bertilsson L, et al. Br J Clin Pharmacol 2002 Feb;53(2):111-122
- Lundqvist E, et al. Gene 1999 Jan 21;226(2):327-338
- Kirchheiner J, et al. Acta Psych Scand 2001 Sept;104(3):173-192
- Lam YWF, et al. Pharmacotherapy 2002;22:1001-1006
- Samer DF, et al. Mol Diagn Ther. 2013 June; 17(3): 165-184.

CYP2C9

The CYP2C9 gene encodes for the metabolic enzyme of Cytochrome P450, family 2, subfamily C, polypeptide 9. Below tables include some of the clinically relevant examples of substrates, inhibitors, and inducers of CYP2C9.

SUBSTRATES

Angiotensin II Blockers: irbesartan losartan	NSAIDs: celecoxib ** diclofenac ** ibuprofen meloxicam naproxen piroxicam suprofen	Others: fluvastatin ** phenytoin ** rosuvastatin ** sulfamethoxazole tamoxifen ** torsemide
Anticoagulants: acenocoumarol phenprocoumone S-warfarin		
Antidepressants: amitriptyline fluoxetine R-norfluoxetine	Oral Hypoglycemic/Sulfonylurea Agents: glimepiride glipizide glybenclamide glyburide	nateglinide rosiglitazone tolbutamide

** **Prodrug** that is converted to active form or active intermediate

INHIBITORS & DEGREE OF INHIBITION

fluvastatin	+++	probenicid	+
sulfaphenazole	+++	teniposide	+
isoniazid	++	desmethylsertraline	<+
sulfamethoxazole	++	paroxetine	<+
amiodarone	+	sertraline	<+
fluconazole	+	S-norfluoxetine	<+
fluvoxamine	+	zafirlukast	<+
phenylbutazone	+		

+++ **Strong** inhibitor may cause more than 80% decrease in metabolism.

++ **Moderate** inhibitor may cause 50-80% decrease in metabolism.

+ **Weak** inhibitor may cause 20-50% decrease in metabolism.

INDUCERS

Phenobarbital	rifampin	secobarbital
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For a more comprehensive list of drug substrate, inducers, and inhibitors, please consult your local pharmacist.

Ultra-rapid or poor metabolizers may benefit from change to other comparable drugs and/or increasing/decreasing doses of current drugs.

Prodrugs are usually converted to active form by the enzyme, and ultra-rapid metabolizer may be higher at risk of overdose/toxicity.

Inhibitors and inducers should also be considered while determining appropriate treatment course and monitoring response. Inhibitors can decrease the enzyme metabolic rate, and inducers can increase it.

Although DNA testing is highly accurate, it may not predict the effective overall metabolic rate of a patient. Other factors that can alter the rate of metabolism include liver and kidney function, drug-drug and drug-food interactions, smoking, age, gender, race, and/or variations in other genes. The genetic test results can provide adjunctive information to support a more effective and safer treatment decision.

METHOD OF ANALYSIS: DNA is isolated from the *sample* and tested for the variations listed above. Specific regions of the gene are analyzed by Sanger based sequencing. Borderline results are confirmed by repeat sequencing. The assay will test only the variations ordered, including alleles *1 (extensive metabolizer) and *2-6 (intermediate and poor metabolizers). This assay was developed and its performance characteristic determined by FirmaLab. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA), or the FDA has determined that such clearance of approval is not needed. The laboratory is accredited by College of American Pathologists (CAP), and regulated by the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity molecular testing.

References

- Wang B, et al. *Curr Drug Metab.* 2009 Sep;10(7):781-834.
- Van Booven D, et al. *Pharmacogenet Genomics.* 2010 Apr;20(4):277-81
- C. F. Samer, et al. *Mol Diagn Ther.* 2013 June; 17(3): 165-184
- Gage BF, et al. *Thromb Haemostasis* 2004;91:87-94
- Hung CC, et al. *Ther Drug Monit* 2004;(26):534-540
- Llerena A, et al. *Eur J Clin Pharmacol* 2004;(59):869-873
- Johnson JA, et al. *Clin Pharmacol Ther.* 2011 Oct;90(4):625-9
- Cavallari LH, Shin J, Perera MA. *Pharmacotherapy.* 2011 Dec;31(12): 1192-207
- Samer DF, et al. *Mol Diagn Ther.* 2013 June; 17(3): 165-184.