Patient Name	Patient ID	Age	Gender	Order #
SAMPLEREPORT,2C19O A	SA00059750	47	F	SA00059750
Ordering Phys CLIENT,CLIENT				**DOB** 06/10/1966
Client Order # SA00059750	**Account Information**			**Report Notes**
Collected 07/08/2013 00:00	C7028846-DLMP Rochester 3050 Superior Drive Rochester, MN 55901			
Printed 07/23/2013 09:47				

Test	Flag	Results	Unit	Reference Value	Perform Site*
CYP2C19 Genotype, Saliva					
RECEIVED: 07/09/2013 09:18 **REPORTED:** 07/17/2013 15:43					
CYP2C19 Sequencing		Performed			MCR
CYP2C19 Sequence Genotype					
2C19 Genotype Star Alleles		17/17			MCR
2C19 -806C>T (*17)		T/T			MCR
2C19 1A>G (*4)		A/A			MCR
2C19 358T>C (*8)		T/T			MCR
2C19 395G>A (*6)		G/G			MCR
2C19 636G>A (*3)		G/G			MCR
2C19 681G>A (*2)		G/G			MCR
2C19 IVS5+2T>A (*7)		T/T			MCR
2C19 Reviewed by		Jamie Bruflat			MCR
2C19 Interpretation					MCR

This individual has two copies of the gene encoding enzyme with increased transcription of the CYP2C19 gene and increased expression of CYP2C19 enzyme. Metabolism of some drugs is increased by the *17 promoter polymorphism. Patients with the *17 promoter polymorphism should be monitored for signs and symptoms associated with lack of efficacy while receiving drug therapy. Prodrugs, such as clopidogrel, may be activated to the therapeutic metabolite to a greater degree by individuals who carry the *17 allele. Individuals with two copies of the *17 allele who receive clopidogrel therapy are at increased risk for bleeding and should be monitored closely.
A combination of bidirectional and dual monodirectional DNA sequence analysis was used to test for the presence of variants in the promoter as well as exons 1, 3, 4, and 5 of the CYP2C19 gene. These sequencing reactions detect the presence of -806C>T (*17), 1A>G (*4), 358T>C (*8), 395G>A (*6), 636G>A (*3), 681G>A (*2), and IVS5+2T>A (*7). This sequencing assay will not detect all the known mutations that result in decreased or inactive CYP2C19. Absence of a detectable gene mutation or polymorphism does not rule out the possibility that a patient has an intermediate or poor metabolizer phenotype.

Individuals receiving clopidogrel who have one copy (heterozygous) of the null or deficient CYP2C19 polymorphisms detected by this test will likely require a dose increase to achieve effective inhibition of platelet aggregation. Individuals who have two defective copies of

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these CYP2C19 deficient alleles (poor metabolizers) may not achieve effective inhibition of platelet aggregation using the standard doses of clopidogrel. An increased dose of clopidogrel, or switching to other antiplatelet drugs such as prasugrel, should be considered for CYP2C19 poor metabolizers. The presence of the *17 promoter polymorphism will increase the expression of the CYP2C19 enzyme encoded by the allele on which it is found. When found in combination with other polymorphisms, we are unable to ascertain the mode of inheritance to predict which allele includes the *17 promoter polymorphism but will make our best prediction of the impact of the findings.

Patients with an extensive (normal) or intermediate metabolizer genotype may have CYP2C19 enzyme activity inhibited by a variety of medications or their metabolites. The following is a partial listing of drugs known to affect CYP2C19 activity as of the date of this report.

Drugs that undergo metabolism by CYP2C19:
Anticoagulants: clopidogrel
Anticonvulsants: mephenytoin, phenobarbitone, phenytoin, primidone Antidepressants: amitriptyline, citalopram, S-citalopram, clomipramine, imipramine Antineoplastic drugs: cyclophosphamide, teniposide Antiretroviral: nelfinavir Proton pump inhibitors: lansoprazole, omeprazole, pantoprazole, rabeprazole Miscellaneous drugs: diazepam, hexobarbital, indomethacin, progesterone, proguanil, propranolol, R-warfarin (less active isomer) Coadministration may decrease the rate of elimination of other drugs metabolized by CYP2C19.

Drugs known to increase CYP2C19 activity: carbamazepine, norethindrone, prednisone, rifampin Coadministration of these drugs increases synthesis of CYP2C19 and increases the rate of elimination of drugs metabolized by CYP2C19.

Drugs known to decrease CYP2C19 activity: chloramphenicol, cimetidine, felbamate, fluoxetine, fluvoxamine, indomethacin, ketoconazole, lansoprazole, modafinil, omeprazole, oxcarbazepine, pantoprazole, probenicid, rabeprazole, ticlopidine, topiramate. Coadministration will decrease the rate of metabolism of CYP2C19 metabolized drugs, increasing the possibility of toxicity, particularly

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in heterozygous individuals.
Laboratory developed test.

* Performing Site:

MCR	Mayo Clinic Laboratories - Rochester Main Campus 200 First St SW Rochester, MN 55905	Lab Director: Franklin R. Cockerill, III, M.D.