

MEMORANDUM

To: Regional Medical Laboratory, Inc. (RML) Clients
 From: Michelle Terrell, MT, Manager of Microbiology and Molecular
 Cindi Starkey PhD, MD, Director of Molecular Testing
 Subject: Discontinuation of MTHFR, DNA Mutation Analysis (C665T& A1286C)
 [methylenetetrahydrofolate reductase].

Regional Medical Laboratory will be discontinuing MTHFR, DNA Mutation Analysis (C665T & A1286C) [methylenetetrahydrofolate reductase] on **3/1/2021**. Polymorphisms of the MTHFR gene may cause reduced enzyme activity of MTHFR and, as such, may cause mild hyperhomocysteinemia, but this is only one of many factors that has been associated with elevated homocysteine blood levels. Historically, hyperhomocysteinemia has been associated with increased risk for venous thromboembolism, coronary heart disease, stroke and recurrent pregnancy loss. Meta-analyses have disproved an association between the polymorphisms of MTHFR and these conditions and there is significant evidence that MTHFR polymorphism testing has minimal clinical utility and therefore should not be ordered as part of a routine evaluation for thrombophilia. As a result, the American Congress of Obstetricians and Gynecologists and the American College of Medical Genetics Practice Guidelines indicate that MTHFR genotyping is NOT recommended as part of a routine evaluation for recurrent pregnancy loss or thrombophilia^{1,2,3}. In fact, it has been suggested that an elevated homocysteine blood level is a better indicator of increased risk for disorders associated with hyperhomocysteinemia²; and is less expensive to evaluate.

Test Name DISCONTINUATION	Order Name	Test Number	Date of Cessation of Testing
MTHFR, DNA Mutation Analysis (C665T& A1286C)	MTHFR	1515625	3/1/2021

(1)

Preferred Test	Order Name	Test Number	Testing Section
Homocysteine	HOMOCYS	2004575	Chemistry

References:

1. Hickey, SE, Curry CJ, Toriello HV, et al. ACMG Practice Guideline: lack of evidence for MTHFR polymorphism testing. *Genet Med.* 2013; 15 (2): 153-156
2. ACMG Practice Guideline: lack of evidence for MTHFR polymorphism testing Michael T. Bashford, MD, Scott E. Hickey, MD, Cynthia J. Curry, MD and Helga V. Toriello, PhD for the American College of Medical Genetics and Genomics (ACMG) Professional Practice and Guidelines Committee *Genetics in Medicine* (2020) 22:2125
3. ACOG Practice Bulletin No. 197: Inherited Thrombophilias in Pregnancy. *Obstetrics & Gynecology*: July 2018, Volume 132 (1), p e18-e34.