SPECIMEN TYPE: PLASMA

SPECIMEN INFORMATION	**Collected**	**Received**	**Reported**	
	Feb-25-2019	Feb-26-2019	Feb-27-2019	
PATIENT INFORMATION	**MRN#**	**Last Name**	**First Name**	**Date of Birth**
	REDACTED	REDACTED	REDACTED	REDACTED
INSTITUTION INFORMATION	**Ordering Physician**		**Address**	
	REDACTED		REDACTED	

TEST RESULTS

MICROORGANISM NAME	DNA MOLECULES PER MICROLITER (MPM)*	REFERENCE INTERVAL (MPM)**
Escherichia coli	3,291	< 15
Cytomegalovirus (CMV)	590	< 10

* Molecules per microliter = number of DNA fragments present in one microliter of plasma

** Reference Interval = the 97.5th percentile MPM concentration detected in PPT plasma from a cohort of asymptomatic donors

Karius Medical staff are available to answer questions about these results: Phone: (866) 452-7487 | Email: medical@kariusdx.com

TEST DESCRIPTION

The Karius Test can identify:

Bacteria: 883 **DNA viruses:** 102 **Archaea:** 1 **Fungi:** 400 **Eukaryotes:** 63

Full list of organisms is found at:

The Karius Test for infectious disease detects microbial cell free DNA (cfDNA) in plasma from bacteria, DNA viruses, fungi and protozoa using next-generation sequencing (NGS) [1]. The test reports the presence and abundance of microbial cfDNA when statistically significant levels of the associated cfDNA are detected above background.

Microbial cfDNA may be found in plasma when viable microorganisms are not detected in blood by other methods [2]. It can be detected from localized infections [1, 3] or during effective antimicrobial treatment [4]. The reported microorganism(s) may or may not be the cause of patient infection. Results should be interpreted within the context of clinical data, including medical history, physical findings, epidemiological factors, and other laboratory data.

[1] Blauwkamp , et. al. (2019 February) Nature Microbiology
[2] De Vlaminck, et al. (2013). Cell, 155(5)
[3] Hong , et. al. (2018 November) DMID, 92 (3): 210-213
[4] Abril, et al. (2016 Jul 12) Open Forum Infect Dis, 12;3(3):ofw144

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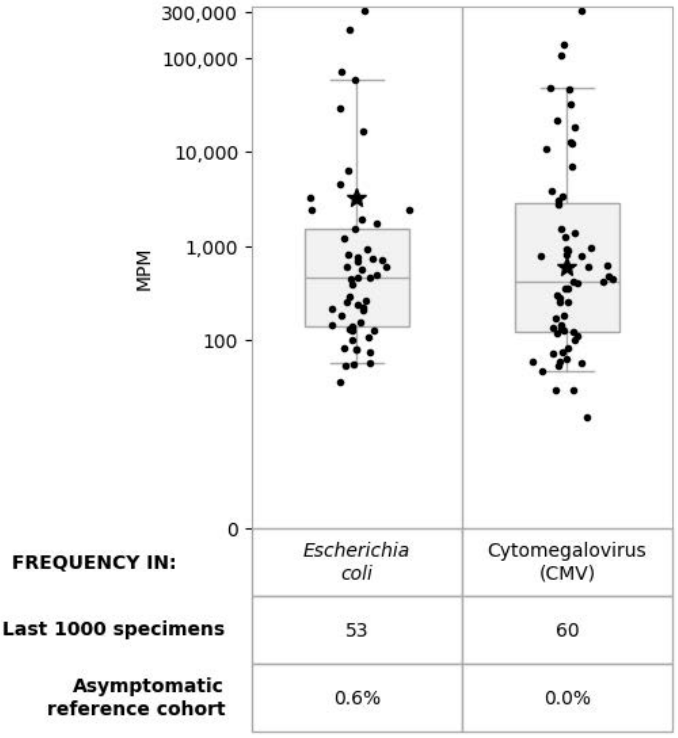
	REDACTED		REDACTED	

RANGE OF MICROORGANISM QUANTITIES REPORTED IN LAST 1,000 SPECIMENS



FREQUENCY IN:	*Escherichia coli*	Cytomegalovirus (CMV)
Last 1000 specimens	53	60
Asymptomatic reference cohort	0.6%	0.0%

The above plot(s) show how the concentration of each microorganism reported here compared to the concentration(s) of the same microorganism reported in the last 1,000 specimens tested by Karius. The star represents the MPM result in this specimen, and the black dots represent the MPM results in other specimens where the same microorganism was reported. The frequencies with which the microorganism is reported in the last 1,000 specimens tested and in a reference range of 167 asymptomatic adult individuals are indicated below the plot.

The plot(s) and other information provided above do not constitute medical advice and are being provided for informational purposes only. Results should be interpreted within the context of clinical data, including medical history, physical findings, epidemiological factors, and other laboratory data.

Analytical Performance Specifications		
Sensitivity	95% at 41 MPM	
Specificity	Per microorganism	> 99.99%
	Per report	98%

For a summary of the analytical validation see: kariusdx.com/validation

Clinical Validation in the SEP-SEQ Trial (N=350) [1,2]		
Positive Agreement	Blood Culture (N=63)	93.7%
Diagnostic Sensitivity	Composite Gold Standard (All microbiology tests and clinical adjudication)	92.9%
Diagnostic Specificity	Composite Gold Standard (All microbiology tests and clinical adjudication)	63%*

*Discordant Karius results included clinically-relevant pathogens such as *Helicobacter pylori*, EBV, and CMV that were determined not to be the primary cause of sepsis via adjudication.

MPM interpretation: Positive results will display the concentration of pathogen cfDNA detected in units of **M**olecules of cell-free DNA fragments of a pathogen **P**er **M**icroliter of plasma (abbreviated MPM). The MPM value may be used to infer the amount of microorganism cfDNA present in an individual. If a report includes multiple microorganisms, they are listed in the order of high to low MPM. Several variables impact the MPM value, including the location of infection, prior or ongoing antimicrobial treatment, and genome size of the microorganism. In cases where multiple microorganisms are reported, comparison of MPM values across organisms in the context of etiology should be done with caution.

Reference Interval: The reference interval is derived from a study of 167 asymptomatic adults. Specific reference intervals are calculated using the MPM value reported for the 97.5th percentile for each microorganism. For example, the reference range of *E. coli* has an MPM value of < 15, which means that across asymptomatic individuals the 97.5th percentile of *E. coli* quantitations was 15 MPM. MPM values reported below the corresponding reference interval may be the cause of infection, for example due to antibiotic pre-treatment or locus of infection.

[1] SEP-SEQ Trial. Determining the Etiology of Sepsis Using an Infectious Disease Diagnostic Sequencing Assay, Data on File (2018)
[2] ClinicalTrials.gov Identifier: NCT02730468

This test was developed and its performance characteristics determined by Karius. This test has not been cleared or approved by the FDA, nor is it required to be. The Karius laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88) and is accredited by the College of American Pathologists (CAP) to perform high-complexity clinical laboratory testing.

Karius Laboratory | 975 Island Drive, Suite 101, Redwood City, CA 94065
Toll Free: (866) 452-7487 | Fax: (866) 246-6567 | Email: help@kariusdx.com
CLIA # 05D2121236 | CAP # 9497749 | Lab Director: Judith Wilber, PhD, D(ABMM)