KARIUS TEST REPORT

Karius ID: KA-XXXXXX

KARIUS® clarity at speed™ | TEST

SPECIMEN TYPE: PLASMA

SPECIMEN INFORMATION	**Collected**	**Received**	**Reported**	**Specimen ID**
PATIENT INFORMATION	**MRN#**	**Last Name**	**First Name**	**Date of Birth**
INSTITUTION INFORMATION	**Ordering Physician**		**Address**	

TEST RESULTS

MICROORGANISM DETECTED	DNA MOLECULES PER MICROLITER (MPM)*	REFERENCE INTERVAL (MPM)**
Pneumocystis jirovecii	**31,736**	**< 10**

* **M**olecules **P**er **M**icroliter = 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 684 asymptomatic donors

Results can also be accessed via our online secure portal
Karius medical staff are available to answer questions about these results: Phone: (866) 452-7487 | Email: medical@kariusdx.com
Karius is a covered entity under HIPAA

TEST DESCRIPTION

The Karius Test can detect:

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

Full list of organisms is found at: https://www.kariusdx.com/pathogenlist/3.6.0

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 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 or during effective antimicrobial treatment [1, 3, 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 T, et al. *Nat Microbiol*. 2019;4(4):663-674.
[2] De Vlaminck I, et al. *Cell*. 2013;155(5):1178-1187.
[3] Farnaes L, et. al. Diagn Microbiol Invect Dis 2019;94(2):188-191.
[4] Rossoff J, et al. Open Forum Infect Dis 2019;6(8).

KARIUS TEST SPECIMEN COMPARISON

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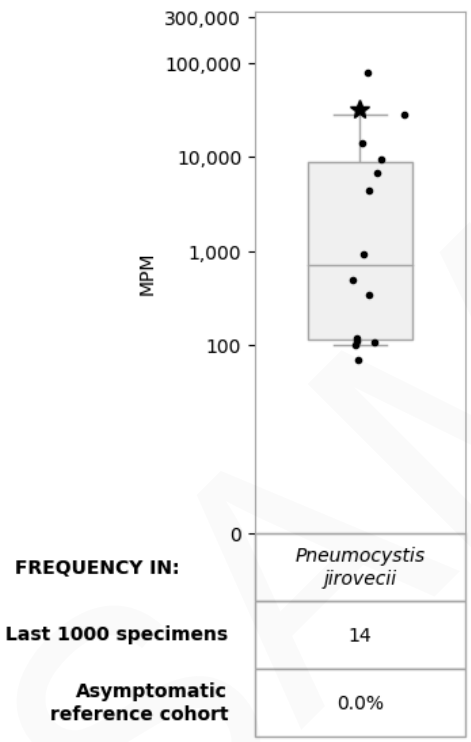
RANGE OF MICROORGANISM QUANTITIES REPORTED IN LAST 1,000 SPECIMENS



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 684 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.

KARIUS TEST RESULT HISTORY

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HISTORY OF KARIUS TEST RESULTS ON THIS PATIENT (MPM VALUES BY DATE COLLECTED)

MICROORGANISM NAME	R.I.	02/07/2020	12/10/2019	08/19/2019	05/20/2019	04/05/2019
Pneumocystis jirovecii	< 10	**31,736**	**9,407**	**5,669**	**5,379**	**33,192**

Notes:

(-) indicates that the microorganism was not detected in statistically significant amounts.

(x) indicates no result was reported for specimen received as it was outside of acceptable quality limits.

Last 6 sample dates and up to 15 microorganisms displayed. For additional results, please contact Customer Success at (866) 452-7487 or help@kariusdx.com.

R.I. stands for reference interval and is measured in MPM.

KARIUS TEST PERFORMANCE 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]		
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 684 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 < 16, which means that across asymptomatic individuals the 97.5th percentile of *E. coli* quantitations was 16 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.

Assay Limitations:

- This test has been validated only for human plasma collected in EDTA anticoagulant.
- Reliable results are dependent on adequate specimen collection, processing, transport, and storage procedures.
- This test has been validated to detect only the microorganisms listed in our pathogen list(https://kariusdx.com/pathogenlist).
- The assay analytical sensitivity is influenced by the depth of sequencing achieved. A minimum sequencing depth is required to pass quality control.Many batches achieve greater than this minimum sequencing depth resulting in enhanced sensitivity.
- MPM values obtained for different microorganisms may not be comparable to each other.
- Co-infecting organisms within a taxonomic family are not reported when detected at less than 25% of the most abundant organismwithin thefamily.
- Co-infecting organisms within a taxonomic superkingdom are not reported when detected at less than 3% of the most abundantorganism within thesuperkingdom.
- False positive or false negative results may occur for reasons including but not limited to sporadic contamination from specimencollection,reagent,and materials or hospital and laboratory environments, technical and biological factors.
- The report of a microorganism signifies the presence of its cell-free DNA in the patient plasma specimen. It may or may not be thecause of aninfection.
- The results obtained from this assay should always be used in combination with clinical examination, patient medical history, and otherfinding.

[1] Blauwkamp T, et al. *Nat Microbiol*. 2019;4(4):663-674.

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