KARIUS

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CODE: **152U**

Test Name: KARIUS TEST

Clinical Laboratory Fee Schedule for 2021 – Virtual Public Meeting
Presentation: June 22, 2020

0152U – KARIUS TEST

Infectious disease (bacteria, fungi, parasites, and DNA viruses), DNA, PCR and next-generation sequencing, plasma, detection of >1,000 potential microbial organisms for significant positive pathogens

PUBLIC COMMENT	RATIONALE
Karius Test (0152U) should be priced by the Gapfill method.	There is no current code which is so close in method and purpose as to be an appropriate and accurate crosswalk.

Purpose	• **Karius Test is a unique and highly complex next generation sequencing test** which based on cell free DNA analysis of plasma (viral, fungal, bacterial). • **Both systemic and localized infections can be identified.** • **The test can be used when** patients are on broad spectrum antibiotics and/or conventional culture/sensitivity testing has failed and/or when biopsy has failed or is contraindicated. • **TAT is very rapid (24 hours).**
Test	• **A complex and highly specialized** extraction technique is required followed by high-depth sequencing of host and microbial cell free DNA followed by bioinformatics analysis of essentially all pathogens with DNA-based genomes (Blauwkamp et al., Nature Microbiol 2019). • **The complexity is similar to an NGS based liquid biopsy analysis** of >50 tumor genes (81455, $2995). The Karius Test list price is $2000.
Lack of Crosswalk	• **Lack of crosswalk:** The complexity (and the methodology) is completely different than the far smaller targeted 12-25 pathogen viral panels (87633), which is NOT an appropriate crosswalk. The technology, scope and comprehensiveness of Karius Test is completely different than this panel. • **Lack of crosswalk:** Test 0010U is an entirely different test and purpose, for strain identification of a known, identified bacteria, e.g. comparison of multiple patients for the strain lineage. Mayo Clinic offers this test with a stated 30-40 day turnaround. https://www.mayocliniclabs.com/test-catalog/Setup+and+Updates/65162

- Discussion

nature microbiology

ARTICLES

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Analytical and clinical validation of a microbial cell-free DNA sequencing test for infectious disease

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Thousands of pathogens are known to infect humans, but only a fraction are readily identifiable using current diagnostic methods. Microbial cell-free DNA sequencing offers the potential to non-invasively identify a wide range of infections throughout the body, but the challenges of clinical-grade metagenomic testing must be addressed. Here we describe the analytical and clinical validation of a next-generation sequencing test that identifies and quantifies microbial cell-free DNA in plasma from 1,250 clinically relevant bacteria, DNA viruses, fungi and eukaryotic parasites. Test accuracy, precision, bias and robustness to a number of metagenomics-specific challenges were determined using a panel of 13 microorganisms that model key determinants of performance in 358 contrived plasma samples, as well as 2,625 infections simulated in silico and 580 clinical study samples. The test showed 93.7% agreement with blood culture in a cohort of 350 patients with a sepsis alert and identified an independently adjudicated cause of the sepsis alert more often than all of the microbiological testing combined (169 aetiological determinations versus 132). Among the 166 samples adjudicated to have no sepsis aetiology identified by any of the tested methods, sequencing identified microbial cell-free DNA in 62, likely derived from commensal organisms and incidental findings unrelated to the sepsis alert. Analysis of the first 2,000 patient samples tested in the CLIA laboratory showed that more than 85% of results were delivered the day after sample receipt, with 53.7% of reports identifying one or more microorganisms.