1. Marvel Genomics PBC Inc.

Presenter: Michael Ronemus PhD

Code: 0156U

0156U: Copy number (eg, intellectual disability, dysmorphology), sequence analysis

Public Comment	Rationale
Crosswalk to 81229 x 1.5 ($1740) Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities	• Consistent code descriptor, same test input, full genome coverage for CNV detection • Superior clinical utility: SMASH can detect smaller CNV events than CMA, resulting in superior diagnostic yield • Increased cost: sample prep, NGS, and analysis

CMS Annual Lab Meeting, Date (June 22, 2020)

Marvel Genomics, Ronemus, Michael PhD

Justification for SMASH Pricing

There are four steps for which performing SMASH incurs additional cost over CPT code 81229.

1. *SMASH sample prep*: the 2-stage process first requires digestion of DNA samples, then reassembly of the fragments. Following this, a standard NGS sample prep is done.
2. *Next-gen sequencing*: SMASH uses next generation sequencing resulting in higher equipment costs over CMA.
3. *SMASH analytics*: this proprietary software package powers the SMASH approach, but requires significant processing capacity. Either a HIPAA-compliant cloud server or a dedicated computational cluster within the CLIA environment is needed for both data processing and long-term storage.
4. *Clinical analysis (labor)*: Marvel's direct comparison of SMASH to CMA has revealed a 70% increase in the number of candidate pathogenic CNV calls by SMASH analysis. Consequently, the time required for clinical geneticists to fully assess SMASH data is approximately increased by roughly 1.5X over CMA.

SMASH Genomic Assay Cost Structure

Step	Cost (USD)	Notes
Biosample acquisition	100	saliva, cheek swab or blood; accessioning & mailing
DNA preparation from biosample	50	standard DNA prep using commercial kit
Two-stage SMASH sample prep	150	custom enzymatic DNA digestion + standard sequencing
Next-gen sequencing	500	multiplexed on NGS instrument
Informatics processing (standard)	25	standard NGS file output
SMASH analytics (custom)	165	HIPAA cloud server or dedicated private cluster
Clinical analysis (labor)	625	2.5 hours of labor @ $250/hour
Clinical report (commercial software)	25	Nx Clinical (BioDiscovery Inc)
Q-PCR validation	100	orthogonal method required for positive tests
Total	**1740**	**see next slide for more information**