Submitted electronically via www.regulations.gov

September 21, 2020

Seema Verma, Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CMS–1736–P
Mail Stop C4–26–05
7500 Security Boulevard
Baltimore, MD 21244–1850

Re: CMS-1736-P — Hospital Outpatient Prospective Payment System, Proposed Rule – Laboratory Date of Service and Packaging Policy

Dear Administrator Verma:

On behalf of the Coalition for 21st Century Medicine (C21), we appreciate the opportunity to comment on the Hospital Outpatient Prospective Payment System (HOPPS) Proposed Rule for Calendar Year 2021. We strongly support the existing laboratory date of service (DOS) policy at 42 CFR 414.510(b)(5) which has expanded beneficiary access to innovative diagnostic testing since implementation in 2018. Likewise, C21 strongly supports CMS' proposal to update the laboratory DOS policy and packaging policy exclusion to include cancer-related protein-based multi-analyte assays with algorithmic analyses (MAAA) tests. We believe this revision will promote similar billing jurisdiction rules for tests that are unrelated to the primary hospital outpatient service. To best promote the consistent application of the laboratory DOS policy, we respectfully recommend two updates to the agency's proposal:

1. **Confirm that the laboratory DOS policy and packaging policy exclusion apply to MAAA tests described by Proprietary Laboratory Analyses (PLA) codes; and**

2. **Make the laboratory DOS policy and packaging policy exclusion applicable to all MAAA tests if they are unrelated to the primary hospital outpatient service.**

C21 comprises many of the world's most innovative diagnostic technology companies, clinical laboratories, physicians, venture capital companies, and patient advocacy groups. C21's mission is to improve the quality of healthcare by encouraging research, development, and commercialization of innovative diagnostic technologies that will personalize patient care, improve patient outcomes, and substantially reduce healthcare costs. C21 has worked with CMS and Congress on the laboratory DOS issue since 2005, and we appreciate the agency's efforts in establishing the current policy at § 414.510(b)(5) and its continued attention to these issues.

I. Laboratory DOS Policy and Laboratory Packaging Exclusions Expand Beneficiary Access to Innovative Diagnostic Testing

In 2017, C21 worked with the agency and other stakeholders on the CY 2018 HOPPS Final Rule to modernize Medicare's policies on laboratory billing jurisdiction in order to address beneficiary access issues that arose from requiring the hospital to bill for precision diagnostic tests performed by an outside laboratory. In response to considerable stakeholder input, CMS promulgated a new regulation at § 414.510(b)(5), under which the DOS for a molecular pathology test or "Criterion A" ADLT performed on a specimen collected from a hospital outpatient is the date of test performance as long as certain conditions are met. This, in turn, allows the performing laboratory to bill Medicare directly for the test, because the test is not considered a hospital service required to be billed to Medicare by the hospital under CMS' "under arrangements" regulations at 42 CFR §§ 410.42 and 411.15(m). Over the past two and a half years, the DOS policy at § 414.510(b)(5) has improved beneficiary access to precision tests and targeted treatment by removing barriers that once led to delayed and canceled orders.

Likewise, C21 continues to support the exclusion of molecular pathology tests and "Criterion A" Advanced Diagnostic Laboratory Tests (ADLTs) from the outpatient laboratory packaging policy. We agree that packaging of these tests is inappropriate, because they "have a different pattern of clinical use, which may make them generally less tied to a primary service in the hospital outpatient setting than the more common and routine laboratory tests that we package."

II. C21 Supports Updates to Laboratory DOS Policy and Packaging Exclusions to Include Protein-Based MAAAs

A. Support Proposal to Include Cancer-Related Protein-Based MAAAs

C21 has long advocated for CMS to update the laboratory DOS policy and laboratory packaging policy exclusions to allow protein-based MAAAs to be billed by the performing laboratory and separately paid on the CLFS. We strongly support CMS' proposal to update the regulation at § 414.510(b)(5) to include cancer-related protein-based MAAAs and to make corresponding changes to the outpatient laboratory packaging policy. We agree with the agency that these tests "have a pattern of clinical use that make them relatively unconnected to the primary hospital outpatient service during which the specimen was collected because the results of these tests are typically used to determine post-hospital care."[1]

Specifically, protein-based MAAA tests (like their DNA- or RNA-based counterparts) are ordered to determine a beneficiary's longer-term care pathway, even if the specimen happens to be collected during a one-day hospital outpatient encounter for convenience's sake. As CMS notes, protein-based MAAAs are "typically used to guide and manage the patient's care after the patient is discharged from the hospital outpatient department because the test results are used to

[1] 85 Fed. Reg. 48772, 49035 (Aug. 12, 2020).

determine potential future oncologic surgical and chemotherapeutic interventions; they would almost never affect the treatment regimen during the same hospital outpatient service in which the specimen was collected, even if the results were available immediately."[2] Instead, this care pathway will typically be determined based on a follow-up discussion between the patient and their care team, in which the test results will be one of several factors under consideration.

Given the similarity in pattern of clinical use between these protein-based MAAAs and the molecular pathology tests and Criterion A ADLTs already subject to § 414.510(b)(5), C21 believes that the agency's proposal will promote parity with respect to billing jurisdiction and separate payment for comparable laboratory tests, helping to ensure that patient access is not impacted by discrepancies in billing regulations. For instance, with respect to cancer-related protein-based MAAAs, the proposal will eliminate the current inconsistency under which molecular pathology tests can be billed by the performing laboratory, but patients continue to face delays in access to similar tests that are based on protein-based MAAA technologies due to the hospital billing requirements of the laboratory DOS and under arrangements regulations.

B. Clarify that Revised Policy Applies to Protein-Based MAAAs Regardless of CPT Code Category

CMS' proposed regulations would revise § 414.510(b)(5) to apply to "a cancer-related protein-based [MAAA]."[3] Based on the text of this definition, **all** protein-based MAAAs should be included in the proposed update to the DOS policy and outpatient laboratory packaging exclusion, regardless of CPT code. However, the Preamble only includes five CPT Category I codes – 81500, 81503, 81535, 81536, and 81539 – as well as "cancer-related protein-based MAAAs that do not currently exist, but that are developed in the future."[4]

CMS should clarify that this policy would also include protein-based MAAAs described by PLA codes, consistent with the proposed regulatory text. The proposed text includes "cancer-related protein-based [MAAAs]," without any distinction by type of CPT code. This language is applicable to protein-based MAAAs regardless of whether they are assigned a Category I or a PLA code. Notably, in the Preamble, CMS explicitly refers to AMA CPT's definition of a MAAA to define the scope of that group of tests.[5] AMA CPT guidance provides that the "PLA Code section…may include a range of medical laboratory tests **including, but not limited to, Multianalyte Assays with Algorithmic Analyses (MAAA)** and Genomic Sequencing Procedures (GSP). The descriptor nomenclature follows, where possible, existing code conventions (e.g. MAAA, GSP)."[6] Based on CMS' use of AMA CPT's definition of MAAA to define the contours of the laboratory DOS policy and the outpatient packaging policy exclusion,

[2] *Id.* at 49036.
[3] *Id.* at 49081.
[4] *Id.* at 49036.
[5] *Id.*
[6] AMA, CPT PLA Codes, *available at* https://www.ama-assn.org/practice-management/cpt/cpt-pla-codes.

the agency should apply § 414.510(b)(5) to **all** tests that AMA CPT would define as protein-based MAAAs.

Including qualifying PLA codes would also align with CMS' existing approach to how PLA codes are treated for purposes of the laboratory DOS policy. A test that would otherwise qualify for these policies as a molecular pathology test or Criterion A ADLT is included **regardless** of whether it is billed using a PLA code. Accordingly, PLA codes are included on the list of codes subject to § 414.510(b)(5) if they qualify as molecular pathology tests or Criterion A ADLTs. The same approach should apply to protein-based MAAAs described by PLA codes, because whether a test is assigned a PLA code or a Category I code has no bearing on the test's pattern of clinical use.

Two of our members' tests, the OVERA test from Aspira Labs (CPT 0003U[7]) and the TissueCypher assay from Cernostics (CPT 0108U[8]), are examples of tests that fall under the DOS policy and the outpatient laboratory packaging exclusion based on the proposed regulatory language. OVERA analyzes five protein biomarkers using an algorithm to detect ovarian cancer risk in women with pelvic or adnexal masses. TissueCypher involves analysis of the expression of 9 proteins from multiplexed immunofluorescence and 15 features derived from the protein biomarkers and morphology, combined using an algorithm to result in a risk score for a Barrett's esophagus patient's progression to high-grade dysplasia or esophageal adenocarcinoma. Both of these tests meet the AMA CPT definition of MAAA, analyze proteins, and are cancer-related. Both have a pattern of clinical use that is unrelated to the primary outpatient service when the specimen is collected at an outpatient encounter.

To implement its proposed regulatory revisions to § 414.510(b)(5) and the outpatient packaging exclusion consistent with the proposed regulatory text, AMA CPT's definition of MAAA, and its current policy with respect to molecular pathology tests and Criterion A ADLTs, CMS should include protein-based MAAAs with PLA codes. We believe the agency should clarify in the Preamble that the definition of "protein-based MAAA" may include any test that meets AMA CPT's definition of the term MAAA, even if the test is assigned a PLA code and included in the PLA section of the codebook rather than the Category I MAAA section of the codebook. Such clarification would confirm that tests described by 0003U and 0108U are included under § 414.510(b)(5) and the outpatient laboratory packaging exclusion, as indicated by the regulatory text. CMS can identify the protein-based MAAAs in the PLA section of the code book by determining which codes' descriptors include **both** multiple proteins and reference to an algorithm. We would also recommend a conforming update to the regulatory text to avoid any ambiguity as to whether protein-based MAAAs with PLA codes are included.

---

[7] Oncology (ovarian) biochemical assays of five proteins (apolipoprotein A-1, CA 125 II, follicle stimulating hormone, human epididymis protein 4, transferrin), utilizing serum, algorithm reported as a likelihood score.
[8] Gastroenterology (Barrett's esophagus), whole slide-digital imaging, including morphometric analysis, computer-assisted quantitative immunolabeling of 9 protein biomarkers (p16, AMACR, p53, CD68, COX-2, CD45RO, HIF1a, HER-2, K20) and morphology, formalin-fixed paraffin-embedded tissue, algorithm reported as risk of progression to high-grade dysplasia or cancer.

III. Recommend Update to Include Non-Cancer Protein-Based MAAAs

C21 also believes that the updates to the laboratory DOS and outpatient laboratory packaging exclusion policies should include all protein-based MAAAs that have a pattern of clinical use that make them relatively unconnected to the primary hospital outpatient service during which the specimen was collected. We are concerned that the limitation to cancer-related protein-based MAAAs is not an appropriate clinical proxy for whether a protein-based MAAA's use is distinct from the primary outpatient service.

Generally, MAAA tests related to complex conditions other than cancer are similar to cancer-related MAAAs in their typical use – the results are used to guide longer-term patient care after the patient's outpatient encounter. In the proposed rule, CMS refers to the Vectra (CPT 81490) test, which is performed by our member laboratory Myriad Genetics, Inc. (Myriad), as an example of a non-cancer related protein based MAAA with a pattern of use potentially "tied to the primary hospital outpatient service."[9] We believe Vectra's pattern of clinical use is as unconnected to the hospital outpatient encounter at which the specimen is collected as the use of the cancer-related protein-based MAAAs listed by the agency as included in its proposal.

Vectra is a MAAA test that analyzes the interrelationship of twelve specific and scientifically selected serum protein biomarkers using a validated algorithm. The test generates a score that represents the level of rheumatoid arthritis (RA) disease activity on a scale of 1-100, with categories of low (<30), moderate (30-44) and high (>44). Typically, a rheumatologist will order Vectra following a physician office visit that involves subjective assessment of the patient's condition through examination of joints and discussion of patient-reported symptoms. After the Vectra test is performed by Myriad, the test report is provided back to the physician. The result is used by the physician to assess RA disease activity and guide future treatment decisions days after the office visit at which the test was ordered.

This pattern of use is as unconnected to a hospital outpatient encounter as the clinical use of a cancer-related protein-based MAAA. Just as the results of a cancer-related MAAA "are used to determine potential future oncologic surgical and chemotherapeutic interventions" outside of the hospital outpatient encounter, Vectra is used by the rheumatologist to make longer-term changes in RA treatment. Given the similarity in clinical pattern of use, it would be inconsistent to demarcate which protein-based MAAAs are included under the revised § 414.510(b)(5) and the outpatient laboratory packaging exclusion based on whether the test is "cancer-related," leaving out similarly complex tests like Vectra.

Moreover, we believe there is very little risk in including protein-based MAAAs in the laboratory DOS policy because the regulations at § 414.510(b)(5) **already** require tests performed and used during the outpatient encounter to be billed by the hospital. Under § 414.510(b)(5)(i) and (iv), the test must satisfy **both** the requirement that it be "performed

[9] 85 Fed. Reg. 48772, 48799 (Aug. 12, 2020).

following a hospital outpatient's discharge from the hospital outpatient department" and the requirement that its results "do not guide treatment provided during the hospital outpatient encounter." If the test is either performed before the outpatient's discharge or guides treatment provided at the outpatient encounter at which the specimen is collected, § 414.510(b)(5) does not apply and the DOS is the date of specimen collection, requiring the hospital to bill for the test. These conditions remain in § 414.510(b)(5), as proposed, and would apply to protein-based MAAAs to the extent they are included in the Final Rule.

IV. Conclusion

C21 strongly supports CMS' laboratory DOS policy at § 414.510(b)(5), which has greatly improved Medicare beneficiary access to valuable precision diagnostic tests that assist physicians in making well-informed treatment decisions. We likewise support the agency's proposal to update the laboratory DOS policy and the outpatient laboratory packaging exclusion to include cancer-related protein-based MAAAs, although we urge CMS to clarify that its proposal applies to these MAAAs irrespective of whether they are described by a Category I code or a PLA code. Furthermore, we believe the policy rationale of promoting access parity between protein-based MAAAs and DNA- and RNA-based tests that are similarly distinct from the primary outpatient service applies with equal force to protein-based MAAAs that are not cancer-related (whether assigned a Category I or PLA code). We respectfully request that CMS update its proposal to include those codes in the revised laboratory DOS and packaging policy exclusion as well.

We have included recommended revisions to the regulatory text below. These proposed revisions would include protein-based MAAAs (whether cancer-related or not, and whether described by a Category I or a PLA code) under § 414.510(b)(5) and the outpatient laboratory packaging exclusion:

> 42 CFR 414.510(b)(5): In the case of a molecular pathology test performed by a laboratory other than a blood bank or center, a test designated by CMS as an ADLT under paragraph (1) of the definition of an advanced diagnostic laboratory test in § 414.502, or a test that is a ~~**cancer-related**~~ protein-based Multianalyte Assays with Algorithmic Analyses **(including Proprietary Laboratory Analysis codes that comprise protein-based multianalyte assays with algorithmic analyses)**, the date of service of the test must be the date the test was performed only if…

Thank you for considering our comments. Please contact me at hmurphy@c21cm.org or (916) 835-5117 should you have any questions or if we can provide you with further information.

Sincerely,

Hannah Murphy
Executive Director
Coalition for 21st Century Medicine