October 19, 2015

Statement of the Coalition for 21st Century Medicine
Advisory Panel on Clinical Diagnostic Laboratory Tests

Session 2: Definition of an Advanced Diagnostic Laboratory Tests

The Coalition for 21st Century Medicine (C21) is pleased to submit these written comments as a supplement to our presentation to the Advisory Panel on Clinical Diagnostic Laboratory Tests for the October 19, 2015 public meeting. As the Advisory Panel and the Centers for Medicare & Medicaid Services (CMS) consider the framework for implementing the provisions of Section 216 of the Protecting Access to Medicare Act (PAMA), we would like to share our perspective pertaining to the definition of Advanced Diagnostic Laboratory Tests (ADLTs) and the ADLT application process.

C21 comprises many of the world's most innovative diagnostic technology companies, clinical laboratories, physicians, venture capital companies, and patient advocacy groups. Given C21's mission to facilitate development and commercialization of innovative diagnostic tests to inform important patient management decisions, we have a keen interest in the transparency and consistency of the agency's policies for laboratory tests, including ADLTs, which are increasingly vital to patient-tailored and effective medical practice.

C21 is a strong supporter of the Section 216 PAMA market based reform of the Clinical Laboratory Fee Schedule (CLFS), and in particular the specific recognition by Congress that innovative ADLTs warrant a "special payment status". C21 believes that implementation of the PAMA ADLT provisions will play a critical role in providing transparency and predictability in the reimbursement for precision medicine. Below we articulate several key elements that we encourage CMS and the Advisory Panel to consider when developing the Final Rule for the Medicare Clinical Diagnostic Laboratory Tests Payment System.

DEFINITION OF AN ADLT

A. The ADLT Definition Is Required to Include Proteins

Congress stated unambiguously in Section 1834(d)(5)(A) (Criterion A) that a clinical diagnostic laboratory test that meets certain other requirements pertaining to its laboratory shall

be an ALDT if it is "an analysis of multiple biomarkers of **DNA, RNA, or proteins** combined with a unique algorithm to yield a single patient-specific result".[1]

While the Proposed Rule reiterates this statutory requirement in full, we are concerned that the following discussion in the Proposed Rule would exclude tests based on proteins from the ADLT definition.[2] CMS declares that "we interpret this provision to require that the test analyze, at a minimum, biomarkers of DNA or RNA," and proposes that an ADLT under Criterion A be "a molecular pathology analysis of DNA or RNA." Notably, proteins — mentioned expressly in the statutory definition — are missing from the proposed regulatory definition.

Congress recognized that multiple analyte protein tests with algorithms play a critical role in precision medicine. The statutory language for an ADLT also closely tracks the AMA CPT definition for "Multianalyte Assays with Algorithmic Analyses" test codes which expressly includes proteins.[3] The MAAA tests are unique laboratory tests that analyze many biomarkers including DNA, RNA or proteins through algorithms.

Where Congress has stated that a test shall be an ADLT if it is "an analysis of multiple biomarkers of DNA, RNA, or proteins," we respectfully suggest that CMS does not have the discretionary interpretive authority to contend otherwise. Congress was not providing CMS with a range of options from which to choose; instead, Congress was articulating the scope of biomarkers that qualify as ADLTs, and plainly intended for these types of protein-based tests to be treated similarly for rate setting purposes.

We recommend that the Final Rule reflect the plain language of the statute, and acknowledge that under Criterion A an ADLT can be an analysis of DNA, RNA, or proteins.

B. The ADLT Definition Should Not Require that the Test Provide New Information

Section 1834(d)(5)(A) requires that to be classified as an ADLT under Criterion A, a test must combine an analysis of multiple DNA, RNA, or protein biomarkers with a unique algorithm. In the Proposed Rule, however, CMS proposes an additional requirement that the test

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[1] Section 1834(d)(5)(A) of Social Security Act (emphasis supplied).
[2] 80 Fed. Reg. 59,397.
[3] The AMA CPT Editorial Panel defines MAAAs as

> procedures that utilize multiple results derived from panels of analyses of various types, **including molecular pathology assays**, fluorescent in situ hybridization assays and non-nucleic acid based assays (eg, **proteins**, polypeptides, lipids, carbohydrates). Algorithmic analysis, using the results of these assays as well as other patient information (if used), is then performed and reported typically as a numeric score(s) or as a probability. (Emphasis added).

must "provide new clinical diagnostic information that cannot be obtained from any other existing test on the market or combination of tests."[4]

In establishing the ADLT definition, Congress was simply concerned that a new test not be duplicative of one another or rely upon the same generic algorithms. Yet the proposed regulatory definition not only goes well beyond the statutory language, it proposes a subjective "novelty" standard that would be near impossible to operationalize. The PAMA statutory definition tracks closely with the MAAA code set definition in AMA CPT. It is clear when these tests utilize a unique algorithm to yield a single patient-specific result. However, the Proposed Rule imposes a higher *subjective* standard — generating "new clinical diagnostic information" — that is neither contained in nor contemplated by the statute.

We recommend that the Final Rule CMS establish an objective standard under Criterion A that a laboratory need only demonstrate or certify that its ADLT algorithm is not duplicative of an existing test. We oppose a subjective "novelty" standard that would exceed the statutory scope.

C. CMS Should Retain Flexibility as to the Utilization of Criterion C

Section 1834(d)(5)(C) grants the Secretary the discretion to establish "other similar criteria" to Criteria A and B by which a test could demonstrate that it qualifies as an ADLT. While the plain language of Criterion C provides significant discretion to CMS, the Proposed Rule proposes that if CMS were to exercise the authority granted by Criterion C in future, "it would be through notice and comment rulemaking".[5]

We believe that Criterion C was inserted by Congress specifically and affirmatively to provide the Secretary with the statutory flexibility necessary to enable CMS policy to reflect with the rapidly-changing technological innovation that characterizes advanced diagnostic laboratory testing. As has become increasingly evident, the traditional notice and comment approach to rulemaking is often an inadequate tool for allowing CMS to maintain pace with the rate of technological development in the advanced diagnostic testing industry. Based on recent innovations in next generation sequencing and other technologies, it is clear that the agency should retain the flexibility under Criterion C to determine to classify new categories of ADLTs.

We recommend that the agency consider other approaches such as authorizing Medicare Administrative Contractors (MACs) to assign ADLT status based on assessment of clinical, technological, and resource similarities to other tests that have already been assigned ADLT status.

[4] 80 Fed. Reg. 59,398.
[5] 80 Fed. Reg. 59,399.

D. The ADLT Definition Should Not Use the Number of CLIA Certificates as a Proxy for a Single Laboratory

Section 1834(d)(5) states that a test qualifies as an ADLT if it meets one of the three criteria and is "***a clinical diagnostic laboratory test covered under this part that is offered and furnished only by a single laboratory and not sold for use by a laboratory other than the original developing laboratory***. . . ." CMS proposes to operationalize the statutory "single laboratory" requirement by requiring that "the laboratory to be a facility with a single CLIA certificate" because "we believe, in most instances, the laboratory's single CLIA certificate will correspond to one laboratory location, or facility." Under the CMS proposed rule, a laboratory with multiple CLIA certificates would not be a single laboratory.[6]

The intent of the statutory requirement is to limit the scope of ADLTs to laboratory developed tests that are only performed by the developing laboratory and not sold commercially as a kit. C21 is concerned that this proposed regulatory definition fails to account for the fact that a single laboratory may often hold more than one CLIA certificate. Based on our own membership, many companies that provide sole source tests have multiple CLIA certificates. For example a single entity may have separate CLIA certificates for both a research laboratory that does not perform the commercial ADLT test, as well as the commercial laboratory that performs and offers the ADLT. A reference to CLIA certificates as a method to operationalize the requirement for a single laboratory would preclude many laboratory tests that are only performed and furnished by the developing laboratory from being ADLTs.

We recommend that the Final Rule avoid using CLIA certificates as a proxy for "single laboratory" that will operate to exclude from the *regulatory* ADLT definition certain laboratories that meet the plain meaning and clear intent of the *statutory* definition.

ADLT APPLICATION PROCESS

A. ADLT Application Should be a Checklist Attestation

Section 1834(d)(5) declares that a test is an ADLT so long as it meets the requirements established therein. In the Proposed Rule, CMS contemplates implementing this provision by requiring laboratories to submit applications for ADLT status.

C21 believes that such applications should be essentially a checklist, limited to requiring laboratories to demonstrate that their tests meet the objective and easily-validated factors contained in the statutory definition. Most of the terms under each criterion can be validated easily through publically-available information. We have attached as an Appendix a model form of an ADLT application.

It is also important to note that classification as an ADLT under Section 1834(d) — in and of itself — does not determine whether an ADLT will be covered by Medicare. Every test

[6] 80 Fed. Reg. 59,396.

classified as an ADLT will still be required to obtain a Local Coverage Determination (LCD), and to demonstrate to its MAC both its analytical and clinical validity. As such, it is reasonable and appropriate that the mere designation as an ADLT be ministerial in nature.

We recommend that the application process by which laboratories would apply for ADLT status to CMS be an objective checklist of the statutory criteria.

B. Confidentiality of Proprietary Information in Application Materials is Essential

The specifications of an advanced diagnostic laboratory test, particularly those details relating to a unique algorithm, are highly confidential and market sensitive. The Proposed Rule suggests that while PAMA provides for the confidentiality of certain information disclosed to CMS by laboratories, PAMA's express confidentiality provision "does not apply to subsection (d) of section 1834A of the Act, which relates to information provided to the Secretary to determine whether a test is an ADLT."[7]

To the extent that laboratories are required to provide proprietary information as part of their applications, we believe strongly that CMS should affirmatively commit to invoking the provisions of 5 U.S.C. § 552(b)(4) that exempt trade secrets from disclosure under the Freedom of Information Act in response to any such public request.

We recommend that the ADLT application clearly state that any proprietary information that is submitted to CMS as part of an ADLT application is protected from public disclosure pursuant to 5 U.S.C. § 552(b)(4).

CONCLUSION

C21 appreciates the time and attention that CMS and the Advisory Panel have devoted to ensuring that the Final PAMA Rule implements the intent of Congress while remaining responsive to the needs to Medicare beneficiaries and diagnostic testing laboratories alike. We encourage CMS and the Advisory Panel to incorporate the above recommendations in the Final Rule, and would be pleased to provide any additional information that may assist in this process.

[7] 80 Fed. Reg. 59,398.

APPENDIX

PROPOSED ADLT Designation Request Form

Applicant must complete Section 1 and one of Criterion A, B, or C.

Section 1 i. Test is offered and furnished only by a single laboratory and not sold for use by a laboratory for use by a laboratory other than the original developing laboratory (or a successor owner)	☐
Applicant Comments:	
ii. Test is Covered by Medicare	☐
Applicant Comments:	
AND (Complete relevant Criterion)	
Criterion A i. Test includes biomarkers of DNA, RNA, or proteins	☐
ii. Test includes an algorithm that provides a single, patient-specific result	☐
Applicant Comments Regarding Criterion A:	
OR	
Criterion B iii. Test is cleared or approved by the FDA	☐
Applicant Comments:	
OR	
Criterion C iv. Test has been proposed for ADLT designation by the regional MAC	☐
Applicant Comments:	