Coalition for 21st Century Medicine
Session 2: ADLT Definition

October 19, 2015

Advisory Panel Meeting

21st centurymedicine

Advanced Diagnostic Laboratory Tests

- C21 strongly supported the enactment of CLFS reform provisions in PAMA, and in particular the Advanced Diagnostic Laboratory Test (ADLT) classification
- C21 agrees with CMS that Congress intended to establish special payment status for these unique innovative tests
- C21 makes the following recommendations on the definition of ADLT to promote continued precision medicine innovation

Statutory Definition of ADLT

ADVANCED DIAGNOSTIC LABORATORY TEST DEFINED.—In this subsection, the term 'advanced diagnostic laboratory test' means 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 (or a successor owner) and meets one of the following criteria:

(A) The test is an analysis of multiple biomarkers of DNA, RNA, or proteins combined with a unique algorithm to yield a single patient-specific result.

(B) The test is cleared or approved by the Food and Drug Administration.

(C) The test meets other similar criteria established by the Secretary.

Social Security Act § 1834A(d)(5)

Criterion A: CMS Proposed Rule

CMS proposes to qualify as an ADLT under criterion A of section 1834A(d)(5) of the Act, a test:

i. **Must be molecular pathology analysis of multiple biomarkers of DNA or RNA;**

ii. **When combined with an empirically derived algorithm, yields a result that predicts the probability a specific individual patient will develop a certain condition(s) or respond to a particular therapy(ies);**

iii. **Provides new clinical diagnostic information that cannot be obtained from any other test or combination of tests; and**

iv. **May include other assays**

Criterion A (i): Biomarkers

STATUTE

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CMS PROPOSED RULE

Criterion A of section 1834A(d)(5) of the Act We interpret this provision to require that the test analyze, at a minimum, biomarkers of DNA or RNA. Tests that analyze nucleic acids (DNA or RNA) are molecular pathology analyses. Therefore, we are proposing that, under criterion A, a test must be a molecular pathology analysis of DNA or RNA. Examples of such tests include those that analyze the expression of a gene, the function of a gene, or the regulation of a gene. The statute also requires that the test analyze ''multiple'' biomarkers of DNA, RNA, or proteins. Therefore, an ADLT might consist of one test that analyzes multiple biomarkers or it might consist of multiple tests that each analyses one or more biomarkers

Criteria A (i): Biomarkers

C21 recommendation:

– "The test must be an analysis of multiple biomarkers of DNA, RNA, or protein"

Rationale:

– Congress recognized that there are protein-based multi-biomarker tests with algorithms

– Clinically, the analysis of proteins provide the current status of a disease state that may not be able to be captured through analysis of DNA or RNA. Protein analysis can be independent of analysis of DNA or RNA.

Criterion A (ii, iii): Unique Algorithm

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CMS PROPOSED RULE

(ii) When combined with an empirically derived algorithm, yields a result that predicts the probability a specific individual patient will develop a certain condition(s) or respond to a particular therapy(ies); and

(iii) Provides new clinical diagnostic information that cannot be obtained from any other test or combination of tests

Criterion A (ii, iii): Unique Algorithm

C21 Recommendation:

- "When combined with an unique algorithm, yields a single patient-specific result"

Rationale:

- 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.
- Insofar as the tests are developed and performed by a single laboratory, they should meet the criterion.
- A "novelty" criterion has no basis in the statute.

Criterion A: C21 Recommendation

C21 Recommends CMS qualify as an ADLT under criterion A of section 1834A(d)(5) of the Act, a test:

i. **Must include multiple biomarkers of DNA, RNA or proteins; and**

ii. **When combined with a unique algorithm, yields a patient specific result**

ADLT Statutory Definition of Criterion A is Clear and Concise

Criterion B: FDA Cleared or Approved

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"(B) The test is cleared or approved by the Food and Drug Administration.

"(C) The test meets other similar criteria established by the Secretary.

CMS PROPOSED RULE

(B) The test is cleared or approved by the Food and Drug Administration.

C21 concurs with CMS

Criterion C: Established by the Secretary

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CMS PROPOSED RULE

(C) No proposal to implement this criterion at this time.

Criterion C: C21 Recommendation

C21 Recommendation:

- Authorize MACs to assign ADLT status based upon MAC's assessment of clinical, technological, resource similarities to other tests assigned to ADLT status

Rationale:

- MACs have experience with laboratories performing in their jurisdiction.
- MACs review substantial amounts of analytical and clinical data when deciding to cover these tests.
- The MACs are, therefore, well-positioned to assess whether a new test is distinct.

ADLT Designation Process

CMS Proposed Rule

- *Appears to contemplate submission to CMS for designation*
- *Details of process not specified*

C21 Recommendations:

1. Checklist type of attestation tracking Criterion A or Criterion B or Criterion C
2. Support required for attestation limited to published and publicly available studies of assay development unless laboratory chooses to provide more information
3. Review and response within 30 days

Rationale:

- Most of the terms under each criterion can be validated easily through publicly available information

Thank you