



ASSOCIATION FOR MOLECULAR PATHOLOGY

Education. Innovation & Improved Patient Care. Advocacy.

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February 10, 2015

The Honorable Fred Upton
Chairman
House Energy and Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Diana DeGette
Member
House Energy and Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515

Sent via e-mail: Cures@mail.house.gov

Re: Regarding the 21st Century Cures Act discussion draft

Dear Members of the Energy and Commerce Committee:

Thank you for the opportunity to submit feedback on the 21st Century Cures Act discussion. The Association for Molecular Pathology (AMP) is an international medical and professional association representing approximately 2,300 physicians, doctoral scientists, and medical technologists who perform or are involved with laboratory testing based on knowledge derived from molecular biology, genetics and genomics. Membership includes professionals from the government, academic medicine, clinical testing laboratories, and the in vitro diagnostics (IVD) industry.

AMP applauds the Energy and Commerce Committee on the 21st Century Cures Initiative and their efforts to take a holistic look at processes through which new cures are developed, and the positive and negative impacts of regulatory policy. In addition to these comments, AMP submitted comments in June in response to the "21st Century Cures: A Call to Action", testimony to the hearing on the topic last September, and last month in response to "A Modernized Framework for Innovative Diagnostic Tests". Links to these documents can be found below.

The 21st Century Cures Act addresses many issues and policies and we are greatly appreciative of the effort of Chairman Upton, Representative DeGette, and the many Representatives that have contributed to this overarching proposed legislation that is intended to accelerate the discovery, development, and delivery of preventive measures, treatments, and cures. Below please find our initial response to three sections that are of particular interest to our members. We look forward to having a continued active role in developing the sections related to the regulation of laboratory developed testing services and the National Institutes of Health (NIH) travel policy when the Committee releases updated legislative language.

Title IV, Subtitle H, Sec. 4161 Improvements in the Medicare Local Coverage Determination (LCD) Process

AMP appreciates the committee's interest in improving the Medicare Local Coverage Determination (LCD) process and agrees with the proposals outlined in this draft legislation. Any changes made to this process must preserve and improve the public's ability to review and comment on these proposed coverage changes. It is just as important that the Medicare Administrative Contractors (MAC) drafting and finalizing these proposals thoughtfully review the public's input to ensure that patients have access to lifesaving diagnostics.

We strongly support the proposal to require at least 45 days for comment on a new or significantly revised LCD and 60 days for LCDs that propose to limit or preclude coverage for an item or service. These requirements will preserve the public's ability to provide input into these proposals, some of which are very complicated in terms of the science and policies involved. Currently, MACs provide comment periods that may be as short as two weeks, making it nearly impossible to provide thoughtful comments. For draft LCDs related to molecular pathology, a thorough review of the literature must be completed before comments can be drafted, making a standard review period of either 45 or 60 days vital for those who wish to comment.

The Association appreciates the committee's proposal to convene an open, public meeting to review the proposed LCD and receive comments from attendees and for MACs to meet upon request with interested stakeholders within the jurisdiction. MACs should also be required to meet with and consider comments from representatives of interested specialty societies. Specialty societies play an integral role responding to draft LCDs by conducting the reviews of the scientific literature that are necessary to provide meaningful comments. Currently, MACs can ignore their comments because they are only required to respond to those who do business in their jurisdiction. We believe that both groups provide critical input to the MACs on their draft policies. AMP would also like to recommend that MACs be mandated to hold webinars on a regular basis to answer questions and provide clarification on draft LCDs. By utilizing the technology available, many more interested stakeholders will be able to participate in the process than may be able to attend a public meeting.

AMP agrees with the committee's inclusion of language requiring MACs to respond to comments with the release of the final LCD the way federal agencies respond to comments upon the publication of final rules, ensuring that all comments are given the thoughtful review they deserve. Palmetto recently published a final LCD on January 1 for which the comment period closed on December 25. This final LCD does not respond to comments. Given the timing of the final LCD's publication and lack of formal response, it is easy to see why AMP and other commenters may be skeptical that our comments were given the consideration they deserve.

We also strongly support the draft legislation's requirement that MACs wishing to adopt another jurisdiction's LCD undertake the full draft LCD process. However, we believe that the other enhancements to this process are necessary to ensure that the second jurisdiction completes a meaningful review. Noridian has proposed and adopted many of the Palmetto's LCDs in the MoDx program, usually without modification. While Noridian provides for a comment period, it appears evident that they generally intend to ultimately adopt the Palmetto policy. A genuine public comment process is even more critical since those in the subsequent jurisdiction (in this case Noridian) cannot participate in the comment process of the first jurisdiction (in this case Palmetto) and typically do not even know about the LCD in the first jurisdiction, exacerbating the sense that what Palmetto does is already a "done deal" in other jurisdictions. Requiring all jurisdictions to hold public meetings, meet with stakeholders within the jurisdiction, potentially hold a webinar, and then respond to comments will help ensure that the comment period is truly meaningful where the public's comments are thoughtfully considered.

Also, we further recommend that the 21st Century Cures Act instructs the Centers for Medicare and Medicaid Services (CMS) to establish a listserv or web-portal where new draft LCDs would be published. AMP is familiar with the current searchable database; however, it is very difficult to navigate. A listserv or web-portal would ensure that those interested would be notified of new drafts upon publication.

Further Comments on the Palmetto MoDx Pilot

AMP has been actively engaged in the LCD process, particularly since the launch of Palmetto's MoDx pilot. The *Protecting Access to Medicare Act of 2014* (PAMA) passed by Congress made changes to the LCD process that AMP supported. However, those changes and the changes proposed in this draft legislation do not address all of the issues our members are experiencing as a result of the MoDx pilot. Its lack of transparency, granularity of coverage decisions, and inappropriate evidentiary requirements have been highly problematic – limiting access

to laboratory tests that are often the standard of care – and should not serve as a model for future coverage decisions – molecular or otherwise.

Greater Coordination among MACs: PAMA § 216 mandated that CMS consolidate to between one and four MACs nationwide. AMP has repeatedly recommended that no fewer than four MACs, if not more, should be maintained for the review of clinical diagnostic laboratory tests. Having multiple MACs will best allow for the discovery and adoption of good practices with effective regional input. If CMS were to elect to have only a single MAC, then the national coverage determination (NCD) process should be followed as any such decision would in actuality be national in scope. The NCD process would involve more highly structured processes for solicitation of input and transparency of consideration than with local determinations. We recommend that Congress urge CMS to maintain at least four, if not more, MACs.

Granularity: CMS has stated that part of the rationale for updating the LCD process for clinical laboratory tests is to bring greater efficiency in the process given that if CMS “require[s] that MACs follow all steps in the current LCD process, we fear that LCDs will not be able to be finalized quickly enough for even a fraction of the thousands of new clinical diagnostic (particularly molecular) tests developed each year.” CMS also asserts that given “multiple molecular diagnostic tests designated to diagnose the same disease may rely on different underlying technologies and therefore, have significantly different performance characteristics,” that Medicare has an “obligation to consider the evidence at a granular level...”

AMP vigorously disputes this underlying rationale. First, there is no meaningful sense in which the statement that there are “thousands of new clinical diagnostic (particularly molecular) tests are developed each year.” This would be like saying that there is no way to develop LCDs that address E&M services because there are hundreds of thousands of practitioners providing them, each in his or her own fashion; indeed, the ability provided by proficiency testing and alternative methods to validate the accuracy and comparability of laboratory tests exceeds that of any other area in clinical medicine. There is no reason tests should be considered for coverage at a more granular level than by CPT code with its associated gene identifiers. If CMS and its MACs consider tests by category for each analyte, as is consistent with the remit of the LCD process of assuring alignment of the service with its medical indications, the volume of tests to be reviewed would be entirely manageable. The standards developed under the *Clinical Laboratory Improvement Amendments*, and not the coverage process, is the best method for addressing the performance characteristics of a given test.

Given the precision of the molecular CPT codes, neither LCD nor NCDs need to be specified beyond the level of the CPT code. The CPT molecular pathology Tier 1, Tier 2 codes with the CPT gene identifiers, and CPT Multianalyte Assays with Algorithmic Analyses (MAAA) codes already cover many of the new tests in current clinical use. These CPT code and CPT gene identifier lists are updated throughout the calendar year and continue to accommodate an expanding list of new tests offered for clinical use that demonstrate a need for new codes. In addition to the resources that are already available in CPT, an official set of gene abbreviation/identifiers have been created for use in the narrative field of the claims form for Tier 2 Molecular Pathology test codes 81400-81408. These CPT molecular pathology code gene identifiers are to give providers, payers, and coders exactly the clinically-relevant level of granularity to facilitate adjudication of claims for all stakeholders. This should provide the granularity that CMS and other payers quite reasonably seek in making molecular coverage decisions. The list was published online on March 12, 2014.

Evidentiary Standards for Coverage: Palmetto has issued guidance on the MolDx coverage process entitled, “TheMolDx Clinical Test Evaluation Process (CTEP),” which provides greater clarity about their process but imposes an evidentiary standard that very few laboratories can meet. This high bar –based on standards for new prescription drugs– is *inappropriate* for laboratory tests, which serve a different function and have a widely divergent economic model, which would impede access to most molecular tests. Further, a double-blinded randomized control trial is not the gold standard for diagnostics as it is for therapeutics, because both

characterizing sufficiently similar patient groups and ensuring sufficiently comparable patient management in a diagnostic (as opposed to a therapeutic) setting is not (and has never been) feasible. Drug trials are generally made against a particular standard of care (placebo or alternate drug), but the clinical utility of outcomes for diagnostics can range over many approaches to a patient's illness.¹ Additionally, as an article by the Cochrane collaborative notes, "... direct measurements of whether a particular diagnostic test does in fact enhance patient health are currently very rare," and suggests an alternate paradigm for assessments of clinical laboratory tests.²

We vigorously oppose any plans to allow or expand adoption of any such CTEP process for the reasons above, for which there was no opportunity to provide comment to Palmetto, as Palmetto issued CTEP without an opportunity for stakeholder input or comment. We urge the committee to mandate that CMS abandon CTEP and not permit the expansion of the MolDx program as currently configured and conducted.

FDA Draft Guidance: This situation is further complicated by the Food and Drug Administration (FDA) draft guidance document to establish a framework of oversight for laboratory developed tests (LDT). Unlike conventional, manufactured, and distributed IVD test kits, LDTs are a medical service throughout the design, performance, and interpretation of the results. As professional services, there are additional opportunities to promote patient safety due to the professional judgment used at every stage. To clearly distinguish the professional services that molecular pathology professionals provide using their education and experience, AMP refers to these services as laboratory developed procedures (LDPs). AMP defines an LDP as "a professional service that encompasses and integrates the design, development, validation, verification, and quality systems used in laboratory testing and interpretative reporting in the context of clinical care."³ The term LDP better represents the nature of complex laboratory testing, which is very much a medical service, and emphasizes the ongoing involvement of appropriately trained and qualified professionals in every aspect of the procedure, in addition to the provided interpretation. The term also acknowledges the inherent connectedness and interdependence amongst the components of the test, the results, and the role of health care professionals. For these reasons, AMP encourages the Committee to refer to these services as LDPs.

AMP is greatly concerned that FDA's proposed risk-based framework for regulating LDPs will severely disrupt physician and patient access to these vital laboratory services. AMP provided extensive comments to the docket on the guidance that will be of assistance to the Committee as you consider legislative language on this policy area and you may access the comments below. Given the significant impact and potential disruption this proposed framework could have on laboratory services and patient care, AMP has requested that FDA adhere to the Administrative Procedures Act and withdraw the draft guidance and instead pursue notice and comment rulemaking. This would help to ensure transparency in the process, that the FDA provides full consideration of the comments received, and that an economic impact study is conducted prior to finalizing any new regulation.

Earlier this year, AMP published a white paper on *A Molecular Diagnostic Perfect Storm: The Convergence of Regulatory & Reimbursement Forces that Threaten Patient Access to Innovations in Genomic Medicine*. The confluence of the effects of both potential FDA regulation and the MolDx program will only further exacerbate health care access issues. Not only does the MolDx program fail to respect the legitimate concern to avoid disruption of beneficiary access to medically necessary services, but combined with the inability to complete the burdensome and resource intensive medical device pathway, laboratories may have no other choice than to drop clinically necessary tests from their menu. The consequences of this would not only be

¹ Personalized Medicine Coalition, "*The Future of Coverage and Payment for Personalized Medicine Diagnostics*," 2014. Downloaded from http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/pmc_the_future_coverage_payment_personalized_medicine_diagnostics.pdf

² L. Di Ruffano et al, "How do tests impact on patient health? Development of an Explanatory Framework," *Cochrane Methods*. *Cochrane DB Syst Rev* 2011 Suppl 1: 1-40

³ Ferreira-Gonzalez et al. (2014). Revisiting Oversight and Regulation of Molecular-Based Laboratory-Developed Tests. *The Journal of Molecular Diagnostics*: 16, 3-6.

felt throughout the healthcare system, but there will be a significant disruption to innovation and investment into developing new or modifying existing tests. Expanding the flawed MolDx program beyond Palmetto and finalizing the draft guidance on LDTs would be a mistake and detrimental to patient care and as such, AMP strongly opposes both policies.

Title, IV Subtitle S Continuing Medical Education Sunshine Exemption

AMP is fully supportive of the inclusion of this provision which would clarify those peer-reviewed journals, journal reprints, journal supplements, and medical textbooks are excluded from the reporting requirement under the Sunshine Act. It is essential that physicians have access to the most relevant, latest emerging scientific knowledge associated with health care delivery. This legislation ensures that physicians' access to the highest quality publications in the world will remain unobstructed. Medical textbooks, consults, conference reports, journal articles and their reprints are written and published for the purpose of building upon and improving clinical understanding. These universally respected publications not only meet the rigorous standards of the highest quality peer-review and editing, but also provide impartial and independent information that provides direct benefit to patients through improved care. We believe the materials listed above are essential components to a physician's continuing medical education and this provision should be preserved in the final version of the 21st Century Cures Act.

Title V, Subtitle D, Sec. 5067 Humanitarian Device Exemption Application to In Vitro Diagnostics

AMP supports this provision which adds language to the Humanitarian Device Exemption so that an exemption can be made for IVDs used to benefit patients in the treatment of diagnosis of diseases or conditions that affect greater than 4,000 individuals in the United States annually. AMP believes the Humanitarian Device Exemption, as it is currently written, fails to adequately capture the full range of IVDs used to diagnose a rare disease or fulfill an unmet need. For example, while cancer is not considered a 'rare' or 'orphan' disease, a number of subtypes of cancer occur less than 1% of the time. Specifically, while lung adenocarcinomas have a rather high incidence, some targetable subtypes are rare and IVDs for these subtypes should be considered rare and eligible for any rare disease exemption. The Humanitarian Device Exemption provision in the 21st Century Cures Act draft removes the 4,000 limit and reaffirms that the exemption is for IVDs for diseases or conditions based on prevalence of that disease or condition, not on the number of times a test is ordered. Additionally, it allows for multiple IVDs to be granted an exemption for the same indication if the Secretary determines they are medically necessary. For these reasons, AMP recommends that this provision be included in the final version of the 21st Century Cures. We note, however, that it will be important for FDA to provide clarity on what information would be required for the Secretary to determine that the severity of the disease or condition requires greater availability of the device to treat or diagnose a disease or condition. In addition, FDA should be required to clarify what a "satisfactory alternative" would be with regards to this exemption.

AMP appreciates the opportunity to provide these comments in response to the 21st Century Cures Act discussion draft. We hope this information helps inform your efforts and that AMP can continue to work with the Committee on other sections that impact molecular pathology professionals and their patients. Please do not hesitate to contact Mary Williams, AMP's Executive Director, at mwilliams@amp.org if we may be of assistance or provide additional information.

Sincerely,

Janina Longtine, MD
AMP President

Additional Material:

- AMP's response to "21st Century Cures: A Call to Action":
http://amp.org/publications_resources/documents/AMPComments21stCenturyCures-ACalltoAction.pdf
- Testimony submitted to Energy and Commerce for the hearing on "21st Century Cures: Examining the Regulation of Laboratory Developed Tests":
http://amp.org/publications_resources/documents/AMP.Testimony.E&C.Hearing.Regulation.LDT.2014-09-08.pdf
- AMP's response to "A Modernized Framework for Innovative Diagnostic Tests":
http://www.amp.org/publications_resources/position_statements_letters/documents/AMPresponsetoECRFifinal.pdf
- MoLDx Clinical Test Evaluation Process (CTEP):
http://www.palmettogba.com/palmetto/MoLDX.nsf/DocsCat/MoLDx%20Website~MoLDx~Browse%20By%20Topic~General~8PKRZF3404?open&navmenu=Browse%5eBy%5eTopic|_|_|
- AMP's comments submitted to the docket on FDA's LDT draft guidance:
<http://amp.org/advocacy/documents/FDAcommentsonLDTguidance-FINAL.pdf>
- AMP's white paper on *A Molecular Diagnostic Perfect Storm: The Convergence of Regulatory & Reimbursement Forces that Threaten Patient Access to Innovations in Genomic Medicine*:
http://amp.org/publications_resources/position_statements_letters/PerfectStorm.cfm