American
Clinical Laboratory
Association

September 28, 2012

Mr. Glenn McGuirk
Centers for Medicare & Medicaid Services
Center for Medicare
7500 Security Boulevard
Mail Stop C4-01-26
Baltimore, Maryland 21244

Dear Mr. McGuirk:

The American Clinical Laboratory Association ("ACLA") is pleased to offer its comments on the Centers for Medicare and Medicaid Services' ("CMS's" or "the agency's") preliminary payment decisions for new and reconsidered Clinical Laboratory Fee Schedule ("CLFS") test codes for CY 2013.[1] ACLA is an association representing clinical laboratories throughout the country, including local, regional, and national laboratories that provide millions of clinical diagnostic laboratory services for Medicare beneficiaries each year. As a result, ACLA members will be affected directly by CMS's decisions on these issues. Our comments focus on CMS's preliminary payment determination for new codes for Tier 1 and Tier 2 molecular pathology tests that are paid under the CLFS and those for codes describing Multi-analyte Assays with Algorithmic Analyses ("MAAAs"). We also comment on the preliminary payment determination for the Galectin-3 test.

In sum, ACLA continues to believe that for the new molecular pathology codes, cross-walking – not gapfilling – is the appropriate approach based on CMS's own regulations. Furthermore, we are very concerned that there are far too many codes to be priced in the very short time available for gapfilling, which could prevent the process from being fair or effective. However, if CMS ultimately decides to direct Medicare contractors to gapfill the tests, the agency should take specific steps to mitigate the potentially adverse impacts of the gapfilling process. With regard to CMS's proposal on the MAAA codes, we believe it is not necessary for CMS to establish a blanket payment policy for all MAAA tests at this time. Before setting a payment policy, it is important for the agency to recognize the function and purpose of the algorithms that are essential to the MAAA tests and why it is not possible to dissociate the algorithms from the so-called "underlying clinical laboratory tests." ACLA disagrees that the Medicare program is precluded from paying for the MAAA tests, and it urges CMS to permit contractors to continue to price and pay for these clinical laboratory tests, as they have for some years. Finally, ACLA disagrees with CMS's proposal to cross-walk the Galectin-3 test to CPT code 83520, a non-specific immunoassay, and believes instead that it should be cross-walked to CPT code 83880, Natriuretic peptide.

[1] Calendar Year 2013, Centers for Medicare and Medicaid Services, New and Reconsidered Clinical Laboratory Fee Schedule Test Codes and Preliminary Payment Determinations (posted Aug. 31, 2012), *available at*: http://www.cms.gov/Center/Provider-Type/Clinical-Labs-Center.html.

I. Molecular Pathology Tests (New codes 812XX through 81408)

Pricing the Tier 1 and Tier 2 molecular pathology codes for CY 2013 is an enormous undertaking in the short amount of time CMS plans to allot to contractors. The agency postponed pricing the tests last year because of the complexity of the task, and the job has not diminished in size. However, CY 2013 begins in just a few months, and neither the agency nor laboratories want to see a lengthy delay in claims processing for molecular pathology tests. Furthermore, regardless of the size of the task, the process should be transparent and should include the participation of interested stakeholders. These circumstances call for a straightforward pricing approach that utilizes information already available to CMS and contractors and that results in as little disruption as possible for stakeholders in the process.

A. The Molecular Pathology Test Codes should be Cross-walked to Existing Codes

ACLA disagrees with CMS's preliminary payment decision for Tier 1 and Tier 2 molecular pathology tests, which is that contractors would price them using gapfilling for CY 2013. The agency acknowledges that commenters at the July 2012 CLFS meeting "generally suggested that these codes be cross-walked back to the stacking codes," but it says that stakeholders did not provide CMS with "specific cross-walks of the stacking codes to the new codes." CMS is concerned that the same test is billed with different stacks and that the stacks may have changed over time; therefore, the agency reasons, gapfilling would allow CMS and contractors the "opportunity to gather current information about the manner in which the tests are performed and the resources necessary to provide them."

ACLA reiterates its previously-stated position that gapfilling is inappropriate for these new codes. Per CMS's own regulations, the new codes must be cross-walked from existing codes. CMS regulations state that cross-walking is appropriate when "it is determined that a new test is comparable to an existing test, *multiple existing test codes*, or a portion of an existing test code."[2] In contrast, gapfilling is to be used "when no comparable existing test is available."[3] The molecular pathology codes are comparable to multiple existing test codes (the stacking codes), some that have been paid under the CLFS for two decades. Therefore, cross-walking is the right approach for these tests. It is not the case that "no comparable existing test is available."

Because the tests are not new, but now simply are represented by new codes, ACLA continues to believe the most appropriate way to price these codes is to cross-walk them to the prices paid for the prior stacking codes. CMS seems to be concerned that laboratories may submit claims using different code stacks for the same test, and it appears reluctant to declare that one set of stacking codes is "more right" than another. These differences result from the fact that different laboratories perform these tests in different ways, based on their own judgment about how best to provide the tests. ACLA continues to believe that the best way to develop a fair, easy, and fast process for pricing the molecular pathology tests is for CMS to determine a

[2] 42 C.F.R. § 414.508(a) (emphasis added).
[3] 42 C.F.R. § 414.508(b).

price for each test based on a utilization-based weighted median of the amounts CMS has been paying for the test. CMS should be able to calculate this based on the cross-walk information provided by laboratories and from its own claims review. Once it has determined the fair price, it would be able to cross-walk to the applicable codes related to that price. This would be an equitable, uncomplicated, and relatively quick way for the tests to be priced, and there is nothing in the regulations or in subregulatory guidance that would preclude CMS from selecting this approach.

B. ACLA's Concerns with the Gapfilling Process

Although ACLA believes it is inappropriate for CMS to direct Medicare contractors to use gapfilling to price the molecular pathology tests, we nevertheless want to share our concerns about such an approach and offer our suggestions on how CMS should provide guidance and direction to contractors if it ultimately selects this approach.

CMS and the Medicare contractors have used gapfilling very rarely in the past decade, and the method generally has been used to price only one code at a time. It certainly has never been used to price more than one hundred new codes simultaneously. It would be a tremendous undertaking for CMS, Medicare contractors, and laboratories alike, and the results of the process would have significant consequences for physicians and patients, as well as for laboratories. ACLA and its members are concerned about the short period of time in which the pricing must be accomplished, and it would be unacceptable – and unnecessary – for there to be a significant lag time between the start of the calendar year and the time when prices finally are established. However, Medicare contractors have a tremendous amount of work to accomplish already, and pricing this many tests in such a short period of time may be unachievable, especially given the need to obtain input from those laboratories for which the contractors process claims.

In the Medicare Physician Fee Schedule proposed rule for CY 2013, CMS stated its concern that it lacks sufficient information about the time and resources required to perform molecular pathology services to allow it to price the tests itself. The Medicare contractors will not be in a better position than CMS to gather this information because the contractors will need the information from laboratories, and it will be extremely difficult for laboratories to assemble such information on a test-by-test basis in such a short time. In particular, it will be extremely difficult for laboratories to provide contractors with information on the resources required for each test; *i.e.*, cost information. It is important to remember that the molecular pathology codes have been paid under the CLFS for many years, and the CLFS is based on *charges*, not on costs.[4] Laboratories simply do not perform the type of micro-costing analysis for each laboratory test that CMS appears to be contemplating. To obtain the information in a consistent way that would be useful to the contractors would be a major accounting undertaking. Even if there were a way to complete such a project, it likely would take far more time than is available, not to mention require a great expenditure of resources.

In addition, it is extremely difficult to quantify the costs involved for each molecular pathology test, in part because a great deal of the cost is in the research and development that

[4] *See* Medicare Claims Processing Manual, Pub. 100-04, Ch. 16, § 20.

goes into a test. A company developing a test may spend tens of millions of dollars developing and validating it. For example, many companies allocate 20 percent of revenue to research and development of new tests and improvement of existing tests. Once a promising test is identified, that test has to be refined and validated. The process that takes a test from discovery to commercial viability is a long and risky one and can take ten years or longer. Once validated, the test may have to meet other regulatory requirements, and the laboratory must educate physicians appropriately to the utility of the test. Also, in order to obtain coverage from payors, laboratories may need to conduct additional studies and data publication to demonstrate the clinical value of the technology. These costs are difficult to quantify in a way that can be captured for these purposes.

ACLA also is concerned that Medicare contractors that have not had an opportunity to familiarize themselves with the molecular pathology tests will be expected to establish fair prices for the tests. The molecular pathology tests are highly sophisticated and specialized. CMS has suggested it will give the same instructions to each of the Medicare contractors, but it will not give contractors much direction for how to approach gapfilling. Some contractors may need more assistance than CMS intends to provide. We also are concerned that prices set by contractors that are not familiar with molecular pathology tests would be included in CMS's calculation of national limitation amounts after the first year.

Further complicating matters are changes among the very Medicare contractors doing the gapfilling. We learned last week that the Medicare Part A and Part B contract for the jurisdiction currently served by Palmetto GBA (J1) has been awarded to Noridian Administrative Services. The notice said that Palmetto "will continue to administer provider claims for up to six months as CMS oversees the transfer of these Medicare contract responsibilities to Noridian Administrative Services."[5] Palmetto will maintain at least some functions for up to six months, but it is unclear whether it will be involved in a gapfilling process for tests furnished by laboratories in the current J1 jurisdiction and if so, whether it could complete the process and what would become of its pricing determinations. This is but one example of how a fluid contractor landscape potentially could affect what already is a complex situation, and there are other jurisdictions in which there may be a change in the Medicare contractor in the midst of the gapfilling process.

Given the potential difficulties presented by a process whereby Medicare contractors would gapfill more than one hundred molecular pathology codes in a short period of time, it is essential that the process be transparent. For stakeholders to trust the process, communication must be open, and CMS, the contractors, and the laboratories must have access to the same information (other than fellow laboratories' proprietary information). For example, ACLA is aware that CMS entered into at least one contract with a consultant "to assist the agency in determining payment rates" for molecular pathology services and to "work with CMS staff to ensure that payment rates for new and existing Clinical Laboratory Fee Schedule codes are set at

[5] Status of MAC Contract Awards (as of Sept. 20, 2012), *available at*: http://www.cms.gov/Medicare/Medicare-Contracting/MedicareContractingReform/Spotlight.html.

accurate levels consistent with the law."[6] ACLA believes it is appropriate, and necessary, for CMS to share the consultants' findings and recommendations with the laboratories that will be affected by them and to give laboratories an opportunity to review and respond to the findings and recommendations.

C. ACLA's Recommendations for a Gapfilling Process

Against the backdrop of our concerns, we offer the following recommendations on how CMS should proceed if it chooses, despite our objections, to direct Medicare contractors to gapfill the molecular pathology codes.

1. Only Contractors With Experience With the Codes Should Be Involved in the Process

Given the complexity of these tests, we believe that only contractors with experience pricing and paying for a given test should participate in the gapfilling process for that test. Some contractors do not process a sufficient number of claims for tests to have the requisite familiarity to develop fair and accurate prices. Because some of the tests are developed as proprietary tests by individual laboratories, one contractor usually has primary responsibility for pricing that test. It seems unnecessary for other contractors to be involved in the process if they have little familiarity with a test. This is especially true given the short amount of time and the large number of tests that would be priced using the gapfill method. Therefore, ACLA believes if a contractor processes only a small number of claims for a molecular pathology test in a given year, that contractor should not be involved in pricing the test.

We also are concerned that payment amounts from contractors unfamiliar with a given test may be factored in to CMS's eventual national limitation amount. To address this issue, CMS should employ a utilization-based weighted median of the contractors' amounts when setting the national limitation amount.

2. CMS Must Give Contractors Clear Directions and Ensure They Meet With Laboratories

CMS should give clear directions to contractors on the process for establishing prices through gapfilling in accordance with regulations and guidance, not only for the sake of fairness, but also for the sake of ease, since there is a limited time to accomplish a great deal. (Our suggestion for how to price the tests is set forth below.) CMS has voiced its intention to give all contractors the same directions; ACLA believes that, at a minimum, CMS must direct all contractors pricing molecular pathology tests to meet with any laboratory that wants to present information and direct all contractors to meet with ACLA.

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[6] Clinical Support for the 2011 and 2012 Updates, Solicitation No. 767-1-1042-04 (posted Jun. 15, 2011), *available at*: https://www.fbo.gov/index?s=opportunity&mode=form&id=37a40a7e35a979d5cfd8947a1b2ee831&tab=core&_cview=0.

Given the short time period in which to price these tests, ACLA believes it will be important for contractors and laboratories to meet to discuss the gapfill process as soon as possible. We recognize that there will be considerable pressure on contractors because of the time and extensive workload involved, but we believe it is essential for contractors to meet with interested parties. If CMS decides that contractors should gapfill the hundred-plus molecular pathology tests, it is important for contractors and laboratories to begin discussions now – not wait until November – to begin the gapfilling process. Additionally, contractors should consider immediately what information they need to gapfill the test codes and whether they already have sufficient information and experience to participate in the process and for which codes. Contractors also should begin to consider how to reallocate internal resources to be able to complete the gapfilling process for a large number of tests in a short amount of time.

ACLA is willing to help facilitate contractors' meetings with laboratories by having preliminary meetings with the contractors. To begin, ACLA can work with contractors to determine which contractors plan to price which tests. A contractor that plans to price tests can describe to ACLA the information it believes it needs in order to gapfill each test code; ACLA then can let the contractor know what information laboratories would and would not be able to provide and why. ACLA and the contractor can determine the best format for the contractor to receive information from laboratories. ACLA also can work with each contractor to develop a schedule for each step in the process: when each contractor will receive information from laboratories, when meetings with laboratories will take place, and when prices will be established. ACLA also can help contractors communicate with a broad swath of the laboratory community to improve the efficiency of the pricing process. If contractors meet with and avail themselves of assistance from ACLA, it is important that such meetings do not take the place of meetings with laboratories who wish to meet with the contractors independently to present information.

3. The Gapfilling Process Must Be Transparent

For a gapfilling process of this magnitude to be credible to stakeholders, it must be open and transparent. This is especially important in light of the fact that gapfilling has been used very rarely in the last decade, and CMS, laboratories, and contractors have little or no experience with such a process. The process can be successful only if all stakeholders communicate openly and frequently.

Laboratories will be sharing information with contractors and with CMS as part of the process, and ACLA and its members ask that CMS and the contractors reciprocate. ACLA requests that CMS provide it with real-time access to the information the agency shares with contractors, including instructions, utilization data, pricing data, and assumptions about resource use. This includes information CMS gets from its molecular pathology test payment rate consultant(s). Additionally, as the process unfolds, both CMS and the contractors should communicate with the laboratory community regularly about the problems and successes of the gapfilling process and work collaboratively to address issues as they arise.

4. Contractors Should Use Cross-Walk Data Submitted by Laboratories, Together with Historical Claims Data, to Identify a Weighted Median to Price the New Tests

ACLA believes that because of the number and complexity of the tests and the short timeframe, the most reasonable method of pricing these codes continues to be basing prices on past payment amounts. Therefore, if gapfilling is used to price the new codes, a hybrid approach utilizing available cross-walk data and historical claims data would expedite appropriate payment determinations. As we have discussed, Medicare has paid for these tests for some time and laboratories have provided cross-walk information to CMS for the new codes. Thus, contractors already have information about how they have paid these tests in the past, and CMS could provide the contractors with laboratory cross-walk data to facilitate historical claims data analysis. Contractors should review claims they have paid for molecular pathology tests to develop a utilization-based weighted median as a basis for a price, and they should use the information they already have at their disposal or to which they have ready access, especially because there is a very short time in which to price a large number of tests. CMS has said that, when using the gapfilling method to price a test, a contractor should look at charges for the test and routine discounts, resources required to perform the test, payment amounts determined by other payors, and relevant information about other comparable tests.[7] The contractors' own claims data, together with cross-walk information provided by laboratories, can yield some of this information and should not be ignored. Rather than starting from scratch, a contractor should determine the historical median amount it has paid for each test, and it should consider the volume of tests it has paid at different prices (if any) when determining the median price. CMS should give contractors clear instructions for how to reach this amount.

II. Multi-analyte Assays with Algorithmic Analyses (New Codes 815XX1 through 815XX7 and XXXX1M through XXXX3M)

ACLA is deeply concerned about CMS's proposal that codes describing MAAAs would not be priced separately.[8] CMS essentially has proposed that the codes would be "inactive" and that only the "underlying clinical laboratory tests on which the MAAA is done" would be paid. The agency's stated rationale is: "Medicare does not recognize a calculated or algorithmically-derived rate or results as a clinical laboratory test since the calculated or algorithmically-derived rate or result alone does not indicate the presence or absence of a substance or organism in the body. Medicare uses other codes for payment of the underlying clinical laboratory tests on which the MAAA is done and we continue to recommend not separately pricing the codes."[9]

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[7] 72 Fed. Reg. 66,276 (Nov. 27, 2007).

[8] Our comments do not address why the Medicare program should pay for MAAA tests, which is an issue that is determined through the usual coverage process. Although we do believe that all of the MAAA tests are reasonable and medically necessary when used in the appropriate clinical circumstances, the only issue we address herein is how the tests should be paid when they are covered.

[9] Calendar Year 2013, Centers for Medicare and Medicaid Services, New and Reconsidered Clinical Laboratory Fee Schedule Test Codes and Preliminary Payment Determinations.

The agency states that "CMS uses other codes for payment of the underlying clinical laboratory tests on which the MAAA is done," but the physician orders the MAAA test – not the "underlying clinical laboratory tests" – and in most instances, the :underlying clinical laboratory tests" are not separable from the MAAA algorithm.

A relatively small number of these codes are being considered for 2013, and the tests represented by the codes differ in their methodologies and approaches. We do not believe that it is prudent for CMS to propose a broad payment policy this year that would apply to all current and future MAAA tests. Rather, CMS should direct Medicare contractors to continue to price and pay for the few MAAA tests for 2013. It is important, however, for the agency to understand what MAAA tests are – and what they are not – when considering a payment approach for this burgeoning category of clinical laboratory tests.

A. Background on MAAA Tests

The American Medical Association's ("AMA's") CPT Code Manual recognizes distinct MAAA codes for the first time in 2013, although these clinical laboratory tests themselves are not new. The AMA has described MAAAs this way: "[MAAAs] are procedures that utilize multiple results derived from assays of various types, including molecular pathology assays, fluorescent in situ hybridization assays, and non-nucleic acid based assays (*e.g.*, 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…[MAAA codes] encompass all analytical services required for the algorithmic analysis (*e.g.*, cell lysis, nucleic acid stabilization, extraction, digestion, amplification, hybridization and detection), in addition to the algorithmic analysis itself."[10]

As the AMA's description demonstrates, MAAA tests vary greatly in their methodologies, in the types of underlying tests to which they are applied, and in the independent value to a physician of the results of any one of the "underlying tests." An algorithm may be applied to the results of a genetic test performed on a tissue sample to determine which of a number of genes show mutations, or an algorithm might be applied to the results of a series of blood or chemistry tests. A physician may understand the implications of one or more of the test results to which a MAAA algorithm is applied, but most often, the results without the algorithm have no meaning to a physician. The MAAA tests are not monolithic, and therefore CMS should proceed cautiously when considering whether to establish broad payment policies for them.

The codes representing the MAAA tests are alike in that they encompass all analytical services performed by a clinical laboratory up to and including the algorithmic analysis. A physician orders a MAAA test itself; the physician does not order each individual service or expect to receive the results of each individual test. Rather, it is the algorithmically-derived probability score that is useful to a physician and that a laboratory reports to a physician. For example, a physician may order a MAAA test that involves the gene expression analysis of

[10] American Medical Association, "Multi-analyte Assays with Algorithmic Analysis Codes," August 2012, *available at*: http://www.ama-assn.org/ama/pub/physician-resources/solutions-managing-your-practice/coding-billing-insurance/cpt/about-cpt/maaa-codes.page.

multiple genes, and the application of that algorithm determines whether a treatment is likely to have therapeutic value. The individual results of each gene's analysis would be of little value to the physician in the context in which the MAAA test is ordered – it is the probability score derived from the algorithm that drives the physician's decision-making. In short, the MAAA tests are far more than the sum of their parts.

It is important to acknowledge that the so-called "underlying tests" to which the MAAA algorithms are applied are not the same as organ- or disease-oriented panels. Those panels are a collection of tests, ordered together. The individual results of each of the test are reported back to a physician, and generally, the physician is capable of making an independent judgment about a patient's condition or prognosis based on the results of any or all of the panel's tests. In contrast, a physician orders the MAAA test, not the "underlying tests." The MAAA tests include a range of tests that may have little or no independent value with respect to the conditions being tested. With few exceptions, physicians cannot analyze the results of the MAAA's "underlying tests" to reach accurate conclusions about their patients' prognoses or susceptibility to therapeutic treatments. The result of the clinically-validated MAAA test is what provides the actionable intelligence about a patient's prognosis or condition.

The MAAA tests represented by the new codes are vital to the development of personalized medicine, which allows health care providers to target care and treatment based on a person's individual genetic makeup. In other words, personalized medicine helps physicians select "the right treatment for the right patient at the right time." As FDA Commissioner Dr. Margaret Hamburg and Director of the National Institutes of Health Dr. Francis Collins wrote in the New England Journal of Medicine, "The success of personalized medicine depends on having accurate diagnostic tests that identify patients who can benefit from targeted therapies…Real progress will come when clinically beneficial new products and approaches are incorporated into clinical practice."[11]

The development and validation of a MAAA algorithm typically takes several years and a significant investment of resources on the part of the developer, sometimes tens of millions of dollars. Ultimately, however, these tests save money, because health care providers will select the best option first, reducing the time and money otherwise required by a trial and error process for selecting effective therapies for patients. An illustration of this is a MAAA test that identifies which early-stage breast cancer patients are at risk of cancer recurrence. It was developed on a decade of outcome data from an untreated breast cancer patient population, ensuring the validity of the results regardless of the treatment regimen ultimately selected. After evaluation of all 25,000 genes in the human genome, 70 genes were identified as the most prognostic breast-cancer specific genes because they affect all steps known to be important for metastasis, including cell cycle regulation, angiogenesis, invasion, cell migration, and signal transduction.[12] This example shows the substantial investment of time and money to develop a test that can significantly improve physician decision-making.

[11] N. ENGL. J. MED. 363;4: 301-304 (Jul. 22, 2010).
[12] *See* van 't Veer, L.J., van de Vijver, M.J. et al., NATURE 2002; 415(31): 530-536.

An example of a MAAA test being priced for 2013 is the OVA1® test, which helps a physician assess the likelihood that an ovarian mass is malignant and determine the course of treatment most likely to be successful for a patient. The OVA1 test is a qualitative serum test that combines the results of five distinct immunoassays into a single numerical result. A higher score equates with a higher probability of malignancy and a greater need for a patient to be referred to a gynecologic oncologist for proper treatment. It greatly increases the chances that a non-gynecologic oncologist can detect malignancies, and it also is highly accurate for identifying women with no malignancies, resulting in fewer unnecessary referrals and complicated surgeries. (A fuller explanation of the OVA1 test is attached as Exhibit A.)

Against this background of the MAAA tests, we address CMS's assertion that the Medicare program cannot pay for the MAAA tests and the agency's proposal that the MAAA codes would be inactive and that codes representing the "underlying tests" could be used, instead.

B. Medicare Is Permitted to Pay for MAAA Tests

The Social Security Act and implementing regulations do not contain CMS's cited limitation on payment for algorithmically-derived results. CMS has not provided a citation for its assertion that a test that does not indicate "the presence or absence of a substance or organism" in the body is not recognized by the Medicare program and payable under the CLFS. ACLA has been unable to determine the source of the statement.[13] There is no such definition of a clinical laboratory service in federal law. Further, Medicare does, in fact, pay for tests that do not indicate "the presence or absence of a substance or organism," such as functionality tests, sensitivity tests, time measurements, and concentration measurements.

C. Laboratories May Not Simply Submit a Claim for a MAAA Test Using Codes for "Underlying Tests"

CMS's proposal that laboratories seek payment for the underlying clinical laboratory tests on which a MAAA is performed does not comport with the way MAAA tests are used and performed, and a laboratory would violate Medicare law in doing so. A physician who orders a MAAA test typically does not order the "underlying tests" – he or she orders the MAAA test. Per Medicare billing rules, a clinical laboratory may submit a claim only for a test ordered by the beneficiary's treating physician.[14] Thus, if a physician does not order the "underlying tests," a laboratory would not be permitted to bill the Medicare program for them. Furthermore, physicians rarely receive the underlying DNA, RNA, or protein measures to which a MAAA algorithm is applied to derive the score, because, generally, there is no value to the physician of those results alone in the context in which the MAAA test is ordered (*e.g.*, deriving a probability

[13] This phrase appears in CLIA regulations in in the definition of "laboratory," but the section in which it appears is irrelevant to payment for tests under the CLFS. *See* 42 C.F.R. § 493.2.

[14] *See* 42 C.F.R. § 410.32(a) ("All diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem. Tests not ordered by the physician who is treating the beneficiary are not reasonable and necessary.").

of malignancy or recurrence). Performance of the "underlying tests" in the first instance is for the sake of applying the MAAA algorithm.

D. Medicare Does Currently Recognize and Pay For Calculated and/or Algorithmically-Derived Results

CMS already pays for other such tests with algorithmically-derived results. For example, in 2005, CMS began reimbursing providers for the HIV bioinformatics code (CPT code 87900, Infectious agent drug susceptibility phenotype prediction using regularly updated genotypic information). This describes a method of determining individually specific and effective drug treatment regimens based on a patient's specific viral load response by applying a predictive model of drug resistance or susceptibility. The AMA's description of the code states, "The prediction of phenotypic behavior derives from comparison of the genotypic patterns of the patient with a large relational database of actual phenotypic and genotypic information that is continuously updated with recent clinical isolates representing the changing nature of the pandemic."[15] Without the HIV bioinformatics information represented by CPT code 87900, the "underlying test" to which the information is applied would have little value for a physician who is trying to determine which treatment regimen will work for a specific patient at a specific time. CMS has recognized – rightly – the value in the complex calculation represented by CPT code 87900.

As you may know, several Medicare contractors already have determined that payment for MAAA tests is appropriate. In setting payment levels, the contractors have looked at a variety of information, including payments received from private payors, the potential savings to the Medicare program due to proper test utilization, and what Medicare would pay for tests that require similar resources (independent of the algorithm). Also, several laboratories currently are in discussions with contractors about payment for different MAAA tests.

Like the HIV bioinformatics code for which the Medicare program already pays, MAAAs are complex calculations with independent predictive value. ACLA recognizes that the Medicare program does not pay health care providers separately for simple calculations, such as the calculation of a patient's low density lipoprotein ("LDL") derived from total cholesterol, high density lipoprotein ("HDL"), and triglycerides, which can be calculated in a physician's office with a pocket calculator. No specialized training is required for such a calculation, and a health care provider does not need to make any investment of time, money, or other resources into developing the calculation. MAAAs, in contrast, are more like the tests with algorithms for which CMS already pays. They weigh numerous variables to arrive at a score, and the relationship between and among the variables are not widely known and must be validated through expensive clinical trials.

[15] American Medical Association, CPT Changes 2006: An Insider's View (2005).

E. A Decision to Make MAAA Codes Inactive Would Negatively Impact Their Development

Dr. Hamburg, Dr. Collins, and many others have recognized the tremendous promise of personalized medicine. However, a broad payment policy not to pay for the MAAA codes could thin the ranks of potential developers of the tests. It would be far too risky for most laboratories to invest years of research and millions of dollars to develop a test that may not be paid by Medicare. Additionally, many commercial contracts instruct laboratories to submit claims in the same way claims are submitted to the Medicare program; the Medicare program's failure to recognize the MAAA codes could eliminate payment by commercial payors. Until now, the Medicare contractors and private payors alike have recognized the value of MAAA tests and have reimbursed providers for them according to their value. CMS's proposal would be a step in the wrong direction and could have a disastrous impact on personalized medicine.

F. CMS Should Maintain the Current Pricing System, Rather Than Establish a Broad Payment Policy for All MAAA Tests

For several years, Medicare contractors have priced the tests now described as MAAAs on a case-by-case basis and generally have developed fair prices for the tests. In general, they have looked at some of the same factors considered in a gapfilling process: charges by laboratories, rates paid by other payors, resource use, and the inherent value of a test to patient management. ACLA recommends that, for the purpose of payment determinations, CMS should continue to defer to Medicare contractors that have expertise with MAAA tests, and the tests should continue to be paid under the CLFS as laboratory tests.

III. Galectin-3 Test

ACLA disagrees with CMS's decision to cross-walk proposed CPT code 827XX ("Galectin-3") to existing CPT code 83520 ("Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified"). We do not believe that code 83520 is an appropriate cross-walk, as it is not comparable technically, clinically, or economically to proposed CPT code 827XX. We support BG Medicine's recommendation that proposed CPT code 827XX be cross-walked to existing CPT code 83880 ("Natriuretic peptide"), as it much more closely resembles the resources and techniques utilized in the performance of the assay.

Furthermore, ACLA disagrees in principle with cross-walking a novel specific immunoassay test to a generic nonspecific immunoassay code. The cost of an immunoassay can vary considerably depending upon the type of assay and the reagents, and CMS must account for these variations in cost and resources in making payment determinations. Payment determinations should take into account the specific nature of each test and CPT code and accurately reflect the resources involved. For these reasons, we respectfully request that CMS instead adopt CPT code 83880 for the Galectin-3 test.

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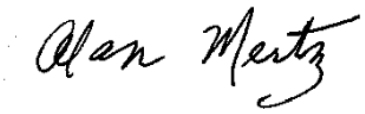
Thank you very much for your consideration of ACLA's comments. We look forward to discussing this with you further and to working with CMS on these important issues.

Sincerely,



Alan Mertz
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Enclosure

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OVA1®, Meeting an Unmet Medical Need

More than 22,280 American women will be diagnosed with ovarian cancer in 2012. More than 15,500 women die annually from ovarian cancer.[1] The overall 5-year survival rate for ovarian cancer is 45%.

The following provides background on OVA1, the medical need it addresses, and how it facilitates the appropriate use of medical resources. Relative to other technologies funded by Medicare, OVA1 is a more efficient use of economic resources (i.e., provides women more years of life per dollar spent by Medicare)[2]. Importantly, this review provides a rationale for the cost of developing the test and that the value it provides is greater than the sum of the individual analytes that are components of the test.

OVA1: What is it?

OVA1 is an FDA-cleared qualitative serum test that combines the results of five immunoassays (CA 125, β2-microglobulin, Transferrin and Apolipoprotein A-1, Transthyretin (prealbumin)) which are incorporated into the OVA1 test score using the OvaCalc® algorithm. OvaCalc is a proprietary FDA-cleared software device that generates a single numerical result between 0 and 10. It is indicated for women who meet the following criteria: over age 18; ovarian adnexal mass present for which surgery is planned, have not had cancer in the past five years, and not yet referred to an oncologist.[3]

The OVA1 test is an aid to further assess the likelihood that malignancy is present even when the physician's independent clinical and radiological evaluation does not indicate malignancy. The test is not intended as a screening or stand-alone diagnostic assay.[3]

A high score indicates a higher probability of malignancy. Specifically, in premenopausal women a score greater than or equal to 5.0 indicates a higher likelihood of malignancy. In postmenopausal women, a score greater than or equal to 4.4 indicates a high likelihood of malignancy. Low scores indicate a lower probability of malignancy (Negative Predictive Value = 94.6%).[3]

OVA1: Clinical Benefits

OVA1 was validated in a prospective, double-blind clinical study using 27 demographically mixed subject enrollment sites with 516 patients. In June 2011, Ueland et al. reported data from this clinical study demonstrating a substantial improvement in sensitivity across a broad range of ovarian malignancies from 75% to 96% when OVA1 results were included in the physician's clinical assessment.[4] The addition of OVA1 also increased the negative predictive value from 89% to 95%, strengthening the prediction disease was absent and giving the generalist confidence to treat patients with a lower risk of malignancy.[4]

OVA1 Facilitates Efficient Use of Medical Resources (Clinical Utility):

OVA1 improves the management of women with an ovarian malignancy. Failure to achieve comprehensive surgical staging and tumor debulking at the time of initial surgery results in serious adverse consequences. Using OVA1 in the management of patients with possible ovarian malignancy, therefore, offers key clinical advantages, including:

1) more appropriate referrals of patients with high probability of malignancy to a gynecologic oncologist[5-7] (Gynecologic oncologists most frequently perform comprehensive surgical evaluation and tumor debulking of early-stage disease (97% of the time) while gynecologists and

general surgeons do so much less frequently (52% and 36%, respectively). Only 9% of patients with early-stage ovarian cancer are treated appropriately according to NIH-recommended surgery and chemotherapy.[8] Only 71% of women with Stage III and 51% of those with Stage IV disease receive recommended surgery and chemotherapy.[8]);

2) fewer unnecessary referrals if the mass is benign[5-7]
3) fewer second surgeries (reoperations occur in about 10% of women who had surgery performed by a non-oncologist.[9,10]);
4) fewer cases where a second surgeon unnecessarily participates in the surgical procedure;
5) more appropriate and efficient use of chemotherapy (Insertion of IP ports occurs in fewer than 10% of women not seen by gynecologic oncologist compared with >40% of women seen by a gynecologic oncologist.)[10;]
6) lower rate of recurrence and expense of treating advanced cancer (the benefit of surgery performed by an oncology expert is found among all FIGO stages)[5-7];
7) longer survival, associated with improved quality of life (women seen by gynecologic oncologists have a relative reduction in annual mortality between 15 and 30%[5-7,11-13]); and· A woman with stage 2 ovarian cancer treated by an expert may gain up to 1.5 years of life. At a population level, OVA1 is expected to add 15-37 years of life per 1,000 women tested.[)]; and
8) Reduced potential to offer fertility sparing procedures in young women with early-stage disease.[14]

Clinical and Analytical Validity:

The biomarker set development and validation was performed on serum samples from over 2,500 women to establish biomarker validity. Each biomarker was discovered, validated and independently validated for its role in Ovarian Cancer, and independent of the original use. The markers function as a unit to provide a single result. Additionally, each marker has been patented for its use in Ovarian Cancer.[15]

The FDA submission included a prospective clinical trial which was led by Dr. Frederick Ueland from the University of Kentucky. The trial involved 27 demographically mixed sites representative of institutions where ovarian tumor subjects may undergo a gynecological examination. The OVA1 test was validated using blood samples from 516 women, 161 of whom had a histologically confirmed malignancy. The study's findings were instrumental to the FDA's decision to clear OVA1 and subsequently led to two peer reviewed publications.[4,16]

Conclusions:

For all of the reasons stated above, the value and the resources to develop and maintain this service is more than the sum of its component tests. Therefore, it is appropriate when making reimbursement decisions to consider the algorithm's value in addition to the component analytes.

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