July 12, 2012

Mr. Glenn McGuirk
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Baltimore, Maryland 21244

Docket # CMS-1441-N

Dear Mr. McGuirk:

The American Association for Clinical Chemistry (AACC) welcomes the opportunity to provide input regarding the new test codes for the calendar year (CY) 2013 clinical laboratory fee schedule (CLFS). Our comments are below:

Multianalyte Assays with Algorithmic Analyses (MAAA)

Rationale for all of the following MAAA codes: The following crosswalk recommendations are based on current coding and coverage rules which require the individual listing and payment for each component test of a panel. The use of algorithmic analysis is generally considered a calculation and is not separately payable.

815XXa Oncology (ovarian), biochemical assays of two proteins (CA-125 and HE4), utilizing serum, with menopausal status, algorithm reported as a risk score

Recommendation: Crosswalk to following 2 component tests:

86304 Immunoassay for tumor antigen, quantitative; CA125	$29.48
86305 Immunoassay for tumor antigen, quantitative; HE4	$29.48
Total:	$58.96

815XXb Oncology (ovarian), biochemical assays of five proteins (CA-125, apoliproprotein A1, beta-2 microglobulin, transferrin and pre-albumin), utilizing serum, algorithm reported as a risk score

Recommendation: Crosswalk to following 5 component tests:

86304 Immunoassay for tumor antigen, quantitative; CA125	$29.48
82172 Apolipoprotein, each	$21.95
82232 beta-2 microglobulin	$22.91
84466 Transferrin	$18.09
84134 Pre-albumin	$20.65
Total:	$113.08

815XXc Endocrinology (type 2 diabetes), biochemical assays of seven analytes (glucose, HbA1c, insulin, hs-CRP, adiponectin, ferritin, interleukin 2-receptor alpha), utilizing serum or plasma, algorithm reporting a risk score

Recommendation: Crosswalk to following 7 component tests:

82947 Glucose, quantitative	$5.56
83036 HbA1C	$13.75
83525 Insulin, total	$16.19
86141 hsCRP	$18.34
83520 Immunoassay NOS (adiponecton)	$18.34
82728 Ferritin	$19.30
84238 Receptor assay; non-endocrine	$51.79
Total:	$143.27

815XXd Fetal chromosomal abnormalities, biochemical assays of three proteins (PAPP-A, hCG (any form), DIA), utilizing maternal serum, algorithm reported as a risk score

Recommendation: Crosswalk to following 3 component tests:

84163 PAPP-A	$21.33
84702 hCG, quantitative	$21.33
83520 Immunoassay NOS (DIA)	$18.34
Total:	$61.00

815XXe Fetal chromosomal abnormalities, biochemical assays of three analytes (AFP, uE3, hCG [any form]), utilizing maternal serum, algorithm reported as a risk score

Recommendation: Crosswalk to following 3 component tests:

82105 alpha-fetoprotein, serum	$23.76
83520 Immunoassay NOS (DIA)	$18.34
84702 hCG, quantitative	$21.33
Total:	$63.43

815XXf Fetal chromosomal abnormalities, biochemical assays of four analytes (AFP, uE3, hCG [any form], DIA) utilizing maternal serum, algorithm reported as a risk score (may include additional results from previous biochemical testing)

Recommendation: Crosswalk to following 4 component tests:

82105 alpha-fetoprotein, serum	$23.76
83520 Immunoassay NOS (uE3)	$18.34
84702 hCG, quantitative	$21.33
83520 Immunoassay NOS (DIA)	$18.34
Total:	$81.77

815XXg Fetal chromosomal abnormalities, biochemical assays of five analytes (AFP, uE3, total hCG, hyperglycosylated hCG, DIA) utilizing maternal serum, algorithm reported as a risk score

Recommendation: Crosswalk to following 5 component tests:

82105 alpha-fetoprotein, serum	$23.76
83520 Immunoassay NOS (uE3)	$18.34
84702 hCG, quantitative (total)	$21.33
84702 hCG, quantitative (hyperglycosylated)	$21.33
83520 Immunoassay NOS (DIA)	$18.34
Total:	$103.10

New Chemistry and Immunology Codes

827XX Galectin-3

Elevated levels of galectin-3 have been found to be significantly associated with higher risk of death in patients with both acute decompensated and chronic heart failure. Galectin-3 is a protein that plays an important role in one of the most common and serious disease processes in heart failure called remodeling. Galectin-3's primary utility is not in predicting poor outcomes but in segmentation and selection of therapy. Patients with elevated galectin-3 have double the mortality rate compared to those with normal galectin-3 levels. The Galectin-3 Assay is a sandwich enzyme immunoassay that uses two highly specific monoclonal antibodies for the direct measurement of galectin-3 in human plasma and serum. The predicate device for 510 FDA approval is BNP.

Recommendation: Crosswalk to 83880 $48.08

Rationale: Galectin-3 is a similar to BNP in that it is a cardiac marker and is determined using EIA methods the same as CPT code 83880 (Natriuretic peptide, BNP). The predicate device upon which FDA based the 510K approval for Galectin-3 was BNP. The cost of the Galectin-3 assay will be similar to that of BNP as well.

861XX Cell enumeration using immunologic selection and identification in fluid specimen (e.g., circulating tumor cells in blood)

Circulating tumor cells (CTCs) represent the point in the metastatic process of solid tumors when cells from a primary tumor invade, detach, disseminate, colonize and proliferate in a distant site. Detection of elevated CTCs during therapy is an accurate indication of subsequent rapid disease progression and mortality in breast, colorectal and prostate cancer. The CellSearch CTC assay involves the automated immunomagnetic selection of CTCs based on an anti-EpCAM antibody cell capture. To perform this assay, a 7.5 ml aliquot of blood is incubated with EpCAM antibody-covered ferroparticles (nanotechnology). Circulating epithelial cells that express EpCAM are isolated in a magnetic field without centrifugation.

Recommendation: Crosswalk to 88239 + 88283 + 88249, $551.39

Rationale: The above three codes, 88239 (Tissue culture, solid tumor), 88283 (chromosome analysis additional specialized banding) and 88249 (chromosome analysis for breakage syndromes, score 100 cells) represent an appropriate crosswalk to achieve reimbursement for the total resources utilized by this testing. These codes align to the circulating tumor cell test for resources, process, clinical similarity and complexity.

867XX Antibody; JC (John Cunningham) virus

The JC virus or John Cunningham virus (JCV) is a type of human polyomavirus that causes progressive multifocal leukoencephalopathy (PLM) in cases of immunodeficiency, as in AIDS or during treatment with immune-suppression drugs. The virus is very common in the general population, infecting 70 to 90 percent of humans; most people acquire JCV in childhood or adolescence. Immunodeficiency or immunosuppression allows JCV to reactivate. In the brain it causes the usually fatal PLM. Several studies since 2000 have suggested that the virus is also linked to colorectal cancer as JCV has been found in malignant colon tumors.

Recommendation: Crosswalk to 86790, $18.25

Rationale: CPT code 86790 represents the typical payment for antibody detection of infectious agents such as JCV. The JVC assay is similar in both purpose and cost to other antibody detection assays.

Tissue Typing - New HLA Codes

The primary use for HLA testing is to match organ and tissue transplant recipients with compatible donors. Different kinds of transplants necessitate different levels of matching between donor and intended recipient. This may determine which HLA tests are performed and which HLA genes are tested for.

868XX1 Antibody to human leukocyte antigens (HLA), solid phase assays (e.g., microspheres or beads, ELISA, Flow cytometry); qualitative assessment of the presence or absence of antibody(ies) to HLA Class I and Class II HLA antigens

Recommendation: Crosswalk to 86807, $56.04

Rationale: CPT 86807 is the code currently used for cytotoxic antibody testing, *standard method*. The methodology is different, but the total cost of work and reagents is comparable and testing is for the same antigens

868XX2 Antibody to human leukocyte antigens (HLA), solid phase assays (e.g., microspheres or beads, ELISA, Flow cytometry); qualitative assessment of the presence or absence of antibody(ies) to HLA Class I or Class II HLA antigens

Recommendation: Crosswalk to: 86808, $42.04

Rationale: CPT 86808 is the code currently used for cytotoxic antibody testing, *quick method*. Methodology is different, but total cost of work and reagents is comparable and testing is for the same antigens.

868XX3 Antibody to human leukocyte antigens (HLA), solid phase assays (e.g., microspheres or beads, ELISA, Flow cytometry); antibody identification by qualitative panel using complete HLA phenotypes, HLA Class I

Recommendation: Crosswalk to: 83516 X 7, $114.38

Rationale: This code is for an immunoassay for an analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method. CPT 83516 is used for a single antigen; however, the new code will be used for a panel of complete Class I HLA phenotypes to identify antibodies to about 80 antigens using a 50+ bead array. The multiple of 7 was selected to approximate the cost.

868XX4 Antibody to human leukocyte antigens (HLA), solid phase assays (e.g., microspheres or beads, ELISA, Flow cytometry); antibody identification by qualitative panel using complete HLA phenotypes, HLA Class II

Recommendation: Crosswalk to: 83516 X 6, $98.04

Rationale: Same code as above. This new code will be used for a panel of complete Class I HLA phenotypes to identify antibodies to approximately 40 antigens using a 30+ bead array. The multiple of 6 was selected to approximate the cost, which is slightly less.

868XX5 Antibody to human leukocyte antigens (HLA), solid phase assays (e.g., microspheres or beads, ELISA, Flow cytometry); high definition qualitative panel for identification of antibody specificities (e.g., individual antigen per bead methodology), HLA Class I

Recommendation: Crosswalk to: 83516 X 11, $179.74

Rationale: Same code as above. This new code will be used for a panel of cloned Class I HLA antigens to identify antibodies to all 80+ HLA ABC antigens using a bead array of up to 98 beads. A multiple of 11 was selected to approximates the cost.

868XX6 Antibody to human leukocyte antigens (HLA), solid phase assays (e.g., microspheres or beads, ELISA, Flow cytometry); high definition qualitative panel for identification of antibody specificities (e.g., individual antigen per bead methodology), HLA Class II

Recommendation: Crosswalk to: 83516 X 10, $163.40

Rationale: Same code as above. This new code will be used for a panel of cloned Class II HLA antigens to identify antibodies to individual HLA DRB1/3/4/5, DQA1, DQB1, DPA1 and DPB1 antigens using a bead array of up to 98 beads. The multiple or 10 was selected to approximate the cost.

868XX7 Antibody to human leukocyte antigens (HLA), solid phase assays (e.g., microspheres or beads, ELISA, Flow cytometry); semi-quantitative panel (e.g., titer), HLA Class I

Recommendation: Crosswalk to: 83516 X 31, $506.54

Rationale: Same code as above. This assay requires a minimum of 3 dilutions. A multiple was selected that approximates the cost, i.e., about 3 times the xx5 code but slightly less than 3x to account for sample preparation.

868XX8 Antibody to human leukocyte antigens (HLA), solid phase assays (e.g., microspheres or beads, ELISA, Flow cytometry); semi-quantitative panel (e.g., titer), HLA

Recommendation: Crosswalk to: 83516 X 28, $457.52

Rationale: Same code as above. Titration using xx6 test to monitor desensitization protocols (for sensitized potential transplant recipients or for monitoring treatment of antibody mediated rejection post transplant) or to assess suitability for desensitization pre-transplant. Likewise, minimum of 3 dilutions required. A multiple was selected that approximates the cost, i.e., slightly fewer than 3x to account for sample prep)

New Microbiology Codes for Respiratory Virus Panels

Patients with respiratory infections frequently demonstrate overlapping signs and symptoms making it difficult to identify a specific microorganism clinically and determine the appropriate therapy.

The following 3 new codes describe multiplexed molecular detection of respiratory virus types and subtypes. Molecular detection is sensitive and specific and the ability to multiplex reactions maximizes cost benefit.

As with influenza virus, most respiratory viruses are RNA viruses and require the additional step of reverse transcription to perform molecular detection as described in the FDA approved assays such as the ProFlu+ from GenProbe, Inc., the xTAG Respiratory Viral Panel from Luminex Corp., and the Verigene Respiratory Virus Nucleic Acid Test from NanoSphere, Inc. These assays use various probe formats to detect the amplified product.

***Infectious agent detection by nucleic acid (DNA or RNA), direct probe technique;* respiratory virus (e.g., adenovirus, influenza virus, coronavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, rhinovirus), multiplex reverse transcription and amplified probe technique, multiple types or subtypes,**

876XX1 3-5 targets

Recommendation: Crosswalk to 87502 + 87503, $148.97

Rationale: The above crosswalk is based on combining 87502 (Infectious agent detection by nucleic acid (DNA or RNA); influenza virus, multiplex for multiple types or sub-types, reverse transcription and amplified probe technique, first two types or subtypes) and 87503 (Infectious agent detection by nucleic acid (DNA or RNA); influenza virus, multiplex for multiple types or sub-types, reverse transcription and amplified probe technique, each additional influenza virus type or subtype), This combination approximates the cost to perform an average of 3 infectious agents.

876XX2 6-11 targets

Recommendation: Crosswalk to 87502 + 5 X 87503, $265.85

Rationale: The above crosswalk is based on combining 87502 (Infectious agent detection by nucleic acid (DNA or RNA); influenza virus, multiplex for multiple types or sub-types, reverse transcription and amplified probe technique, first two types or subtypes) and 5X 87503 (Infectious agent detection by nucleic acid (DNA or RNA); influenza virus, multiplex for multiple types or sub-types, reverse transcription and amplified probe technique, each additional influenza virus type or subtype), This combination approximates the cost to perform an average of 7 infectious agents.

876XX3 12-25 targets

Recommendation: Crosswalk to 87502 + 16 X 87503, $587.27

Rationale: The above crosswalk is based on combining 87502 (Infectious agent detection by nucleic acid (DNA or RNA); influenza virus, multiplex for multiple types or sub-types, reverse transcription and amplified probe technique, first two types or subtypes) and 17X 87503 (Infectious agent detection by nucleic acid (DNA or RNA); influenza virus, multiplex for multiple types or sub-types, reverse transcription and amplified probe technique, each additional influenza virus type or subtype), This combination approximates the cost to perform an average of 17 infectious agents.

New Microbiology Codes for Infectious Agent Genotype Analysis Procedures

Infectious agent resistance to direct acting antivirals continues to grow and expand with the development of new drug therapies.

The UL97 phosphotransferase gene and UL54 DNA polymerase gene mutations are well known to confer resistance to ganciclovir and related therapies in treatment of cytomegalovirus infections in transplant and immunocompromised patients

The polymerase/reverse transcriptase gene confers resistance to antiviral therapies using nucleoside/nucleotide analogs including entecavir and tenofovir for chronic hepatitis B infection. These mutations along with pre-core/core promoter region variations are also required for genotyping.

Similar to the HIV genotyping codes, the following two codes recognize the identification of drug resistance mutations through DNA sequencing of the patient's viral organisms and evaluation of the potential drug resistance.

879X1 Infectious agent genotype analysis by nucleic acid (DNA or RNA); cytomegalovirus

Recommendation: Crosswalk to 87901, $362.28

Rationale: CPT code 87901 (Infectious agent genotype analysis by nucleic acid, HCV) also involves the analysis of two targets (UL97 phosphotransferase and UL54 DNA polymerase genes) as is the case for cytomegalovirus and involves similar costs.

879X2 Infectious agent genotype analysis by nucleic acid (DNA or RNA); hepatitis B

Recommendation: Crosswalk to 87901, $362.28

Rationale: CPT code 87901 (Infectious agent genotype analysis by nucleic acid, HCV) also involves the analysis of two targets (UL97 phosphotransferase and UL54 DNA polymerase genes) as is the case for hepatitis B and involves similar costs.

By way of background, AACC is the principal association of professional laboratory scientists--including MDs, PhDs and medical technologists. AACC's members develop and use chemical concepts, procedures, techniques and instrumentation in health-related investigations and work in hospitals, independent laboratories and the diagnostics industry worldwide. The AACC provides international leadership in advancing the practice and profession of clinical laboratory science and its application to health care. If you have any questions, please call me at (804) 828-0375, or Vince Stine, PhD, Director, Government Affairs, at (202) 835-8721.

Sincerely,

Greg Miller, PhD
President, AACC