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# DIAGNOSTIC TESTING & Emerging Technologies

New Trends, Applications, and IVD Industry Analysis

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## Molecular Testing Avoids Significant Pay Cuts in 2017 CLFS

The Centers for Medicare and Medicaid Services (CMS) issued the final 2017 Clinical Laboratory Fee Schedule (CLFS) on Nov. 21, providing an early holiday present for a small group of labs that provide new specialty molecular tests, and dodged deep cuts proposed in the preliminary schedule.

Here is a look at some key changes you need to know about going into 2017:

### Seven Molecular Assays Stave Off Big Cuts

16 CPT codes for molecular tests that CMS added to the CLFS were the subject of debate earlier this year as CMS proposed interim gap-fill prices for these esoteric and pricey assays, at a discount from their regionalized prices. Led by providers of the assays, the industry asked CMS to reconsider the interim rates. "The proposed gapfill rates are inconsistent with rates established by commercial payers and the Protecting Access to Medicare Act of 2014," contended The Coalition for 21st Century Medicine.

*Continued on page 2*

## 21st Century Cures Act Signed into Law

In a show of bipartisanship and further support of precision medicine and health care innovation—including genomics and other diagnostic innovations, the 21st Century Cures Act has become law. After the House of Representatives and Senate overwhelmingly voted to approve the legislation, President Obama signed it into law on Dec. 13, 2016.

Billions of dollars of funding will support precision medicine initiatives and other efforts to discover, develop and deliver treatments and cures for cancer, Alzheimer's and rare diseases. As the American Clinical Laboratory Association pointed out in a 2014 letter to the Energy and Commerce Committee supporting the 21st Century Cures legislation, diagnostics "are an essential component to providing the most effective and highest quality care" with laboratory testing innovations helping physicians by "providing more accurate diagnoses,

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## Molecular Testing Avoids Significant Pay Cuts in 2017 CLFS, *from page 1*

CMS apparently took heed, dropping the rate cuts and either restoring or increasing the regional prices for seven of the 16 tests listed. Companies benefiting from the change included:

- **CareDx**, which instead of a 77 percent cut got a 47 percent increase on its AlloMap test to identify heart transplant recipients at low risk of rejection (CPT 81595);
- **Biodesix**, which got a 57 percent hike on its Veristrat lung cancer aggressiveness test (81538);
- **Genomic Health**, which got a 51 percent hike on its Oncotype DX colon cancer recurrence test (81525);
- **BioTheranostics**, which got a 23 percent hike on its metastatic tumor origins diagnostic test (81540);
- **Invitae**, which avoided a 33 percent cut on its hereditary breast cancer panel (81432);
- **CardioDx**, which instead of a 28 percent cut got a modest 1.4% increase on its coronary artery disease risk test Corus CAD (81493); and
- **Veracyte**, which instead of a 22 percent cut got a 12 percent increase on its thyroid nodule assessment assay Affirma (81545).

**2017 Medicare Rate for New Molecular Diagnostic Tests**
(Boldface tests are those for which discounts were proposed but not adopted)

| CPT Code | Test | Final National Limitation Rate | Proposed National Limitation Rate | 2017 Price |
|---|---|---|---|---|
| 81412 | 9-Gene Ashkenazi Jewish Screen | $597.91 | $597.91 | $597.91 |
| **81432** | **Hereditary Breast Cancer Panel, 14 Genes** | **$925.00** | **$622.53** | **$925.00** |
| 81433 | Hereditary Breast Cancer, Duplications/Deletions Panel | $159.48 | $159.48 | $159.48 |
| 81434 | Hereditary Retinal Disorder Screen | $597.91 | $597.91 | $597.91 |
| 81437 | Hereditary Neuroendocrine Tumor | $597.91 | $597.91 | $597.91 |
| 81438 | Hereditary Neuroendocrine Tumor, Duplications/Deletions | $597.31 | $597.31 | $152.21 |
| 81442 | Noonan Gene Screen | $597.91 | $597.91 | $597.91 |
| 81490 | Vectra Screen | $586.50 | $586.50 | $597.91 |
| **81493** | **Corus CAD** | **$1,035.10** | **$741.01** | **$1,050** |
| **81525** | **Oncotype DX** | **$2,062.10** | **$848.86** | **$3,104** |
| **81538** | **Veristrat** | **$1,341.87** | **$283** | **$2,112** |
| **81540** | **bioTheranostics** | **$2,355.46** | **$1,522.17** | **$2,900** |
| **81545** | **Affirma** | **$2,864.45** | **$2,240.16** | **$3,200** |
| **81595** | **AlloMap** | **$1,920.98** | **$732.00** | **$2,821** |
| 0009M | VisibiliT | $132.86 | $132.86 | $598 |
| 0010M | 4K Score | $260 | $260 | $260 |

CMS also increased pricing for fetal aneuploidy trisomy risk testing (CPT 0009M) from $132.86 to $598.

### New Pricing Formula for Differential Drug Testing G Codes

The other significant development in the final CLFS affects pricing of the four definitive drug tests capable of identifying individual drugs and distinguish between structural isomers, for which CMS issued HCPCS G codes in 2016—G0480, G0481, G0482 and G0483. To pay for these tests, CMS used a crosswalking formula under which: i. the first two tests performed were paid at the full price of the crosswalk CPT code 82542; and ii. remaining tests within that code were paid at 25% of the crosswalk price.

Proposed deep cuts in molecular diagnostic tests were not implemented—in several cases, CMS actually granted significant price increases.

Industry asked CMS to modify the formula for 2017 claiming that it understates the true costs of performing accurate tests. They expressed concerns that physician office labs without quality control and multiple calibrations were generating high volume of G0483 claims in the first part of 2016. CMS made two proposals to address their concerns:

- **Proposal 1:** Change the crosswalk formula to allow four tests to be priced at the full crosswalk price; and
- **Proposal 2:** Create a new G code to recognize labs that perform a less sophisticated version of differential drug tests.

In the end, CMS opted for Proposal 1. Allowing the four tests to be priced at the full crosswalk price should adequately recognize the resources required to perform these procedures, CMS explains.

**New Formula for Crosswalking Price of G Code Differential Drug Tests**

| CPT Code | 2017 Crosswalk Formula* |
|---|---|
| G0480 | 4 x 82542 + 3 x .25 x 82542 |
| G0481 | 4 x 82542 + 10 x .25 x 82542 |
| G0482 | 4 x 82542 + 17 x .25 x 82542 |
| G0483 | 4 x 82542 + 25 x .25 x 82542 |

* Note: 82542 = full crosswalk price for CPT code 82542

***Editor's Note:*** For information about revamped G Codes for Definitive Drug Testing and changes in the crosswalking of 14 existing CPT Codes, see http://www.g2intelligence.com/molecular-testing-avoids-significant-pay-cuts-in-2017-clfs.

*Takeaway: Here are the three key things to know about the newly finalized CLFS:*

1. *Proposed deep cuts in molecular diagnostic tests were not implemented—in several cases, CMS actually granted significant price increases.*
2. *The pricing formula for the four differential drug test G codes has been changed to allow for billing at the full crosswalk price of CPT 82542.*
3. *CMS crosswalked 14 G and CPT codes into existing CPT codes to eliminate duplication.*

# Quest Diagnostics Leads Personalized Medicine Developments

Public support for personalized and precision medicine (PM) is running ahead of the health care industry's plans to develop and implement PM-based clinical strategies. At least that is the conventional thinking, supported by two recent studies. (See "Public Ahead of Providers in Support of Personalized Medicine," *Diagnostic Testing & Emerging Technologies*, Oct. 26, 2016, for details on the study findings.) But based on the deals we are seeing, the theory that the industry is dragging its feet on PM simply does not hold up—at least within the diagnostics realm.

> *"In today's consumer-driven health care environment, people want to play a more active role in managing their own health and wellness."*
>
> — Steve Rusckowski, CEO, Quest

And it is not just startups and research institutions. Now the giant labs are stepping up and launching actionable PM clinical solutions. Quest Diagnostics has been among the most active on this front. Last month, Quest made national headlines by partnering with IBM Watson Health to launch a new precision medicine service combining genomic tumor sequencing with cognitive computing. (See *Diagnostic Testing & Emerging Technologies*, May 11, 2015, for more about IBM's Watson and genomic analysis for cancer care.)

On Nov. 21, Quest announced another PM blockbuster: QuestDirect, a pilot service in Colorado and Missouri that allows patients to order certain lab tests without a physician's order by downloading a special order form posted on the company's website. "In today's consumer-driven health care environment, people want to play a more active role in managing their own health and wellness," Quest CEO Steve Rusckowski explained in a statement.

Although the Quest deals command the attention, the real impetus for development of PM solutions that consumers can use now, either directly or via their physician, is coming from the growing volume of smaller deals that fly under the radar. Here are just a few of the notable recent PM deals.

### Notable Personalized/Precision Medicine Deals from November

- Genomics startup Helix partners with Mount Sinai for apps enabling consumers to assess their risks of transmitting genetic disorders similar to the deal it made with Invitae earlier this year;
- Amazon begins sales of VeriYou, Good Start Genetics' next-generation sequencing (NGS) test that couples planning to have children can use to screen for cystic fibrosis and spinal muscular atrophy;
- Cancer Genetics launches Focus: Renal, an NGS panel for PM in renal cancers;
- Phillips announces a pair of partnerships involving its IntelliSpace Genomics solution for personalized cancer treatments—one with Westchester Medical Center Health Network, the other with interpretation services provider N-of-One;
- Paradigm Diagnostics closes a $7 million Series B financing to fund rapid commercial expansion of its PCDx tumor sequencing test enabling physicians to offer personalized treatment to cancer patients;
- OneOme launches RightMed, a 22-gene pharmacogenomics assay designed for integration into routine clinical care;
- CombiMatrix secures New York State approval for its NGS screening test for women prior to *in vitro* fertilization.

*Takeaway: The popular perception that personalized medicine is more of a consumer attitude than a clinical reality is being belied—at least within the diagnostics realm—not just by lab giants like Quest but the literally dozens of smaller genomic deals.*

INSIDE THE DIAGNOSTICS INDUSTRY

# New Guidelines Suggest Tiered Approach to Standardize Interpretation and Reporting of Sequence Variants in Cancer

A constant refrain within the diagnostics industry is a need for standardization. Rapidly developing technology and testing methods, the call for interoperability, and the vast amount of data and information producible via molecular testing makes this even more important. The capabilities of next generation sequencing have provided both opportunities and challenges as clinical laboratories interpret and report results of cancer-related sequencing tests.

> *"Cancer genomics is a rapidly evolving field so the clinical significance of any variant in therapy, diagnosis, or prognosis should be reevaluated on an ongoing basis by all of the key stakeholders."*
>
> — Marina N. Nikiforova, MD,

Now, the Association for Molecular Pathology (AMP) has released guidelines developed by an industry working group that recommend standard classification, annotation, interpretation and reporting for somatic sequence variants in cancer. The AMP was joined in this effort by the American College of Medical Genetics and Genomics (ACMG), American Society of Clinical Oncology (ASCO), and College of American Pathologists (CAP).

"Cancer genomics is a rapidly evolving field so the clinical significance of any variant in therapy, diagnosis, or prognosis should be reevaluated on an ongoing basis by all of the key stakeholders," said one working group member, Marina N. Nikiforova, MD, Professor of Pathology at University of Pittsburgh Medical Center, in a statement announcing the release of the guidelines. Nikiforova is also the 2016 AMP Clinical Practice Committee Chair and adds, "These new recommendations resulted from the successful ACMG, AMP and CAP efforts on germline variant interpretation and were additionally informed by the diverse perspectives expressed at the ASCO, AMP and CAP Genomic Roundtable stakeholder discussions."

## Working group gathers industry professionals

Recognizing the need for standardization to maximize the benefits of cancer gene sequencing, AMP gathered industry experts in a working group to review literature, data, laboratory surveys and input from industry via public meetings. The result is a report, "Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology and College of American Pathologists" (Guidelines). The Guidelines will be published in the January 2017 issue of *The Journal of Molecular Diagnostics* but were released online by AMP in December.

"We worked diligently to ensure the cancer genomics community was well represented and it is our hope that we will soon see the widespread adoption of these guidelines leading to improved communication between molecular pa-

thologists, oncologists, pathologists, and most importantly, patients," said Marilyn M. Li, MD, AMP Member and Chair of the Working Group in a statement. Li also serves as Vice Chief of the Division of Genomic Diagnostics and Director of Cancer Genomic Diagnostics at Children's Hospital of Philadelphia. To gain insight into the real world operations of varying laboratories the working group solicited surveys from AMP members. The surveys focused on technical issues and reporting issues. They received 67 responses on technical issues and 44 for reporting issues. Survey responses revealed variation among NGS techniques used and the annotation and reporting of variants.

The U.S. Food and Drug Administration has similarly led industry-wide discussion of standards for NGS interpretation and reporting. Recognizing the vast amount of information that can be yielded from NGS, the difficulty in interpreting results of NGS testing and lack of evidence in some cases linking genetic variants to specific diseases, a recent FDA workshop discussed how best to make use of the results of NGS testing—based on patient and provider preferences. The goal, according to the announcement of the workshop, is "to learn when results are generated in a CLIA-compliant laboratory, which results are of importance to patients and providers, how these results should be returned and how much and what types of evidence supporting interpretation of those results is necessary."

*"It is our hope that the guidelines presented herein will achieve widespread use in the cancer genomics community and engender significant improvements in the practice of genomic testing and precision care for cancer patients."*

— Association for Molecular Pathology

## Need for standardization grows with testing capabilities

The Guideline document explains the significant volume of information regarding genetic variations that NGS yields and the clinical benefits in terms of diagnosis and treatment, concluding "therefore, it is imperative to unify the interpretation and reporting of molecular results among laboratories performing these tests."

The guidelines declared standardization is needed for the following quality of care related reasons: "accurate reporting of tumor response to targeted therapy; establishment of national guidelines for patient care; and collaborative institutional clinical trials, thereby supporting the need for standardization among laboratories performing these tests."

The authors conclude "It is our hope that the guidelines presented herein will achieve widespread use in the cancer genomics community and engender significant improvements in the practice of genomic testing and precision care for cancer patients."

## Tiered classification system

The Guidelines share several recommendations for laboratories involved in such NGS variant testing for cancer. To categorize variants, the guidelines recommend using a four-tiered system that categorizes somatic variants accord-

## INSIDE THE DIAGNOSTICS INDUSTRY

> *"It is important to recognize that molecular genetics in cancer is a rapidly evolving field; therefore the level of evidence in therapy, diagnosis, and prognosis should be continuously evaluated based on evolving research data and modified accordingly."*
>
> — Association for Molecular Pathology

ing to their impact on clinical care—using "currently available evidence."

- **Tier I** would be variants with strong clinical significance based on evidence regarding FDA approved therapy and "well-powered studies with consensus from experts in the field."
- **Tier II** covers variants of potential clinical significance based on evidence from FDA approved treatments but for different tumor types or investigational therapies, small published studies having some consensus, and preclinical trials or case reports without consensus.
- **Tier III** includes variants of unknown clinical significance when there is no "convincing published evidence of cancer association" and the variant isn't "observed at a significant allele frequency in the general or specific subpopulation databases, or pan-cancer or tumor-specific variant databases."
- **Tier IV** is for benign or likely benign variants when there is a lack of published evidence of cancer association and the variant is "observed at significant allele frequency in the general or specific subpopulation databases."

With regard to the evidence relied upon to categorize the variants, the authors note "It is important to recognize that molecular genetics in cancer is a rapidly evolving field; therefore the level of evidence in therapy, diagnosis, and prognosis should be continuously evaluated based on evolving research data and modified accordingly." The authors discuss levels of evidence and indicate specific sources can shift between evidence categories as more becomes known about the source.

### Tiered System

- **Tier I** Variants with strong clinical significance
- **Tier II** Variants with potential clinical significance
- **Tier III** Variants of unknown clinical significance
- **Tier IV** Variants deemed benign or likely benign

### Other observations and recommendations

With regard to variant identification and annotation, the guidelines recommend laboratories pay close attention to the bioinformatics pipeline used and emphasizes the need for validation of that pipeline. The authors recommend against *in silico* prediction algorithms being "used as the sole evidence for variant classification or clinical decision making."

When relying on databases to review genomic information, the guidelines caution laboratories to fully understand the database in terms of its content, how it is aggregated, the limitations of the database, how genome information is annotated, the source of the data and data quality of the diagnosis provided. The report then surveys various types of databases and their usefulness with recommendations

## INSIDE THE DIAGNOSTICS INDUSTRY

*Consider using tables to provide information about "genomic coordinates, genome build and transcript reference sequence."*

for evaluating the data within the databases. The authors also address internal laboratory databases and "urge clinical laboratories to contribute their well-curated variants to public variant databases to facilitate accurate interpretation of somatic variants."

In discussing how test results should be reported the Guidelines offer a few tips for laboratories:

- Contain all necessary information for patient and physician explaining what was done, results and factors influencing interpretation as well as what the test doesn't reveal;
- Keep reports "short, simple, and to the point";
- Make sure most critical information is provided clearly, conspicuously, and at the start of the report so it is "seen and understood";
- Include standard and colloquial nomenclature;
- Don't limit reports to just positive findings;
- Consider using tables to provide information about "genomic coordinates, genome build and transcript reference sequence";
- Explain distinction between somatic and germline alterations;
- Clearly indicate date of issue for the report;
- Indicate method, assay performance characteristics and "critical quality metrics for assay run";
- Don't just list gene names but explain what was tested; and
- Provide results in format capable of being incorporated into the electronic health record (pdfs or other formats that have to be scanned are not ideal).

### Guidelines Recommend Policies Needed Regarding Germline Variants

In discussing germline variants, the authors recommend laboratories adopt some specific policies that:

- discuss "detection, disclosure/nondisclosure, and interpretation/reporting of germline variants" when the laboratory conducts testing with "a normal, matched control tissue ... sequenced along with the tumor" which then reveals germline variants;
- address "testing a germline sample for a genetic variant found in a malignancy to confirm the germline or somatic origin of the variant using a clinically validated germline test after appropriate patient consent is received or per request of a clinician";
- direct how to report "variants of unknown significance and disclosure of secondary findings, including under what circumstances such findings will or will not be reported."

*Takeaway: Industry tackles complexities of somatic variant testing and key organizations provide consensus on standards for interpreting and reporting results to assist patients and clinicians in decision-making.*

21st Century Cures Act Signed into Law, *from page 1*

quicker; allowing physicians and patients to choose the best treatment, first and sooner."

*"Passage of this important legislation is a milestone in improving the innovation ecosystem for medical technology and ensuring the availability of new life-saving, life-enhancing devices and diagnostics for patients."*

— AdvaMed

There are four main parts to the legislation: Part I addresses discovery, innovation and opioid abuse; Part II addresses research and development, patient access to new products, protection for human research subjects, and data sharing; Part III addresses health care delivery, interoperability and telehealth; and Part IV addresses Medicare and Medicaid reforms. Here are some highlights of the legislation:

- $4.8 billion in funding for NIH; funds will in part support the Precision Medicine Initiative ($1.5 billion) and the Cancer Moonshot ($1.8 billion)
- $500 million for the FDA to modernize its regulatory efforts and secure the best talent
- Measures that promote electronic health records and interoperability so patient care is seamless
- $1 billion to states for opioid abuse prevention and treatment programs including improvement of drug monitoring programs

Summing up comments of many stakeholders in the life sciences industry, AdvaMed praised the law stating: "Passage of this important legislation is a milestone in improving the innovation ecosystem for medical technology and ensuring the availability of new life-saving, life-enhancing devices and diagnostics for patients."

But not all are happy with the legislation. An online opinion article in *STAT* criticizes what it claims are weakened FDA oversight measures for new drugs and devices: "These provisions would unravel the FDA, turning it from the treatment watchdog it is today into a puppet of the pharmaceutical and medical device industry. If the 21st Century Cures Act is passed as written, clinicians could be given potentially deadly drugs and devices to prescribe to their patients, blessed by this new version of FDA approval."

*Takeaway: Precision medicine initiatives get a significant show of support from both political parties.*

## Child-Parent Screening Effective to ID Familial Hypercholesterolemia

Child–parent hypercholesterolemia (FH) screening is a practical and effective way of conducting population-based screening to identify the condition associated with premature cardiovascular disease, according to a study published Oct. 27 in the *New England Journal of Medicine*. Screening for both cholesterol and genetic mutations found that about one in 270 kids has FH, which is higher than previous estimates.

The researchers used a strategy that screens young children (aged one to two years) for cholesterol during routine immunization visits. This offered the

advantage of eliminating the need for an additional office visit and occurred at a time when measurement of cholesterol is most discriminatory. Parents were only screened if a child had positive results.

*"This is the first demonstration that child-parent screening works on a large scale."*
— David Wald, F.R.C.P.

In the study, more than 10,000 children were screened (March 2012 through March 2015) at 92 general medical practices in the United Kingdom. Heel-stick capillary blood samples were used for both measurement of cholesterol and for testing for FH mutations in children. Based on previous meta-analysis, it was estimated that a total cholesterol cutoff value of 1.53 multiples of the median (MoM) would correspond to levels at approximately the 99.9th percentile. All children were tested for 48 FH (FH48) mutations. Children with a cholesterol level of at least 1.53 MoM plus either an FH mutation or a repeat cholesterol level of at least 1.53 MoM were considered positive for FH. Parents were considered positive if they had the same FH mutation as the child, or if no mutation was identified, the parent who had high cholesterol.

The researchers found that 92 children had a cholesterol level of at least 1.53 MoM. Thirteen of these children had an FH48 mutation, and seven additional children had an FH mutation identified during DNA sequencing, a finding that indicates the incremental value of sequencing, the authors say. Among 10,003 children who had a cholesterol level of less than 1.53 MoM, 17 had an FH48 mutation. All the children were heterozygous for the familial hypercholesterolemia mutation.

In 27 of the 32 parents, the parent with the higher cholesterol level had the FH mutation. Ninety percent of the parents who had positive FH screening results had cholesterol values above the 75th percentile. Twenty-seven of the 28 parents with positive screening results for FH subsequently started statin treatment. All parents reported that they thought the screening was worthwhile with no negative effects.

Using an initial cholesterol cutoff value of 1.35 MoM (the 95th percentile, instead of 1.53 MoM, the 99th percentile) identified 12 more children with FH. Eight of these children had an FH48 mutation. The 1.35 MoM cutoff also identified 12 more parents who had positive screening results for FH.

In addition to being effective, the authors say their FH screening strategy is affordable. They estimate cholesterol testing costs $7 and DNA sequencing costs $300 per sample, yielding a cost of $2,900 per person identified as having positive screening results for FH, without an additional service delivery cost when screening is combined with immunization.

"This is the first demonstration that child-parent screening works on a large scale," said lead author David Wald, F.R.C.P., from the Queen Mary University of London in the United Kingdom, in a statement. "It's the only screening method that stands a reasonable chance of covering the whole population and identifying those at highest risk of an early heart attack."

*Takeaway: A population-based, familial screening strategy for FH is effective at identifying children and parents that may be at high risk for cardiovascular disease.*

## G2 INSIDER

### Epigenetic Testing Predicts Aging, Mortality

Epigenetic changes, measured by DNA methylation, may be a predictor of biological age, according to a study published in the September issue of *Aging*. The multicenter study found that epigenetic age predicts all-cause mortality above and beyond chronological age and traditional risk factors.

The meta-analysis included 13 different cohorts, including large studies like the Framingham Heart Study and the Women's Health Initiative, for a total sample size of 13,089 individuals, (non-Hispanic whites, n=9,215; Hispanics, n=431; and Blacks n=3,443). Epigenetic age was measured using two methods—relying upon markers assessing methylation of cytosine linked to guanine by a phosphate group (CpGs). Additionally, the researchers examined whether incorporating information on blood cell composition, which changes during aging, into the epigenetic age metrics improves predictive power for identifying mortality risk. Chronological age was compared to the blood's biological age, creating an epigenetic clock (AgeAccel) to predict each person's life expectancy. A positive value of AgeAccel indicated that the epigenetic age was higher than expected, based on chronological age.

*"[O]ur results suggest that at least one of the mediating processes relates to the epigenetic age of blood tissue and that this process is independent of age-dependent changes in blood cell composition."*

— Brian Chen

The researchers found that measures of epigenetic age acceleration were significantly predictive of mortality, independent of chronological age and traditional risk factors (e.g. smoking status, physical activity status, or major chronic diseases), across all racial and ethnic groups. Incorporation of blood cell composition into epigenetic age measures resulted in even more accurate estimations of time to death.

"While epigenetic processes are unlikely to be the only mediators of chronological age on mortality—in fact, multiple risk factors have stronger effects on mortality—our results suggest that at least one of the mediating processes relates to the epigenetic age of blood tissue and that this process is independent of age-dependent changes in blood cell composition," write the authors led by Brian Chen, a fellow from the National Institute of Aging in Baltimore, Md.

About five percent of the participants aged at a faster biological rate, which is associated with approximately a 50 percent increased risk of death and a shorter life expectancy. In contrast, 20 percent of participants age at a slower biological rate, which was tied to a decreased risk of death.

Principal investigator Steve Horvath, Ph.D., Sc.D., from University of California, Los Angeles, explains that if two 60-year-old men both smoked to deal with high stress, but one of the man's epigenetic aging rate ranks in the top 5 percent, while the second's aging rate is average, the likelihood of the first man dying within the next 10 years is 75 percent compared to 60 percent for the second.

*Takeaway: A population-based, familial screening strategy for FH is effective at identifying children and parents that may be at high risk for cardiovascular disease.*

## CDRH Emphasizes Biomarkers and Precision Diagnostics in 2017 Priorities

Precision medicine and biomarkers can help the U.S. Food and Drug Administration (FDA) ensure safety of medical devices. That's according to the FDA Center for Devices and Regulatory Health's (CDRH) Fiscal Year 2017 regulatory science priorities.

The agency says these priorities "help focus the Center's attention on the most important regulatory science gaps or needs." The priority most relevant to the diagnostics sector is an emphasis on using precision medicine to improve device review and monitoring and predict device-drug interactions. "Development of clinical diagnostic assays, software and other tools that promote standardization of in vitro tools for a precision medicine approach that predicts clinical performance are necessary to expedite the use and to improve the quality of medical devices," according to the CDRH. Additionally, "[c]haracterization data of existing samples and analytes is needed where no agreed-upon reference standards exist."

Further, the agency emphasizes the importance of biomarkers for diagnosing mild forms of trauma and early stage disease to take advantage of "critical therapeutic windows."

Other items on the FDA list of priorities include:

- Using Big Data to assist in regulatory decision-making
- Making improvements to clinical trial design
- Increasing medical device cybersecurity and advancing digital health
- Advance tests and methods for predicting and monitoring medical device clinical performance

The full document addressing the CDRH's priorities for 2017 can be found on the FDA website.