G2 INTELLIGENCE
A DIVISION OF PLAIN LANGUAGE MEDIA

NATIONAL INTELLIGENCE REPORT™

Covering Government Policy For Diagnostic Testing & Related Medical Services

Celebrating Our 37th Year of Publication

Vol. 16, Iss. 14, July 28, 2016

INSIDE THIS ISSUE

National Academies' Report Offers Hope for Scrapping Proposed Changes to Research Regulations 1

CMS Report to Congress Cites Program Integrity for $42 Billion in Savings, $12.40 ROI 1

Lab and Pathology Industry Responds to Proposed MACRA Rules 3

FDA Issues Draft Guidelines for Companion Diagnostics 4

FDA Seeks Public Comment on Blood Donor Deferral Policy to Decrease HIV Transmission 5

FDA Approves Rapid Molecular Diagnostic Test for Detecting Antibiotic Resistance 6

www.G2Intelligence.com

G2 INTELLIGENCE Upcoming Events

Lab Institute 2016
Oct. 26-28, Hyatt Regency
Washington on Capitol Hill
www.labinstitute.com

National Academies' Report Offers Hope for Scrapping Proposed Changes to Research Regulations

The National Academies of Sciences, Engineering and Medicine released a report last month critical of a controversial proposal to revise regulations that protect people who participate in medical research. The National Academies further recommends that the Obama administration withdraw its proposal and, with Congress, appoint an independent commission to examine and update the ethical, legal, and institutional frameworks governing research involving human subjects.

Known as the Common Rule, these regulations set ethical standards for federally funded researchers who work with human subjects. However, these regulations were put in place in 1981 and have lacked substantial updates over the last several decades, a time in which research technology and sharing of data has changed dramatically. This prompted the U.S. Department of Health and Human Services (HHS) to propose major revisions and "modernizations" to the rules in September 2015. But, the research community largely criticized the revisions as being complex and potentially onerous.

One of the most controversial new requirements would require scientists to obtain explicit consent from patients before using their blood or tissue for research, even when the samples are not linked with any information that could be used to identify the patients. The Common Rule currently allows for

Continued on page 2

CMS Report to Congress Cites Program Integrity for $42 Billion in Savings, $12.40 ROI

In a new report to Congress, the Centers for Medicare & Medicaid Services states the Program Integrity activities have saved Medicare and Medicaid $42 billion during Fiscal Years 2013 and 2014 (Oct. 1, 2012 - Sept. 30, 2014). The agency claims $12.40 was saved for every dollar spent on program integrity efforts. Those efforts included a focus on ensuring providers seeking to enroll in Medicare are properly screened, using predictive analytics to identify fraud and abuse, and coordination with law enforcement. Specifically, the agency credited assistance from Medicare contractors, state Medicaid agencies and law enforcement for these successes.

Continued on page 8

National Academies' Report Offers Hope, *from page 1*

research to be conducted using previously collected biospecimens (e.g., blood, urine, or tissue samples) without informed consent as long as the specimens are de-identified. The proposed revisions require "broad," written consent from specimen donors for future unspecified uses of their de-identified biospecimens—a change in practice that the National Academies calls a "significant departure" from current practice.

> *"Research on excess or residual biospecimens has contributed enormously to the growth of medical knowledge for nearly a century and a half, improving human health with little evidence of harm to individuals whose biospecimens were used in this way."*
>
> — National Academies

"Research on excess or residual biospecimens has contributed enormously to the growth of medical knowledge for nearly a century and a half, improving human health with little evidence of harm to individuals whose biospecimens were used in this way," the National Academies' report says. "Moreover, implementation of the proposed rule would necessitate maintaining a link between the consent document and the biospecimens—a proposal that raises substantial risks of re-identification and loss of privacy."

Experts say with broad consent, patients or research participants give their blanket consent to the use of their biological sample and/or clinical data in research that may not be underway or even specified at the time of consent. By comparison, narrow consent is limited to a specific research endeavor and based on concrete information about planned or currently active research. Given the rise of "big data" and biobanks enabling large-scale genomic research, changes to consent could have enormous implications to the research.

Several recent efforts have tried to illustrate the public's preferences regarding consent. A systematic review published Nov. 19, 2015 in *Genetics in Medicine* found that only a minority of respondents favored broad consent when other options, such as tiered or study-by-study consent, were offered. While undeniably some participants objected, broad consent was often preferred over tiered or study-specific consent, when samples were de-identified, logistics of biobanks were communicated, and privacy was addressed, the Vanderbilt University authors found. Interestingly, individuals were generally willing for data or biospecimens to be shared with other academic researchers, but individuals were less willing for their data to be shared in federal databases or with commercial enterprises.

Another study evaluating consent for biobank research was published in *BMC Medical Ethics* in September 2015. It showed the majority of research participants opted for some version of limited consent, when given the possibility. Consent preferences were influenced by information about pharmaceutical industry sponsorship of biobank research and participants' perceived trade-off between privacy and perceived utility. This review found, however, participants' understanding and recall regarding the consent procedure was lacking.

Currently, HHS is reviewing the National Academies' report as well as more than 2,000 other public comments on the proposed changes to the Common Rule. It remains unclear if the Obama administration or the health agency will scrap its plans. A final decision is expected this fall.

Takeaway: Proposed changes to rules regarding consent for use of biospecimens in medical research continue to draw criticism. While joining those criticizing the regulatory revisions, a new National Academies of Sciences' report suggests an alternative—an independent commission to review and update research rules.

Lab and Pathology Industry Responds to Proposed MACRA Rules

Last year the long-maligned Sustainable Growth Rate payment formula was replaced with the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA), a system where providers are paid in part based on the quality of care they deliver.

"This is the biggest change in how physicians are paid ... since the creation of DRGs," said Emily Volk, M.D., a pathologist and chief quality officer for the Baptist Health System in San Antonio who also sits on the board of governors for the College of American Pathologists.

"All of the items in MACRA and going back to the (Affordable Care Act) have the secondary impact of increasing administrative costs. Does this hit a smaller practice more than a larger one? No doubt that it does."

— Emily Volk, M.D.

MACRA won't be fully implemented until 2019 at the earliest (and likely later than that), but the U.S. Department of Health and Human Services released draft regulations for how the new law would be implemented earlier this year. The agency received nearly 4,000 comments on the proposed regulations from members of the public. The vast majority were physicians, but a handful were pathologists or groups representing that medical specialty as well as laboratories.

The sector is taking a fairly cautious wait-and-see attitude. The CMS will take months digesting the comments it received (although hundreds of them were template submissions from members of the Texas Medical Association). It will likely be the end of the year or even 2017 before the final regulations are announced.

"I'm not getting exorcised about it right now," said Barry Portugal, president of Health Care Development Services, a Florida-based consulting firm to pathology practices. For the moment, Portugal said he is most concerned about the record-keeping required for quality measures, particularly for smaller practices.

"It's a (challenge) keeping track of all of that work and trying to statistically infer how well you're doing," he said.

Concern about Smaller Practices

The consensus among many in the health care industry is also that smaller or solo medical practices will be overwhelmed by the many reporting requirements.

"All of the items in MACRA and going back to the (Affordable Care Act) have the secondary impact of increasing administrative costs," Volk said. "Does this hit a smaller practice more than a larger one? No doubt that it does."

CAP represents the group of laboratory-oriented clinicians who will be most impacted by the rule. It submitted 27 pages of comments, one of the lengthiest documents submitted by commenters. The organization wants an expansion of potential quality measurement categories for pathologists and a minimization of clinical practice improvement activities until more specifics for meeting the objectives are created.

"Pathologists for years have been making contributions to delivering value, but the current program was designed with primary care physicians in mind and not our group," Volk said.

Both Volk and Portugal suggested that pathologists might be measured in areas such as blood management and conservation, as well potentially reducing duplicative testing. Perhaps most importantly, CAP wants a liberalization of the definition of non-patient facing physicians to automatically default pathologists to that category, where scor-

ing is weighted in a manner more favorable to clinicians that don't regularly interact with patients. Under the current proposal, physicians or group practices qualify for a non-patient facing designation if they have less than 25 patient encounters a year.

"If there is a change in someone's status (late in the year), it would be difficult for them to retrospectively meet the reporting requirements," Volk said.

Quality Improvement Possibilities Seen

COLA, the laboratory quality and safety organization, sees a potential opportunity in MACRA to improve the objectives of its mission.

"There are opportunities to expand and improve upon the rule's existing list of clinical practice improvement activities to recognize the significant impact laboratory medicine plays in the delivery of quality care," said COLA Chief Executive Officer Douglas Beigel.

Of particular interest is the measurement category known as clinical practice improvement activities, which would comprise 15 percent of a clinician's score for an incentive or penalty.

"A CPIA that focuses on enhancing practice safety in waived testing through educational support, training and practice management tools will undoubtedly make a clear impact on the quality of care received by patients by encouraging clinicians to take a closer look at the existing waived testing practices," Beigel said.

Another area where a CPIA would make sense is in improving quality control during the pre-analytic phase of testing. According to Beigel, up to 68 percent of all testing errors occur during this phase.

"A CPIA that highlights initiatives focused on quality control measures and proper training for the entire care team will help to enhance practice safety," he said.

Takeaway: The laboratory/pathology sector has taken its first look at the proposed MACRA regulations and has asked for relatively few changes so far.

FDA Issues Draft Guidelines for Companion Diagnostics

The U.S. Food and Drug Administration (FDA) released another draft guidance addressing diagnostics. Earlier this month, two guidances addressed next generation sequencing and variant databases that support clinical validity of genetic tests. July 15, the agency issued draft guidance addressing companion diagnostics: "Principles for Codevelopment of an In Vitro Companion Diagnostic Device with a Therapeutic Product."

The FDA indicates the document is intended to guide in vitro diagnostic device (IVD) and therapeutic product sponsors in codeveloping their products and seeking "contemporaneous marketing authorization." The new draft is a follow-up to a 2014 guidance document which defined in vitro diagnostic devices and encouraged earlier development of companion diagnostics. The FDA's announcement of this latest guidance indicates it "provides general principles for addressing issues that may arise when codeveloping a therapeutic product and a corresponding IVD companion diagnostic. It also provides considerations for planning and executing clinical trials and successfully fulfilling FDA regulatory requirements."

Reiterating the 2014 definition of IVD companion diagnostics, this new guidance highlights four uses for these diagnostics:

- Determining who will benefit from a therapy
- Detect those who might suffer adverse reactions to products
- Monitor and guide adjustment to treatment
- ID patients for whom a product is safe and effective

Noting that "[c]odevelopment of IVD companion diagnostics and therapeutic products is critical to the advancement of precision medicine," the FDA indicates that it won't approve a therapeutic product or a new indication for one if a companion diagnostic is "essential to assuring safety or effectiveness" and hasn't already been approved or is contemporaneously being approved for market. The 13-page 2014 guidance focused on defining IVD companion diagnostics, describing general FDA policies regarding review of therapeutic and companion diagnostic products, and ensuring consistency between labeling for the therapy and the diagnostic. This latest 48-page guidance document covers codevelopment planning, clinical trial design considerations, development of IVD companion diagnostics later in the process of developing a therapeutic product, contemporaneous marketing authorizations, as well as labeling and post market considerations.

An Aug. 18 webinar will provide more information about the guidance and answers to questions. Public comments on the guidance should be submitted by Oct. 13, 2016 to be considered before issuance of the final guidance. For more information about the FDA's webinar see www.fda.gov/CDRHwebinar.

Takeaway: Recognizing the importance of diagnostics to precision medicine, FDA provides guidelines for contemporaneous development and approval of companion diagnostic and therapeutic products.

FDA Seeks Public Comment on Blood Donor Deferral Policy to Decrease HIV Transmission

While the annual rate of new diagnosed cases has declined in the last 10 years, HIV still remains a significant concern. The Centers for Disease Control and Prevention (CDC) reports approximately 44,000 people were diagnosed with HIV in 2014 in the U.S. and more than 1.2 million currently have the virus, with the CDC estimating that 1 in 8 of those having the infection don't know it.

> *"Ultimately, FDA concluded that the 12-month deferral period is supported by the best available scientific evidence, at this point in time, relevant to the U.S. population."*
> — FDA

In December 2015, the U.S. Food and Drug Administration (FDA) released "Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products; Guidance for Industry" (Recommendations). This month, it published a notice in the Federal Register soliciting comments on that document and suggestions for making sure blood donor deferral policies keep up with scientific developments and continue to reduce risk of HIV transmission. Specifically, the FDA seeks:

- Scientific evidence to support alternative policies regarding blood donor deferral
- Feedback on the "feasibility of moving from the existing time-based deferrals related to risk behaviors to alternate deferral options, such as individual risk assessments"

- Suggestions for studies to evaluate different policy options

The December 2015 Recommendations switched to a 12-month rather than an indefinite deferral period for men who have had sex with other men (measured since the last sexual encounter). This new period is more in keeping with the deferral period for men and women at risk due to blood transfusion or accidental needlestick infection, the agency said. "Ultimately, FDA concluded that the 12-month deferral period is supported by the best available scientific evidence, at this point in time, relevant to the U.S. population." But the FDA remains "committed to continuing to reevaluate and update blood donor deferral policies as new scientific information becomes available."

With that in mind, the FDA is interested in public feedback on the merits of a deferral policy based on individual assessments—acknowledging that stakeholders indicated a preference for that basis for deferral. If individual assessments are used to determine donor deferral, the FDA explains that donors would need to be asked several questions to detect high risk behaviors. Therefore, the FDA asks for public comment on the following issues:

- The types of questions that would identify potential donors "at risk of transmitting HIV through blood donation"
- Suggested questions that would uncover recent risk behavior "such as within the 2 to 4 weeks" prior to blood donation
- Appropriate level of specificity for questions "regarding sexual practices while remaining understandable and acceptable to all blood donors" (for example, consider whether donors would accurately answer explicit questions about their sexual practices)
- Whether a short deferral period would be appropriate for high risk behaviors and if so, how long that period should be (the FDA seeks "scientific rationale" to support any such recommendation)
- Changes needed at the blood collection sites "to assure that accurate, individual HIV risk assessments are performed"
- Suggestions for designing studies to evaluate alternative deferral policy options

The notice document is published in the July 28, 2016 Federal Register. Comments need to be submitted by Nov. 25, 2016. To review the FDA's 2015 Recommendations, see the Dec. 23, 2015 Federal Register.

Takeaway: Keeping HIV on the public radar, the FDA solicits public comment on any necessary updates to policies regarding deferral of blood donations.

FDA Approves Rapid Molecular Diagnostic Test for Detecting Antibiotic Resistance

Last year, the White House unveiled a comprehensive, federal plan to combat the growing threat of antibiotic-resistant bacteria, with diagnostics playing a prominent role. To fund those activities outlined in the action plan, the President's Fiscal Year 2016 Budget requested $1.2 billion of federal funding, nearly a doubling of prior requests for federal funding to combat and prevent antibiotic resistance. The 2017 budget request also included antibiotic resistance efforts in its $2.8 billion request for medical product safety initiatives.

The U.S. Centers for Disease Control and Prevention says that CRE infections most commonly occur from exposure in healthcare settings, such as hospitals and long-term care facilities.

Earlier this year, *National Intelligence Report* highlighted an international call for attention to developing tools to fight antibiotic resistance. Global representatives of the diagnostics and pharmaceutical industries issued a joint declaration at the World Economic Forum in Davos, Switzerland, calling on governments to take action, along with private companies, to support investment in the development of products to combat antimicrobial resistance (AMR). (See "Dx Industry Joins Global Call for Incentives to Combat Antibiotic Resistance," *National Intelligence Report*, 1/28/16, p. 1.) Commercial drug and diagnostic developers agreed on a common set of principles for global action to promote antibiotic conservation and the development of new drugs, diagnostics, and vaccines.

One answer to that global call for tools to fight antibiotic resistance can be found in the U.S. Food and Drug Administration (FDA) recent approval of the first rapid molecular test for detection of antibiotic resistance directly from patient samples. The expanded clearance for the Xpert Carba-R assay (Cepheid, Sunnyvale, Calif.), enables rapid detection of genetic markers associated with carbapenem-resistant Enterobacteriaceae (CRE) from patient specimens. This can help hospitals and long-term care facilities identify colonized patients and aid infection control efforts.

The Xpert Carba-R assay uses real-time polymerase chain reaction technology to detect five of the most prevalent genes associated with carbapenemase, an enzyme produced by CRE. The test does not detect the bacteria itself and is one of 20 proprietary tests approved for use on the GeneXpert System.

The U.S. Centers for Disease Control and Prevention says that CRE infections most commonly occur from exposure in healthcare settings, such as hospitals and long-term care facilities. Patients requiring ventilators, urinary catheters or intravenous catheters, and patients who are taking long courses of certain antibiotics for severe infections are at greatest risk for CRE infections. Carbapenemase-producing organisms, commonly known as "superbugs," are often resistant to many classes of antibiotics, posing a significant public health threat.

Cepheid received initial clearance for the Xpert Carba-R assay in March for use of the assay with pure bacterial isolates, but this expanded clearance now enables users to detect carbapenem resistance genes directly from rectal swab specimens. Traditional methods to identify colonization with CRE or other resistant organisms require growing the bacteria from fecal material in cultures, which are then subjected to antimicrobial susceptibility testing—a process that can take three to five days. But the Xpert Carba-R assay can produce results in 48 minutes, the company says.

While this marks a dramatic improvement in delivery of results that can impact patient care and the fight against antimicrobial resistance, the FDA still recommends the Xpert Carba-R Assay be used in conjunction with other tests.

"Labs should continue to perform standard bacterial culture in conjunction with the Xpert Carba-R Assay," the FDA said in a statement. "In addition, concomitant cultures are necessary to recover organisms for epidemiological typing, antimicrobial susceptibility testing, and for confirmatory bacterial identification."

Takeaway: The fight against antibiotic resistance continues with FDA approval of a new rapid molecular diagnostic test.

CMS Report to Congress Cites Program Integrity, *Continued from bottom of p.1*

> *"This development means that more taxpayer dollars intended to care for the beneficiaries are not being paid at all, avoiding the need to recover improperly paid amounts from health care providers and suppliers."*
>
> — Shantanu Agrawal, M.D.

"CMS has achieved this impact by using a multifaceted approach ranging from provider enrollment and screening standards, to use of enforcement authorities, to use of advanced analytics such as predictive modeling," said Shantanu Agrawal, M.D., deputy administrator and director, Center for Program Integrity, in a CMS Blog post announcing the report.

The report also claims savings due to preventing fraud and abuse increased to 74 percent. Prior year's savings was 68 percent. "This development means that more taxpayer dollars intended to care for the beneficiaries are not being paid at all, avoiding the need to recover improperly paid amounts from health care providers and suppliers," explained Agrawal.

Earlier this year, CMS touted the successes of using predictive analytics in its Fraud Prevention System, saying it identified $1.5 billion in inappropriate payments "through new leads or contributions to existing investigations" since the FPS was first put into use. In a blog post this year, the agency claimed the FPS streams 4.5 million pre-paid claims daily and yielded an $11.60 return on investment in 2015 for each dollar spent on the system. The agency reported that for 2015 alone the FPS "helped identify or prevent $654.8 million in inappropriate payments … through actions taken due to the FPS or through investigations expedited, augmented, or corroborated by the FPS." That savings was 44% higher than the prior year under the program.

In February, the agency also highlighted its heightened provider enrollment screening activities, thanks to the Affordable Care Act's provision of "tools to enhance our ability to screen providers and suppliers upon enrollment and identify those that may be at risk for committing fraud, including the use of risk-based screening of providers and suppliers."

CMS indicated it was also increasing site visits to enrolled providers and using data monitoring and IT solutions to ensure enrollment compliance and thanked the Government Accountability Office for its recent report identifying "areas for improvement in our Provider Enrollment, Chain, and Ownership System (PECOS)—the IT system for Medicare enrollment—regarding verification of provider or supplier practice locations."

Takeaway: CMS continues to report that its Medicare fraud and abuse prevention and enforcement activities are successfully preventing and detecting inappropriate Medicare payments and claims robust returns on its investment.

National Intelligence Report (ISSN 2332-1466) is published by G2 Intelligence, Plain Language Media, LLLP, 15 Shaw Street, New London, CT, 06320. Phone: 1-888-729-2315 • Fax: 1-855-649-1623. Web site: www.G2Intelligence.com.

Kelly Hardy Briganti, JD, Editorial Director, Kelly@plainlanguagemedia.com; Barbara Manning Grimm, Managing Editor; Lori Solomon and Ron Shinkman, Contributing Writers; Randy Cochran, Corporate Licensing Manager; Michael Sherman, Director of Marketing; Jim Pearmain, General Manager; Pete Stowe, Managing Partner; Mark T. Ziebarth, Publisher.
Receiving duplicate issues? Have a billing question? Need to have your renewal dates coordinated? We'd be glad to help you. Call customer service at 1-888-729-2315.