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DOJ Memo Emphasizes Focus on Individual Liability for Corporate Misconduct

Given the number of individuals charged in the Biodiagnostic Laboratory Services case it should be no surprise that the government is interested in holding individuals and not just entities accountable for wrongdoing. A recent government memo to prosecutors and others involved in enforcing federal laws reinforces that commitment. What is being referred to as the Yates memorandum addresses "Individual Accountability for Corporate Wrongdoing" and emphasizes that "[o]ne of the most effective ways to combat corporate misconduct is by seeking accountability from the individuals who perpetrated the wrongdoing."

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AACR Calls to Up Federal Research Funding 7%, Improve Regulatory Science Behind Personalized Medicine

Enhanced federal investment in cancer research is necessary, according to the new report *Cancer Progress Report 2015: Transforming Lives Through Personalized Medicine* from the American Association for Cancer Research (AACR).

The report, released Sept. 16, serves to both educate the American public and further AACR's advocacy efforts in Congress. It highlights the progress made in the last year towards improving cancer care and calls for increased funding for "robust, sustained" budgetary increases of at least 7 percent for the National Institutes of Health (NIH), National Cancer Institute (NCI), and U.S. Food and Drug Administration (FDA) in fiscal year 2016 and thereafter to further future advances.

Among the progress cited in the past year is the FDA approval of nine new anticancer therapeutics and new uses for six previously approved anticancer therapeutics, including four targeted therapies, as well as one new cancer-screening test. AACR says that the number of FDA-approved molecularly targeted anticancer therapeutics more than doubled in the past five years, reaching 52 as of July 31, further cementing a role for molecular diagnostics in the future of cancer care.

"During the past five years, the pace of progress against cancer has accelerated dramatically," the report authors write. "As the research landscape

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DOJ Memo Emphasizes Focus on Individual Liability for Corporate Misconduct, *from page 1*

The memo discusses "challenges unique to pursuing individuals for corporate misdeeds" and seeks to promote consistency in enforcement efforts. Those challenges include difficulty proving "beyond a reasonable doubt" that individuals had the required criminal intent when corporate decision-making is often "made at various levels" and high-level executives in particular may be distanced from "day-to-day activity in which the misconduct occurs."

Criminal and civil investigators should be communicating with each other about corporate investigations, allowing the government to consider "the full range of . . . potential remedies."

Addressed to US Attorneys, the FBI director and assistant attorneys general for the civil, criminal, antitrust, tax and other divisions of the Department of Justice, the memo describes six "steps to be taken in any investigation of corporate misconduct"—some new and others already in use. The memo's guidance is intended to apply not just to criminal but to civil cases as well. Here's an explanation of the six measures the memo says those involved in enforcement should be taking to ensure culpable individuals are held accountable for corporate misdeeds.

Hinge cooperation credit on identification of culpable individuals. Corporations must provide "all relevant facts relating to individuals responsible for the misconduct" to receive any credit for cooperating with an investigation. The memo emphasizes that companies "cannot pick and choose what facts to disclose" but must provide all facts regarding the misconduct and identify all individuals involved or responsible "regardless of their position, status or seniority." This applies to civil cases as well as criminal cases. But, the memo warns, attorneys should not wait for or rely on the company's disclosure but should be "proactively investigating individuals at every step of the process."

Plea agreements and settlements that occur before cases against individuals have been fully resolved must also include requirements that the company provide information about all culpable individuals and impose penalties for failure to comply with that obligation. The memo's focus on cooperation reiterates statements made earlier this year by Assistant Attorney General Leslie R. Caldwell who explained entities seeking benefits of cooperation must conduct their own internal investigation and share with prosecutors "all available evidence of wrongdoing" including identification of all culpable individuals, even high level executives. (See *NIR*, May 28, 2015, p. 1).

Begin with a focus on individual liability. Civil and criminal investigators should start looking for culpable individuals from the very beginning of their investigations. The memo asserts that "a corporation only acts through individuals" so starting investigations with a focus on individuals "is the most efficient and effective way to determine the facts" and increases the chances of identifying the individuals involved at the higher levels of corporate organizations.

Coordinate civil and criminal investigations. Criminal and civil investigators should be communicating with each other about corporate investigations, allowing the government to consider "the full range of … potential remedies." The memo advises civil and criminal attorneys to alert each other to potential claims the other branch may have with regard to individuals and engage in early coordination of efforts on potential concurrent civil and criminal investigations.

Don't let individuals off the hook when resolving corporate liability. Culpable individuals can't be released from liability when either a civil or criminal matter is

resolved as to the corporation except in extraordinary circumstances or due to an approved policy. That means any resolution or civil settlement of the corporation's liability can't include immunity deals, dismissed charges or civil releases that compromise the government's ability to pursue individuals.

Memorialize plans to pursue individuals. If the government resolves matters with a corporation before it has completed investigations of individuals, DOJ attorneys should do so only with a documented "clear plan to resolve related individual cases." Therefore, details of the status of individual investigations and what remains to be done as well as a plan for completing those investigations should be stated in the resolution of corporate investigations. Any decision not to pursue individuals must be explained and approved by the U.S. Attorney or Assistant Attorney General involved in the investigation.

Don't focus on individual financial solvency. In civil cases, attorneys shouldn't consider an individual's ability to pay when deciding whether to pursue individual liability. The memo emphasizes two "equally important" objectives of enforcement efforts are to return funds to the government and deterrence of future misconduct. Therefore, decisions should be based on the seriousness of the conduct, the sufficiency of evidence and whether pursuing a case is consistent with federal interests and resources.

Takeaway: Promoting accountability and deterrence, the Department of Justice emphasizes the importance of coordinated and consistent efforts to pursue individuals involved in corporate misconduct rather than simply the corporate entities.

Federal Appeals Court Rebuffed Unfair Competition Claims But Didn't Decide Stark, AKS Liability

The Eleventh Circuit Court of Appeals ruled that a federal court didn't have jurisdiction to hear state law claims of unfair competition in a lawsuit that led to a multi-million dollar jury award against Millennium Health. But it didn't issue any opinion on whether the conduct in dispute violated the federal Anti-kickback Statute or Stark law. The appeals court explained that Ameritox had really raised *state* law issues when it argued that point-of-care testing (POCT) cups Millennium supplied to referring physicians for free violated state unfair competition laws because those practices violated *federal* AKS and Stark law. Declaring that the federal trial court's decision to hear the "novel and complex state-law claims" was an abuse of discretion, the appeals court said it "resulted in the needless creation of new law for nine states and permitted parties that were either ignorant of the law or disingenuous to waste scarce judicial resources."

Millennium and Ameritox are competitors who provide drug testing to physicians' patients. POCT cups include chemically activated strips that detect drugs in urine samples. These strips allow the physicians to obtain limited information in their office about whether drugs are present in the urine. They then send the sample in the POCT cups to the laboratory for confirmatory testing. Physicians can bill Medicare

for the testing performed in office using the POCT cups. Using a standard specimen cup would not allow such billing because the physicians wouldn't be performing a test. Millennium provided the POCT cups for free to physicians who signed Free Cup Agreements (FCA) agreeing to send those used cups to Millennium for confirmatory testing and agreeing not to bill federal programs for the in-office test. The provision of these cups could violate AKS and Stark if considered remuneration in exchange for referrals. Millennium's position was that because the physicians agreed not to bill for the in-office test, these arrangements didn't violate the AKS or Stark. Most of Millennium's physician customers paid for the cups but approximately 10% took advantage of the free cups and the FCA, according to Millenium. Ameritox filed a lawsuit in federal court alleging Millennium's arrangements violated state unfair competition laws and involved kickbacks in violation of state and federal law. The jury found Millennium tortiously interfered with Ameritox business in multiple states and its conduct was unfair competition under state law and awarded more than $14 million in damages. Millennium appealed.

"Allowing the state-law claims to be tried using the Stark/AKS theory was egregious, constituting a clear error of judgment."

— 11th Circuit Court of Appeals

The issue on appeal was whether a violation of the AKS or Stark law proved unfair competition or deceptive business practices in violation of state laws. The appeals court said, "Allowing the state-law claims to be tried using the Stark/AKS theory was egregious, constituting a clear error of judgment." The court said Ameritox either didn't know it would base its state law claims on violations of federal AKS and Stark law or it concealed that intention. Thus, the court said Ameritox was responsible for waste of judicial resources and it would create "perverse incentives" to allow Ameritox to claim the case should now stay in federal court to avoid a waste of resources by starting all over again in state court.

What the court refused to decide was whether the conduct at issue did violate the Stark law or AKS or other state law or whether violations of Stark and the AKS should support claims of unfair competition under state law. However, while claiming it expressed "no opinion whatsoever" about violations of Stark, AKS or state law and "no view as to whether it would be wise" to allow Stark and AKS violations to prove violations of state law, the court did say: "It certainly does not require any great leap of logic to believe that a company that profits by declining to comply with government regulations enjoys an unfair advantage vis-à-vis its competitors who choose to obey the law." The court also left the door open for the parties to litigate their claims "in a proper forum."

Takeaway: Federal court rules in favor of Millennium on procedural issue but leaves some uncertainty by refusing to decide whether conduct violated AKS & Stark law.

CMTP Issues Draft Framework for Covering NGS Testing

An influential not-for-profit group has issued a draft framework for how next-generation sequencing tests for oncology care should be reimbursed by payers.

The report from The Center for Medical Technology Policy (CMTP) comes at a time when anxiety regarding the rates of reimbursement for molecular-based tests has been running high. Many of the regional fiscal intermediaries for Medicare have lagged in providing guidance on payment, prompting many commercial insurers to not cover many tests themselves, or offer payments at rates far lower than what the laboratories consider reasonable. And intermediary Palmetto GBA's efforts to create standardized

codes for such tests through its MolDX system has also caused the laboratory sector additional anxiety. Meanwhile, many labs have been releasing and touting tests and platforms that rely on next-generation sequencing.

At the same time, the report suggested that labs may not be in the ideal position to advocate for their own products. "At issue is a growing flood of new genomic variants in need of study and a lack of economic and commercial incentives for testing companies and laboratories to perform the kinds of studies payers and health technology assessment groups generally expect to see," the report noted.

"NGS testing methods are potentially important new tools to enable clinical genomics and the realization of personalized medicine," said Donna Messner, a CMTP vice president and director, who led the guideline development effort, in a statement. "However, there is currently substantial uncertainty over future health plan coverage policy for genomics and how to accelerate evidence development for this testing."

Through its Green Park Collaborative, CMTP developed the guidelines in consultation with the laboratory, provider, and insurer sectors through a variety of phone calls and conferences held in the summer of 2014 and last spring. The working group reached consensus on two specific points: Coverage should be provided for panels of up to 50 genes that are analyzed for a subset of five or more genes that are considered to be standard-of-care for use with a given diagnosis such as stage four lung adenocarcinomas and other forms of advanced cancers (although payers had expressed concerns about covering any panel with 50 or more genes at all). And whole exome and whole genome sequencing should still be considered investigational assays and therefore should not be covered by payers.

"The lack of predictable coverage and reimbursement policies that anticipate the rapid emergence of new genomic tools could become a hindrance to cancer care."

— Sean Tunis, CEO, CMTP

Among the other recommendations in the framework:

- Payers should require laboratory accreditation through the College of American Pathologists, particularly for all NGS-related requirements mandated by that organization.
- The cost of performing NGS should not exceed the cost of individual sequencing of the target genes by other methods.
- Payers should consider compensating labs that submit new variant data to well-curated, public access databases of somatic mutations.

CMTP is now accepting public comments on the guidelines. The organization said it would use those comments and continued meetings with the major laboratory and payer organizations and the U.S. Food and Drug Administration to try to solidify more details for NGS-related coverage, data sharing from NGS testing, and even coverage of NGS-related off-label use for certain targeted cancer therapies that are employed as the result of the tests.

"The lack of predictable coverage and reimbursement policies that anticipate the rapid emergence of new genomic tools could become a hindrance to cancer care," said CMTP CEO Sean Tunis in a statement. "Getting agreement on guidelines for coverage of targeted NGS gene panels is a crucial first step toward more comprehensive and forward-looking policies for genomics in clinical medicine."

Takeaway: The CMTP is trying to provide some coherence for the lab and insurer sectors regarding coverage for NGS-based testing. G2

AACR Calls to Up Federal Research Funding, *Continued from bottom of p.1*

has changed, the regulatory and clinical trial landscapes have adapted to keep pace." AACR credits the FDA for advancing regulatory science in supporting the use of genomics and adaptive clinical trial designs, which identify the patients most likely to benefit from a given therapy. It is hoped these emerging trial strategies will reduce the number of patients required to enroll in a trial to demonstrate a therapy's effectiveness and trim the costs associated with conducting trials. In turn, it is hoped these new trial designs can accelerate the pace anticancer therapeutics enter clinical use.

In addition to innovative trial design, the FDA has developed four evidence-based strategies to expedite the evaluation of therapeutics for life-threatening diseases, including cancer. AACR says that breakthrough therapy designation was awarded to 26 anticancer therapeutics as of July 31, 2015, and nine of these therapeutics have received FDA approvals after receiving this designation.

AACR sees the FDA as an "integral part" of the biomedical research community and believes that adequate funding is imperative for the agency to keep pace with the rapid progress in biomedical research.

"The revolution in cancer research can be meaningful for patients only if the regulatory bodies that approve the resultant novel therapies adapt as the research landscape changes," the report claims. "The regulatory science initiatives of the FDA are aimed at promoting and developing evidence-based regulatory policies that balance innovation and the expedited approval of medical products with patient safety."

FDA's Expedited Review Strategies

These evidence-based strategies were developed to expedite assessment of therapeutics with potential for life-threatening diseases:

- **Accelerated Approval**—earlier stage assessment based on a surrogate endpoint, but further testing required following approval (i.e., Olaparib for BRCA-associated ovarian cancer)
- **Fast Track**—based on preclinical data for drugs filling an unmet clinical need (i.e., Ipilimumab for metastatic melanoma)
- **Breakthrough Therapy**—designation awarded based on early clinical studies showing substantial improvement over available treatment, making it eligible for fast track (i.e., blinatumomab for acute lymphoblastic leukemia)
- **Priority Review**—following clinical trials review occurs within six months, as opposed to the usual 10 months, given the potential improvement in safety or effectiveness. (i.e., dichloride for metastatic prostate cancer)

The AACR report highlights the importance of molecular diagnostic testing in cancer care and calls for expanded FDA regulation of laboratory-developed tests saying that a "single, predictable, risk-based regulatory framework implemented by the FDA to evaluate diagnostic tests will not only safeguard patients, but it will also further advance precision medicine."

AACR research shows that current funding for biomedical research and its subsequent regulation is inadequate and proposes "robust, sustained, and predictable" funding increases for the FDA and health-related granting agencies. The Biomedical Research and Development Price Index (BRDPI) incorporates the rising cost of personnel, supplies, and equipment required to conduct biomedical research. AACR says that since 2004 the NIH budget has fallen behind BRDPI and has lost approximately 25 percent of its ability to fund research. This, combined with "budget stagnation" for NIH and NCI since 2003 has resulted in a decline in research grant awards, which reached the "lowest 'success rates' on record" in 2014—a one in seven chance of obtaining NCI funding.

Takeaway: Given the FDA's recent advances in regulating tests and therapies associated with personalized cancer care, and the potential future regulation of laboratory-developed tests, AACR calls for ongoing increases in funding for the FDA and health-related federal granting agencies. G2

New FDA Advisory Committee Gives Patients a Voice in Device Approval Process

Recognizing the shift to "patient-centered medicine," the U.S. Food and Drug Administration (FDA) is establishing the first-ever Patient Engagement Advisory Committee (PEAC) to advise the FDA Commissioner on issues regarding medical devices, their regulation and use. A recent *FDAVoice* blog announcing the new committee acknowledged the increasing involvement of patients in health care "decision-making and priority-setting." PEAC will address how best to involve patients in device development and assessment and how to improve communication between FDA, sponsors and patients.

FDAVoice blog authors, Nina L. Hunter, Ph.D., a regulatory scientist in the FDA's Center for Devices and Radiological Health and Robert M. Califf, M.D., deputy commissioner for Medical Products and Tobacco, wrote: "Americans are becoming increasingly active consumers of health care, making choices about their doctors, diagnostics, treatments, and healthcare experiences rather than simply allowing health care providers to make the decisions for them."

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>
> — Nina L. Hunter, Ph.D., FDA Center for Devices and Radiological Health and Robert M. Califf, M.D., deputy commissioner for Medical Products and Tobacco

Hunter and Califf touted the new committee as "a new and exciting opportunity to foster patient partnerships with FDA," adding that it "complements other efforts at FDA to bring the patient into the medical device regulatory process" such as studies of patient preferences regarding medical devices, and draft guidance on patient preference information for PMAs, HDE applications and de novo requests. The authors cautioned, however, that while patients can help the agency "define meaningful benefits or unreasonable risks" of new devices, patient preference information won't be used "to justify approval of unsafe or ineffective devices."

Notices in the Sept. 21 Federal Register describe the committee as having a core of nine voting members serving up to four-year overlapping terms. Members will be chosen by the Commissioner for their knowledge of clinical research, patient care, and the needs of patient groups. Some committee members will be selected for their experience with patient and health professional organizations and methods of soliciting patient preferences and communicating risks and benefits. Nominations for voting members are due by Nov. 20, 2015 to receive first consideration for membership. Nominations received after that date will be considered for future vacancies. Voting members can include a consumer representative and non-voting members can include individuals nominated by industry for temporary committee membership.

The FDA is soliciting comments through Nov. 20, 2015 regarding potential topics for the Committee to address. Topics proposed for comment include:

- Where in the process and how should patient input be provided?
- Should patient input be solicited once products are already available in the market?
- Should labeling indicate only a portion of patients in a preference study "were willing to accept certain risks in order to achieve probable benefits?"
- How can patient preference information be conveyed in an understandable format?

Takeaway: FDA reaffirms its role in the process but acknowledges relevance of the patient's perspective in its medical device approval processes. G2

Two FDA Workshops Focus on Precision Medicine Issues

Earlier this year, panelists at an FDA workshop on next-generation sequencing standards advised the FDA that it should involve multiple stakeholders in crafting any standards and pressed for flexibility in the standards to accommodate the rapidly developing nature of the technology. (See *NIR*, Mar. 9, 2015, p. 1) Building on the discussions started at that February 2015 workshop, the FDA has announced two workshops it will be holding this fall regarding next-generation sequencing standards and use of databases to establish clinical relevance of genetic variants.

For both workshops, attendees must register for in person or webcast attendance by October 30, requests to make public comment must be made by Oct. 26, and written comments on the issues can be submitted until Nov. 25, 2015.

The first workshop, to be held November 12, will focus on potential analytical standards for next generation sequencing based in vitro diagnostic tests, including laboratory developed tests. The FDA seeks "sufficiently flexible assay performance standards that can accommodate innovation, including test modifications, while assuring NGS test safety and effectiveness." The workshop will focus on regulatory strategies for assessing analytical validity of NGS tests that yield information about variations in the human genome. The FDA promises a white paper in advance of the workshop that will cover its "current thinking for a standards-based approach to analytical performance evaluation of NGS diagnostic tests."

A second workshop will be held the next day, November 13, addressing use of databases to establish clinical relevance of human genetic variants. Curated databases have been highlighted as potential means for demonstrating clinical relevance of genetic testing.

At the February workshop, attendees were asked to comment on the use of "highly curated genetic databases that provide information on genetic variants and their association with disease." Several attendees supported the use of shared databases, with some suggesting participation in publicly shared databases should be mandatory.

The November workshop will focus on development, operation and curation, and use of databases of genetic variants. A discussion paper to be released prior to the workshop will address possible uses for such databases and the issues to be addressed at the workshop. For both workshops, attendees must register for in person or webcast attendance by October 30, requests to make public comment must be made by Oct. 26, and written comments on the issues can be submitted until Nov. 25, 2015. Registration, agendas and other information for both workshops can be found on the FDA's website.

Takeaway: The FDA continues to seek public input on standards for assessing next-generation sequencing and ensuring its utility and safety. G2

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