MEDICAL DEVICE DAILY™

THE DAILY MEDICAL TECHNOLOGY NEWS SOURCE

FRIDAY, MAY 27, 2016 VOLUME 20, NO. 103

UBL OFFERS UP MED-TECH AS A CAUTIONARY TALE

Former AdvaMed CEO says diagnostics are an underappreciated part of medicine

Varun Saxena, Staff Writer

WASHINGTON – Former Advamed CEO Stephen Ubl discussed the need to create a sound regulatory and reimbursement environment for personalized medications in his new role as the head of PhRMA, the main trade group representing the pharmaceutical industry. The May 25 keynote address occurred in downtown Washington at an annual conference sponsored by the Personalized Medicine Coalition.

Ubl gained familiarity with personalized medicine at AdvaMed, where he launched AdvaMedDx, which represents the interest of makers of diagnostic testing equipment that enable physicians to customize treatment to the needs of individual patients.

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PRECISION CANCER CARE IN 2016

New technologies offer hope to patients with difficult-to-treat cancer

By Diana Tucker, Staff Writer

Santa Monica, Calif. – Patients with difficult-to-treat cancers have faced little hope for their future; however, leaders in surgical oncology along with their collaborative teams presented incredible out of the box technologies that may change all that. For the first time ever, John Wayne Cancer Institute at Providence Saint John's Health Center, in Santa Monica, Calif. sponsored a

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70% STOP PPIS WITHIN SIX MONTHS

Meta-analysis supports TIF procedure for GERD

By Amanda Pedersen, Senior Staff Writer

Technology supported by a lot of different clinical studies is a good thing, especially the more robust the data is and the longer the follow-up is, but it also can make it difficult to see the forest from the trees. That's why some researchers prefer to pool all the available studies together and analyze the collective data for a bird's-eye view of the outcomes. One doctor who uses this research technique,

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STRONG PANEL SUPPORT

EMDAC goes 2 for 2, supporting approval of Sanofi's fixed-ratio combo diabetes product

By Mari Serebrov, Regulatory Editor

The FDA's Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC) gave qualified support Wednesday for Sanofi SA's fixed-ratio combination diabetes product, voting 12-2 to recommend approval. (One panelist had

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CONFLICT OF INTEREST HALTED

House panel probes changes to how HHS handles cybersecurity

By Liz Hollis, Staff Writer

WASHINGTON –Information security took center stage at a congressional hearing this week, with House members championing the idea of elevating the Department of Health and Human Services' chief information security officer (CISO) to the same level as the chief information officer (CIO).

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IN THIS ISSUE

HOLIDAY NOTICE

Medical Device Daily's offices will be closed Monday, May 30, in observance of Memorial Day. No issue will be published that day. The next issue of *MDD* will be dated Tuesday, May 31.

DIAGNOSTICS EXTRA

Staff Writer Omar Ford on one of med-tech's key sectors

Read this week's Friday Special

OTHER NEWS TO NOTE

3M of St. Paul, Minnesota, said that a court in Düsseldorf, Germany, has ordered an injunction and damages claim reaching back to December 2008 against **Dental Direkt GmbH**, of Hamburg, Germany, for infringement of technology that enables the coloring of ceramic-based dental restorations. The court decision is based on a German patent and on the German portion of a European patent. The court ordered Dental Direkt to reimburse 3M for its litigation costs. While Dental Direkt may appeal the court decision and has filed an opposition against the European patent enforced by 3M, the company has decided to preliminarily enforce the court's decision by providing a security bond.

Guardant Health Inc., of Redwood City, Calif., reported the launch of Project LUNAR, which will extend the technology behind the company's Guardant360 liquid biopsy, into early-stage cancer detection. LUNAR is an umbrella protocol that Guardant Health is launching with researchers from the Massachusetts General Hospital, Perelman School of Medicine at the University of Pennsylvania, the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, UC San Francisco, Samsung Medical Center, the University of Colorado Anschutz Medical Campus, and other institutions that will study the ability of Guardant Health's technology to detect cancer at early stages in high-risk populations. Guardant Health has already collected samples from multiple trial sites in breast, ovarian, lung, pancreatic, and colorectal cancers, with pilot data expected in the second half of 2016. Guardant expects to enroll thousands of patients in multi-site, multi-arm prospective clinical trials that will demonstrate first the feasibility and then efficacy of early detection of the deadliest cancers, through the use of cell free DNA, imaging, germline risk assessment, and other highly complementary technologies.

Pelvalon Inc., of Sunnyvale, Calif., reported publication of a peer-reviewed analysis of the company's Eclipse system in *The Journal of Medical Devices: Evidence and Research.* In a clinical trial of women who used the insert for one month, Eclipse was effective in 86 percent of those successfully fit with the insert. The most common adverse event was discomfort, most frequently associated with the fitting process and typically resolved by just removing the insert. At the end of the study, 96 percent of participants successfully fit with the insert found the Eclipse to be comfortable, and 98 percent reported that they would recommend it to a friend.

Rosetta Genomics Ltd., of Rehovot, Israel, said data from the analytical validation of the its novel, microRNA-based assay for the classification of indeterminate thyroid nodules have been published online in the peer-reviewed journal, *Cancer Cytopathology*. The article, "Analytical Validity of a microRNA-based Assay for Diagnosing Indeterminate Thyroid FNA Smears from Routinely Prepared Cytology Slides," highlights RosettaGX Reveal, a test that stratifies indeterminate thyroid lesions as "benign," "suspicious for malignancy by microRNA" or "positive for medullary carcinoma" in preoperative Fine Needle Aspirate (FNA) by utilizing existing cytology smear samples. The article reports on more than 800 FNA slides that were evaluated for intra-nodule concordance, effect of stain type, minimal acceptable RNA amounts, performance on low number of thyroid cells, effect of time since sampling, analytical sensitivity, specificity, and reproducibility. The results showed that the assay can be run on FNA slides for which as little as 1 percent of the cells are thyroid epithelial cells as was the case with most of the samples.

MEDICAL DEVICE DAILY

Medical Device Daily™ (ISSN# 1541-0617) is published every business day by Thomson Reuters, 115 Perimeter Center Place, Suite 1100, Atlanta, GA 30346 U.S.A. Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement.

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BUSINESS OFFICE

Donald R. Johnston (Senior Director, Current Awareness), Sarah Cross (Marketing Director), Penney Holland (Web Production Manager)

Ubl

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"I start off with the proposition that diagnostics are the least appreciated aspect of health care. Two percent of spending drives 72 percent of decision-making, but the magic happens somewhere else. So if you go to the doctor's office or you get a blood test, you don't hear anything, hopefully, or if you do, you don't appreciate how that blood sample got you to a treatment outcome," he said.

Ubl explained that molecular diagnostics and biomarkers can help improve clinical trials.

"On the FDA side, as has been discussed before, we think there are pragmatic steps that can be taken to more rapidly validate and qualify biomarkers, to use those biomarkers as surrogate endpoints, to harness the power of real-world evidence so that we don't have to try to answer all the questions up front, but can keep learning as we go. These are steps that we think can lower development costs and enhance competition by bringing products to patients more quickly," he said.

In addition, Ubl called for adaptive clinical trials that deploy biomarkers to assign patients to various arms, potentially eliminating the need for a placebo group. He noted that new FDA commissioner Robert Califf is an expert on the topic.

Ubl devoted a substantial portion of his remarks to criticism of a proposed payment demonstration for Medicare Part B drugs that would curtail the reimbursement of high-cost pharmaceuticals. He touted diagnostics as an alternative means of cost-control and resource optimization, saying, "we need diagnostics to make sure that we're allocating resources appropriately in the health care system. That is the right way to solve the cost challenge, not the wrong way like the Part B Demo, or gravitating towards price controls or what have you, but getting the right drug or the right intervention to the right patient at the right time."

As the dad of a child with Type 1 diabetes, Ubl said that industry needs to become more patient-centric. Although A1C levels are the main biomarker used to determine the severity of diabetes over time, he said the metric isn't that useful on a day-to-day basis.

"We have to get a lot better at understanding what patients really want and value, and right now that's not happening," Ubl said.

UBL LEANS ON DEVICE INDUSTRY EXPERIENCE

The speech was with references to lessons learned from his days at AdvaMed, which ended in September after a 16-year term.

"One of the things that I bring from device experience to pharma is that there's nothing that chilled investment like uncertainty. In the device space, over the last five years investment in start-up medical technology companies, the true early stage companies fell by something like 72 percent," he said.

Ubl blamed the poor state of med-tech venture capital on uncertainty around medical device regulation and reimbursement, informing the audience of pharmaceutical company employees and other stakeholders of a fact that that's well known in the device world. Medical devices are routinely approved in Europe years before they are made available in the U.S.

"My point is just that we shouldn't take progress for granted," Ubl said. "We need a robust policy ecosystem to continue to support innovation because investors and supporters of [the pharmaceutical] industry can move to other places, as they did in the device space, something that I know my former colleagues at AdvaMed are very focused on in terms or rehabilitating that particular ecosystem."

He also cited an early study of angioplasty that found the now-routine procedure to be ineffective and uneconomical as justification for proceeding with caution when it comes to new payment models that could restrict the pricing of innovative medications. "My point is that new pharmaceutical interventions and innovations are [also] not all well understood at launch," he said.

The pharmaceutical industry is ahead of the device industry in terms of real-world evidence generation and post-market surveillance. The FDA's device arm is putting increasing emphasis on the topics in an effort to catch up, and its drugs and biologics arm are pushing for more of both as well.

"I will say that on the device side [real-world evidence generation] it is a little more complicated because of the heterogeneity of the products involved and the complexity of getting the information captured, whereas on the drug side you have much more granular information that facilitates access to RWE in a more user friendly way. But I think that at the end of the day, both industries will benefit from having real-time capability of answering questions that can't be answered up front," Ubl said. He added that the issue could be addressed on the device side in the impending 21st Century Cures bill, or the upcoming FDA medical device user fee negotiations with industry.

Ubl also said the regulatory and legislative agendas of the two industries are broadly aligned. He cited a number of initiatives on Capitol Hill that would benefit both sides, such as the Precision Medicine Initiative, 21st Century Cures bill and the National Cancer Moonshot Initiative.

As head of AdvaMed, Ubl used to routinely cite studies showing that medical devices account for a small portion of health care spending, and that the price of implants is growing substantially slower than the rate of health care inflation.

There are few studies

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Precision

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multidisciplinary cancer conference: Precision Cancer Care in 2016.

"We've come a long way in the past 10 years in how we treat our cancer patients," an oncology nurse of 20 years who was in attendance told *Medical Device Daily*. "It used to be that we would tell patients with difficult-to-treat cancers to go home and have a vacation. Now with all the advances, we see a much greater survival rate and the biggest difference of all is that with precision therapy we can offer them more hope."

OPTIMIZING RESPONSES VIA MOLECULAR SELECTION

Targeted therapies – drugs that are specific to a tumor – are now the mainstay of modern oncology; often followed by immunotherapy, the newest tool in the cancer arsenal. The combination of correlating sensitivity and resistance of a biomarker with a molecular pathway-specific drug, followed by immunotherapy is about as precise and personal as one can get to treat that patient's tumor. Having said that, there remain challenges such as tumor heterogeneity that result in mixed responses. In addition, treatments must be adapted as each unique tumor profile evolves.

This paradigm shift allows us to understand that cancer recurrences following surgery are not necessarily (if at all) the pathologist's misdiagnosis or the surgeon's failure to remove the entire tumor. Modern thinking is that there is an underlying molecular/biologic pathway causing the recurrence.

For instance in a study conducted and presented by Anton Bilchik, Chief of Gastrointestinal Research at the John Wayne Cancer Institute, he found that in a cohort of similar colon cancer patients (all stage 2, no metastasis, negative nodes) 25 percent had a recurrence, while 75 percent were cured by surgery alone. The question was how to predict which ones would have a recurrence and which patients could be cured by surgery alone. Although they investigated a myriad of variables including pathological, surgical, and biomarkers – all of which added valuable information--the patients' immunoprofiles were more prognostic in the progression of colon cancer than anything else.

Supporting that evidence is the fact that even though there has been a dramatic reduction in deaths from colon cancer overall, the group between 40-50 years old has significantly increased death rates. One theory is that those are the patients with high BMIs and it has been well documented that obesity carries an associated compromised immunity. It has also been widely noted that cancer occurs many times more in transplant patients and those with HIV due to the fact that they are immunosuppressed.

THERAPEUTIC PROGRESSION TOWARDS IMMUNOTHERAPY

Bilchik concluded by pointing out the progression of indicators that have been utilized for colon cancer staging that determines the necessity and responsiveness of chemotherapy. "We began by counting nodes, then to measuring the amount of micrometastases, followed by identifying molecular biomarkers and now immuno-profiling, each one being more prognostic than the prior," he stated. Molecular diagnostics direct which drug to use for which tumor but oftentimes resistance develops that leads to a recurrence. "Providing immunotherapy specific to that patient's cancer will help curb that phenomenon. Precision medicine will reduce both the overall cost and the side effects that accompany generic chemotherapy," he concluded.

RADIOSURGERY IN BRAIN CANCER TREATMENT

Daniel Kelly, Professor of Neuroscience and Neurosurgery, emphasized the importance of precision brain tumor treatment since brain cancer is the most difficult to treat due to the blood brain barrier (BBB). In order to deliver enough drug to the tumor, the dosage becomes so high it is toxic, so other measures need to be taken to target brain tumors. Stereotactic Radiosurgery (SRS) is one of those newer options.

Although there are only 43,800 primary brain tumor occurrences annually in the U.S., there are 190,000 newly diagnosed metastatic brain tumors each year in the U.S. from melanoma, lung, breast and other cancers. "It used to be that once brain mets were detected, the only thing you could provide the patient was hope and prayer. Then with minimally invasive endoscopic surgery (often through the nose or optic orbit) and whole brain radiation therapy you could give them a survival of 6 months. Now there are targeted radiotherapy systems available that go even further," said Kelly. (See Table 1).

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TABLE 1: STEREOTACTIC RADIO SURGERY OPTIONS (SRS)

Technology	Company	Product
Highly focused gamma rays	**Elekta** (Sweden)	Gamma Knife
Linear Accelerators (LINAC)	**Varian Medical Systems** (NYSEVAR; Palo Alto, Calif.)	Trilogy
	Brainlab AG (Feldkirchen, Germany)	Novalis
	Accuray (Sunnyvale, Calif.)	Cyberknife
Low intensity alternating electric fields	**Novocure** (NVCR)	Optune
Proton Beam Therapy	**Ion Beams Applications SA** (Belgium)	
Source: Medical Device Daily, industry contacts		

GERD

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called a meta-analysis, presented her findings on the trans-oral incisionless fundoplication (TIF) procedure at Digestive Disease Week (DDW) in San Diego.

"So if one study has 30 patients and another study has 100 patients, in order to summarize what the overall effect is you can use meta-analysis," Lauren Gerson, a gastroenterologist at California Pacific Medical Center in San Francisco told *Medical Device Daily*. "This is a way to take a large amount of data and show it in a quantitative fashion."

The TIF procedure is a treatment option for patients with gastroesophageal reflux disease (GERD) that is performed with the Esophyx device from Endogastric Solutions Inc., of Redmond, Wash. According to the company, more than 60 peer-review papers from more than 50 centers have been published on more than 1,100 TIF patients. The Esophyx device was cleared by the FDA in 2007 and earlier this month the company reported FDA clearance for the Esophyx Z, the third generation of the device.

For the meta-analysis, Gerson and Karim Trad, a clinical professor of surgery with The George Washington University School of Medicine and Health Sciences, used research databases to examine data from three randomized clinical trials and seven cohort studies from the past eight years that examined the TIF procedure and outcomes at least six months after the procedure. In total, 492 patients and 426 TIF procedures were included in the analysis. The results showed the procedure effectively treats the underlying cause of GERD while, in most cases, ending patients' reliance on proton pump inhibitor (PPI) drugs. The pooled prevalence for complete discontinuation of PPI therapy was 70 percent, Gerson said, and the confidence interval of the studies that measured that was about 66 percent to 75 percent.

"What we tried to look at was basically did patients' quality of life get better, did their erosive esophagitis heal and did their PPI usage change significantly," Gerson said.

For most of the patients included in the analysis, the answer to all of these questions was yes. Gerson said there was a significant difference in overall quality of life scores in the randomized controlled trials as well as the cohort studies. The researchers also noted that after the TIF procedure a greater number of patients had a reduction of distal esophagus acid exposure and healing of erosive esophagitis. Going forward, the researchers plan to look at the data at 12-month follow-up for as many patients as possible, she said.

She noted that one question that remains is how long these treatment benefits will last.

While the reduction in PPI reliance is an important benefit of the procedure, Gerson said she is less concerned than other physicians may be about the safety of PPI therapy.

"PPIs now are getting a lot of bad press," she said. "The latest thing that came out was [a link to] dementia. In the past, PPIs have been blamed for bone density loss and infections."

Gerson said there is about a two-fold increased risk for certain types of infection but "all the other major risks that have been attributed to PPIs, like heart attacks, are not a major factor when you look at meta-analysis."

Still, the TIF procedure offers GERD patients many quality of life benefits that are important to consider, given that this is a disease that wakes patients at night, interferes with their diet and can reduce their work productivity.

"People want to feel better and not be bothered by this and be able to consume regular meals and have a normal lifestyle," Gerson said.

In other DDW news, Cdx Diagnostics, of Suffern, N.Y., reported results from a multi-center, prospective, randomized clinical trial demonstrating that wide area transepithelial sampling with 3-D tissue analysis (WATS3D) sharply increases, by four times, the detection of esophageal dysplasia (pre-cancer). The study compared WATS3D with the Seattle random forceps biopsy protocol used for the endoscopic surveillance of patients with Barrett's esophagus. According to Cdx, the Seattle protocol leaves "the vast majority of the esophagus untested and is completely random."

For the study, which was conducted at 14 academic GI centers, 160 high-risk patients undergoing Barrett's esophagus surveillance received both Seattle protocol random forceps biopsy and WATS3D. WATS3D found 4.1 times more high-grade dysplasia and esophageal adenocarcinoma than the Seattle protocol biopsies, detecting 29 cases while the Seattle random biopsies method detected only seven cases. //

Sanofi

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to leave before the vote.)

While the panelists agreed that the insulin glargine (Lantus)/lixisenatide combo demonstrated safety and efficacy in type 2 diabetes, several expressed concerns about the Solostar pen devices used to deliver the once-daily injection. Those concerns resulted in the no votes and a number of qualified yes votes.

The Paris-based drug company has proposed making the combo available via two Solostar pen devices. One would inject the drugs on a 2:1 ratio with an insulin range of 10-40 units/mL, with the second one providing a 3:1 ratio with an insulin range of 30-60 units/mL.

Xultophy, a similar combination by Bagsvaerd, Denmark-based Novo Nordisk A/S, which EMDAC unanimously supported Tuesday, would be available in only one pen, with a cap of 50 units/mL of insulin. While Sanofi's two pens would provide more flexibility, they also could lead to medication errors. The FDA noted that in a small human factors trial, a pharmacist chose the wrong pen.

Michael Reed, director of the Rainbow Clinical Research Center at the University Hospitals Case Medical Center, voted for approval of the Sanofi combo, saying the basal insulin/glucagon-like peptide-1 (GLP-1) receptor agonist product "may have the opportunity to change the paradigm" of diabetes treatment. But he added, "I struggle tremendously with the device."

Ellen Seely, professor of medicine at Harvard Medical School, agreed. "The pen needs to be redesigned," she said.

Kenneth Burman, director of the integrated endocrine training program at Medstar Georgetown University Hospital, cited the trial errors with the pen device as the reason for his no vote. However, he said Sanofi and the FDA should be able to work those problems out.

The panelists had no issue with having two different pens, but they want more differentiation. Color was a big issue. While the pens are different colors, several panelists worried that the difference might not be apparent to people who are colorblind or to elderly patients with vision problems.

Summarizing the panelists' views about the pen, EMDAC Chairman Robert Smith, an endocrinology professor at Brown University's Alpert School of Medicine, said no one was objecting to the construct of the pens, but they were concerned about how they were labeled, colored and structured.

If the agency agrees that the current pen design is a problem, the question is whether it can be resolved by the product's August PDUFA date. In its race to market against Novo Nordisk, Sanofi cashed in a $245 million priority review voucher to cut four months from the FDA review time of its combo.

EDUCATION, LABELING

Another concern is how to educate all the people who might have to interface with a novel insulin/GLP-1 combination – whether it's the Sanofi or Novo product. Sanofi is planning a comprehensive education campaign for health care providers and will include live support for patients. But panelist Steven Meisel, system director of patient safety at Fairview Health Services, questioned how the sponsor could effectively educate 5 million doctors, nurses, pharmacists and others who might have to interact with patients using the combo.

The committee members reiterated a labeling concern they raised Tuesday when they considered Xultophy, a once-daily, single injection that combines insulin degludec (Tresiba) and liraglutide (Victoza). They again urged the FDA to come up with a standardized vocabulary for measuring the doses, especially since insulin is measured in units and GLP-1 agonists are measured in micrograms. If the numbers on the dial-a-dose injector pens correspond with insulin units, the fear is that patients and health care providers will see the combos as another insulin product and ignore the GLP-1 component.

"This apparently is the wave of the future," patient representative Barbara Berney said of the combo drugs. Thus, the FDA needs to quickly figure out how to measure such products, she told agency staff.

Sanofi had a tougher row to hoe this week than Novo Nordisk as it also had to convince EMDAC of the merits of lixisenatide, which has yet to be approved by the FDA. The GLP-1 agonist, in-licensed from Zealand Pharma A/S, has a July PDUFA date. However, it's already been approved in more than 60 countries, including Japan and the EU, where it's marketed as Lyxumia.

In presenting lixisenatide and the fixed-ratio combo, Sanofi stressed that the GLP-1's ability to reduce postprandial glucose levels complements the insulin action on fasting levels. And the drug's apparent ability to counter the weight gains associated with insulin was seen as a real selling point for patients.

Although the committee didn't vote on approval of lixisenatide as a standalone drug, the members were asked to discuss issues related to its efficacy and safety. While they stressed the need for monitoring for allergic reactions, the panelists welcomed the drug as another advance in the field.

Getting to market is just the first step. Should both combos be approved, Novo's Xultophy could have an edge as patients and doctors already are familiar with liraglutide, which was approved in the U.S. as Victoza in 2010.

Since 2012, Victoza has been the most oft-dispensed GLP-1 at outpatient retail pharmacies in the U.S., according to data the FDA presented Tuesday. Prescriptions have scaled up every year it's been on the market. In the 12 months ended March 31, 2015, nearly 600,000 patients picked up Victoza at U.S. pharmacies.

If approved, the combo products also could compete with regimens using once-daily insulin injections with a weekly GLP-1 injection such as Bydureon (exenatide, Amylin Pharmaceuticals Inc./Eli Lilly and Co.). Bydureon was the second most frequently dispensed GLP-1 agonist at U.S. retail pharmacies, with prescriptions dispensed for about 200,000 patients in the 12 months ended March 31, 2015. //

Security

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During a May 25 hearing of the House Energy & Commerce Subcommittee on Health, lawmakers scrutinized the HHS Data Protection Act (H.R. 5068), which would establish the Office of the Chief Information Security Officer within the Department of Health and Human Services. The bill was introduced April 26 by Rep. Billy Long, R-Mo., and is cosponsored by Rep. Doris Matsui, D-Calif.

If signed into the law, the Office of the Chief Information Security Officer would have primary responsibility over the cybersecurity programs within HHS. The HHS Secretary also would have to submit a report to E&C and the Senate Health, Education, Labor and Pensions Committee detailing how the CISO plans to oversee and coordinate departmental information security programs, as well as the steps being taken within each operating division of the department.

Rep. Joe Pitts,R-Pa., the subcommittee's chairman set the tone for the hearing, maintaining that HHS currently prioritizes information operations over information security, thus putting internal data at risk. He spoke out strongly against the department's organizational structure, with the CISO reporting to the CIO. "In other words, the official in charge of building complex information tech systems is also the official in charge of ultimately declaring those systems secure. This is an obvious conflict of interest," Pitts maintained.

FDA BREACH

The hearing marked the latest step in attempts to mitigate cyber threats within HHS and comes almost a year after a blistering study unveiled by E&C. The study discussed an October 2013 breach of the FDA's internal network that gave an unauthorized party access to the account details of more than 14,000 users of one of agency's information systems.

"While the breach did not result in substantial harm to the agency's network and users, it highlighted the susceptibility of FDA's network to attacks and raised questions about the adequacy of FDA's information security program," the report noted. These questions prompted a December 2013 committee investigation into the agency's information security.

That investigation uncovered department-wide problems, with "five HHS operating divisions have been breached using unsophisticated means within the last three years." Further, agency officials could not adequately describe the scope of the security incidents to committee investigators.

Investigators did find that many of the security issues shared the same root cause: security concerns were not given the same priority as operational concerns.

Rep. Michael Burgess, R-Texas, said the ongoing threats are unacceptable, given data held by HHS affects all Americans. It's imperative to combat cyberthreats now, rather than be "tasked with examining the smoking ruins" following an attack, he said.

He added that companies might start feeling uneasy if they couldn't trust that the FDA's data on clinical trials are vulnerable to theft by bad actors. "There is no limit to the cavalcade of harsh headlines if we don't get serious about data security at the Department of Health and Human Services before it is too late," he said.

A POLITICIZED ROLE?

While agreeing on the need for cybersecurity enhancement, one expert argued against a provision in the bill that would make the HHS CISO a presidential appointee. Marc Probst, who spoke on behalf of the College of Healthcare Information Management (CHIME) argued that making the CISO a presidential appointment can politicize the role, thus making it harder to produce effective changes in the department. He highlighted the experience of Marilyn Tavenner, who in 2013 became the first Centers for Medicare & Medicaid Services administrator to win congressional backing since Mark McClellan did in 2004. "That lack of official leadership creates uncertainty in the industry," according to his testimony.

McClellan also testified that having secure systems should be paramount, not arguing about roles. "If the strategy is by raising a particular position and that somehow is going to raise cybersecurity," it's not going to work, he said.

Samantha Burch, senior director of congressional affairs at the Chicago-based Healthcare Information and Management Systems Society (HIMMS), said in her testimony that the bill represents "a great opportunity to better position HHS to meet the growing challenges of securing health information." Further, if the CISO "is appropriately positioned within the department," he or she would go far in ensuring a strong security architecture and enhancing cooperation internally and with other government bodies.

"However, it is important to note that it is not simply the organizational change of the CISO which will dramatically improve the security posture of an organization," she noted. "The right people, processes and technology must also be in place."

CONFLICTS WITH OTHER AREAS OF GOVERNMENT

Pitts took issue with the idea that changing the structure at HHS would hamper the ability of the department to coordinate cybersecurity efforts with other federal entities, because the roles of the CIO and CISO are "well established" throughout government. He noted that this structure isn't "novel or untested," highlighting that a branch of the Department of Defense already has implemented a similar structure.

Mac McMillian, chairman and CEO at Cynergistek, who also was at the Defense Threat Reduction Agency (DTRA), agreed that this should not have to be an issue. As security head at DTRA, he worked with the CIO on a level playing field to deploy secure systems. "Both the CIO and I were peers and were expected to

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Precision

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Other non-invasive, non-drug therapeutics in development for brain cancer are high intensity focused ultrasound (HIFU) and lasers. Robotics have been explored but without much optimism due to limited access. Current endoscopic procedures use 2 cm keyholes and robots would need 4 cm but that leads to loss of resolution.

NOVEL ADVANCES FOR TREATING BRAIN CANCER

"Neuro-oncology is now a distinct specialty," began Santosh Kesari, Professor of Neuro-sciences and Director of Neuro-oncolgy, "but it is only one part of an organized squadron that is required to treat brain cancer in the most efficacious fashion. Brain cancer treatments have been less successful than other cancers due to [the blood brain barrier]that creates an immunosuppressive micro-environment."

Kesari told *Medical Device Daily* "I was not an automatic fan when Novocure started their clinical trial using alternating electrical frequencies to disrupt mitosis in tumor cells in the brain, but when I saw that they were getting 43 percent tumor reduction while the control group was experiencing 29 percent I became a believer. This was the only trial stopped early because of one benefit only: progression free survival was significantly better."

Novocure Inc., of Malvern, Pa., introduced an entirely novel modality for antimitotic therapy that non-invasively applies low intensity alternating electric fields to tumor cells, termed tumor treating fields (TTF). Cleared by the FDA in 2011, this device interferes with mitosis only of the cancer cells and is administered by placing electrodes that produce an electric field on the outside of a person's head (for brain cancer). The device is intended as an alternative to standard medical therapy for glioblastomas after surgical and radiation options have been exhausted.

Other applications of this same technology are being developed for ovarian and pancreatic cancer; consensus thinking is that it should be effective for all cancers given a suitable external delivery system can be produced. The effects on the tumor cells are frequency specific and inversely related to cell size, so each type of cancer responds specifically to a certain frequency

IMMUNOTHERAPY CHALLENGES

Genomic characterization defines the pathways and identifies hundreds of mutations or deletions allowing for targeted therapeutics, and the FDA provides an accelerated approval of drugs when the genome can be identified; but once again it is difficult for these "designer" drugs to cross the blood brain barrier when intending to treat brain cancer.

Recent findings also indicate that the biology of the tumor can change its genomic characteristics rapidly, so that it is critical to be able to understand which patient groups will respond and which ones are prone to mutations that will become immune to that drug. It is now clear that tumors develop immune-checkpoint pathways as a mechanism of immune resistance, particularly against T cells that are specific for tumor antigens; a finding that is leading to advanced immunotherapy for brain cancers along with combination drugs that can hit both the existing molecular pathway as well as the possible checkpoint pathway.

"The days of non-specific chemotherapy is in the past," said Steven J. O'Day, Professor of Medical Oncology and Director of Immuno-Oncology in his closing statement. "The immune-oncology revolution is prevalent across all cancers today." //

Ubl

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with similar findings to cite when it comes to pharmaceuticals and biologic drugs.

"We have to have headroom for innovation," Ubl said when asked about high drug prices. "We have to have incentives in the system so that we have an incentive for breakthrough innovations like PCSK9 inhibitors. I just think that relentless education about the way the marketplace has evolved (is needed). Today you have a situation where you have rapidly consolidating payers and PBMs (pharmacy benefit managers). There's absolutely fierce marketplace competition that's driving down costs."

He also said an "honest" discussion around the quality of insurance plans is needed so that patients have more transparency about costs and which medications are covered in-network. //

APPOINTMENTS & ADVANCEMENTS

Ceterix Orthopaedics Inc., of Menlo Park, Calif., said Edward Graubart has joined the company as vice president of sales. Graubart was most recently vice president of sales for the Western United States at Nuvasive Inc. Ceterix develops surgical tools for minimally invasive orthopedic procedures.

DAILY M&A

Amulet Capital Partners LP, of Greenwich, Conn., acquired **Syntheracthcr Holdings Corp**., of San Diego, a contract research organization focused on clinical trials for emerging to mid-sized biopharma clients in the U.S., Europe and Asia. Terms of the transaction were not disclosed.

IMS Health Holdings Inc., of Danbury, Conn., has acquired **Privacy Analytics Inc**., of Ottawa, to extend its real-world evidence capabilities.

PRODUCT BRIEFS

Instamed, a health care payments network, released new updates to its Instamed estimator solution, designed to allow providers to estimate patient responsibility, secure a payment method and automate payment collection. The Philadelphia-based company said the enhancements are intended to augment the way Instamed simplifies the health care payments lifecycle for providers, payers and consumers.

Waltham, Mass.-based **Neurometrix Inc.** reported the launch of the Quell Health Cloud for Android. The updated Android app is designed to allow consumers to set up accounts on the Quell Health Cloud where their data is automatically backed up to secure storage. According to the company, this eliminates consumer worry about losing their therapy or sleep data and allows them to review their data on multiple mobile devices. With the updated launch, users of both the Android and iOS apps can tap into the Health Cloud capabilities, the company said.

Ortho Kinematics Inc., a diagnostics company focused on spine imaging informatics, received Health Canada authorization for its lead product, Vertebral Motion Analysis (VMA). The Austin, Texas-based company said the VMA is now available in the U.S., European and Canadian markets. The VMA is a diagnostic test for the assessment of spinal motion and radiographic instability. The VMA is designed to increase the sensitivity in detecting radiographic instability without a decrease in specificity.

San Diego-based **Pathway Genomics** said its researchers have initiated a clinical trial for the detection of thyroid cancer using its liquid biopsy test, the Cancerintercept Detect. This is the company's third ongoing study for the technology.

FINANCINGS

Great Basin Scientific Inc., of Salt Lake City, has priced a public offering of 3.16 million units at a public offering price of $1.90 per unit. The company said the gross proceeds of the offering of the units will be about $6 million. Each unit will consist of one share of common stock and one series G warrant.

Zebra Medical Vision, of Kibbutz Shefayim, Israel, reported an additional financing round of $12 million led by Intermountain Healthcare, with the participation of existing investors. Intermountain Healthcare, an integrated care providers in the U.S., plans to work with Zebra to accelerate the creation of imaging algorithms to improve patient care.

OTHER NEWS TO NOTE

The **Velocity Group**, of Mason, Ohio, said that member company **Oakley Die & Mold Co.**, which delivers tooling and machined parts to customers in Medical, Safety, Transportation, Industrial Machine and other industries, has received ISO 13485 certification.

Security

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work collaboratively to meet the Agency's mission," he said.

Although he could not comment specifically on HHS's current structure, he recommended that if the proposed structure is implemented, that CISOs make sure to coordinate with their counterparts across the government.

WHERE'S HHS?

Conspicuously missing from the hearing were representatives from HHS, a point not lost on Rep. Gene Green, D-Texas. While expressing gratitude to Long and Matsui for their work in cybersecurity, Green said he was "a bit surprised by my colleagues' decision to have a hearing today on H.R. 5068," particularly in light of HHS's ongoing efforts in this area.

Having someone from the department testify would "greatly enhance our evaluation of the current cybersecurity improvement efforts," Green said.

He expressed concern that the current effort could conflict with the Cybersecurity Security Information Sharing Act (CISA), which also provides direction for HHS in terms identifying cyberthreats. CISA, which was part of the spending package signed in December by President Barack Obama, has instructed the HHS Secretary to designate an official to lead and coordinate cybersecurity efforts between the department and industry. A task force already has been set up for this effort, and a report is expected early next year. Green wanted to ensure that their work isn't overshadowed by the proposed legislation.

Rep. Frank Pallone, D-N.J., echoed Green's concerns, adding that stakeholders had not had time to fully vet the bill. Pitts promised that there would be a consultation with HHS before the bill moved forward. //

DIAGNOSTICS EXTRA

Keeping you up to date on recent developments in diagnostics

By Omar Ford, Staff Writer

Paper used as sun sensor

Summer is around the corner – time for cookouts and sunbathing. But too much sun can result in sunburn, which is the main cause of skin cancer. Because the time it takes to get burned depends on many factors, it is not easy to tell when to seek shade. To help people stay safe, researchers report in ACS Sensors the development of a paper-based sensor for monitoring sun exposure given different skin tones and sunscreen levels. Most currently available UV sensors require high-tech gadgets to operate, such as smartphones or wearable devices. Recently, single-use, disposable sunburn sensors have come onto the market. However, some of these sensors use substances that are potentially harmful to people or the environment. Others are only good for specific skin tones. Justin Gooding and colleagues set out to create a disposable sunburn sensor that is inexpensive, is composed entirely of safe and benign materials and can be easily calibrated to take into account different skin tones and SPFs of sunscreens that are applied on the skin. The group created a sun-exposure sensor by ink jet printing titanium dioxide, a nontoxic and inexpensive compound, and a food dye on paper. When enough UV radiation hits the sensor, titanium dioxide causes the dye to change color, warning people to get out of the sun or apply more sunscreen. To adjust the sensor for various skin tones and sunscreen use, the group added UV neutral density filters that can speed up or slow down the discoloration time of the sensor.

Multiphoton microscope and endoscope could help with stronger disease detection

Two new optical devices could reduce the need to take tissue samples during medical examinations and operations and to then send them for testing – potentially speeding up diagnosis and treatment and cutting health care costs. One is a lightweight handheld microscope designed to examine external tissue or tissue exposed during surgery. One example of its use could be to help surgeons compare normal and cancerous cells (during an operation). A key advantage is that the device can acquire high quality 3-D images of parts of the body while patients are moving, enabling it to be applied to almost any exposed area of a patient's body. The second instrument, a tiny endoscope incorporating specially designed optical fibers and ultra precise control of the light coupled into it, has the potential to be inserted into the body to carry out internal cell-scale examination, for example during neurosurgery. Ultimately, this new approach may be able to provide high resolution images enabling surgeons to see inside individual cells at an adjustable depth beneath the surface of the tissue. Both prototypes have been developed by Imperial College London in collaboration with the University of Bath and funded by the Engineering and Physical Sciences Research Council.

Brain imaging links poverty and depression

A long line of research links poverty and depression. Now, a study by Duke University scientists shows how biology might underlie the depression experienced by high-risk adolescents whose families are socio-economically disadvantaged.
The study, published May 24, 2016 in the journal *Molecular Psychiatry*, combined genetics, brain imaging and behavioral data gathered as adolescents were followed for more than three years as part of a larger study. The results are part of a growing body of work that may lead to biological predictors that could guide individualized depression-prevention strategies. Adolescents growing up in households with lower socioeconomic status were shown to accumulate greater quantities of a chemical tag on a depression-linked gene over the course of two years. These "epigenetic" tags work by altering the activity of genes. The more chemical tags an individual had near a gene called SLC6A4, the more responsive was their amygdala – a brain area that coordinates the body's reactions to threat – to photographs of fearful faces as they underwent functional MRI brain scans. Participants with a more active amygdala were more likely to later report symptoms of depression. The study included 132 non-Hispanic Caucasian adolescents in the Teen Alcohol Outcomes Study (TAOS) who were between 11 and 15 years old at the outset of the study and came from households that ranged from low to high SES. About half of the participants had a family history of depression.
The group's previous work, published last year in the journal *Neuron*, had shown that fMRI scan activity of the amygdala could signal who is more likely to experience depression and anxiety in response to stress several years later. That study included healthy college-aged participants of Hariri's ongoing Duke Neurogenetics Study, which aims to link genes, brain activity, and other biological markers to a risk for mental illness. This study asked whether higher activity in the same brain area could predict depression in the younger, at-risk TAOS participants. Indeed, about one year later, these individuals (now between 14 and 19 years of age) were more likely to report symptoms of depression, especially if they had a family history of the disorder.

Lipid testing underutilized in adults taking antipsychotic medications

Too few adults taking antipsychotic medications are being screened for abnormalities in lipids, which include cholesterol and triglycerides, new research from the University of Colorado

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Anschutz Medical Campus finds. The biggest gap in screening is among adults age 40 and younger, the group for whom early detection and intervention has been shown to be effective when additional cardiovascular risk is present. Adults with serious mental illness die 20 to 30 years earlier than their peers, largely due to increased risk for diabetes, high cholesterol, high blood pressure and heart disease. Taking antipsychotic medication increases that risk. The American Diabetes Association and American Psychiatric Association recommends more intensive diabetes and cholesterol lipid screening for patients receiving antipsychotics, but rates of screening have remained low. Compared with prior reports, progress has been made to improve diabetes screening, but lipid screening remains particularly underutilized. The study, published May 11 in the journal *JAMA Psychiatry*, included 9316 Missouri Medicaid patients to identify factors associated with failure to receive annual glucose and lipid testing during treatment with antipsychotics. Another notable study finding is understanding who is prescribing antipsychotic drugs. About 75 percent of patients initiated therapy with a prescriber not practicing in a Community Mental Health Center and about half initiated therapy with a non-behavioral health care professional. Federal and state investment to prevent and reduce cardiovascular disease among those with mental illness has focused on psychiatrists practicing in community mental health settings.