OFFICE OF THE COMMISSIONER

External Meeting: Advanced Medical Technology Association (AdvaMed)
(August 7, 11:00 a.m. – 12:00 p.m., WO-Bldg. 1, Room 2102)
CONFIDENTIAL

Location: White Oak, Building 1, Conference Room 2102

Invitees: *FDA:* Stephen Ostroff, Robert Califf, Sally Howard, Jeff Shuren, and Josephine Tropea

External Group(s): Steve Ubl, AdvaMed; Janet Trunzo, AdvaMed; Nadim Yared, CVRx; Gary Pruden, Johnson & Johnson; and Michael Rousseau, St. Jude Medical

Purpose: AdvaMed will share their key priorities for this year and review results of their CEO survey regarding the impact of the regulatory environment on product development decisions.

AdvaMed's Proposed Agenda:

I. Introductions
II. AdaMed's Priorities
III. Review Results of AdvaMed's Impact of Regulatory Environment on Product Development Survey

Background:

21st Century Cures:

The Agency has been meeting with AdvaMed regularly during the 21st Century Cures legislative process. The House passed the 21st Century Cures Act on July 10. CDRH representatives and AdvaMed worked together on proposed language for most of the device provisions in 21st Century Cures, including:

- Priority Review for Breakthrough Devices
- Third-party quality system assessment
- Valid scientific evidence
- Least burdensome concept training and oversight
- Recognition of standards
- Easing regulatory burden with respect to certain class I and class II devices
- Advisory committee process
- Humanitarian device exemption application
- Health software

- Clinical Laboratory Improvement Amendments (CLIA) waiver study design guidance for in vitro diagnostics

For the Senate version of 21st Century Cures, CDRH is currently working with AdvaMed to refine their regulatory strategy in a way that is agreeable to both parties.

Attached is a document written by AdvaMed entitled "21st Century Cures: Myth vs. Fact on Medical Technology Regulation & Proposed Legislative Changes."

MDUFA IV:

FDA is on track to meet all of its Medical Device User Fee Act (MDUFA) performance goals.

Discussions about reauthorization of MDUFA have been underway at the Agency since early 2015. Discussions officially kicked off at the July 13 public meeting, at which FDA, industry, patient and consumer groups, health care professionals, and other stakeholders spoke. The reauthorization negotiations with industry—and concurrent meetings with patient and consumer groups—will begin in September and continue through March 2016. At that time, FDA plans to submit the Agency's recommendations (including commitments from FDA and industry) to HHS and OMB before transmitting to Congress in early 2017. FDA will host another public meeting to explain the outcome of the negotiations. FDA will also brief Congressional committees in advance of Congress voting on the reauthorization bill.

National Medical Device Postmarket Surveillance System (MDS):

Beyond clinical trials, real-life patient experience may reveal unanticipated device risks and confirm long-term benefits. A strong postmarket surveillance system can provide more robust and timely benefit-risk profiles for devices so that providers and patients can make better informed health care decisions. In 2012, CDRH laid out a strategy to strengthen the nation's postmarket surveillance system for devices that consists of a national system that quickly identifies poorly performing devices, accurately characterizes and disseminates risk and benefit information about real-world device performance, and efficiently generates data to help support premarket clearance or approval of new devices and new uses of currently marketed devices.

Achieving a national system requires thoughtful input and active participation from many key national and international stakeholders. In 2013, the Agency published an update that described the five major steps FDA would take to create a MDS. The five steps included establishing a multi-stakeholder MDS Planning Board, establishing an unique device identification system; promoting the development of national and international device registries; modernizing adverse event reporting and analysis; and developing and using new methods for evidence generation, synthesis, and appraisal.

The Agency has begun implementing the UDI rule, including development of a Global UDI Database as the repository for information that unambiguously identifies devices through their distribution and use. FDA continues to build registry capabilities both domestically (such as the National Breast Implant Registry) and internationally (such as the International Consortium of

Vascular Registries) and established a Medical Device Registry Task Force consisting of key registry stakeholders under CDRH's Medical Device Epidemiology Network Program. The Agency also commissioned the Engelberg Center for Health Care Reform at the Brookings Institution to convene and oversee deliberations of the Medical Device Postmarket Surveillance System Planning Board. In February 2015 the Planning Board's report entitled Strengthening Patient Care: Building an Effective National Medical Device Surveillance System was released. The report outlines recommended steps toward achieving the MDS and strategies for implementation. It also provides a pathway to realizing a national system that harnesses novel data sources, modern analytical techniques and the participation of all stakeholders to optimize patient care. Interested stakeholders will be able to share their feedback on the report through a public docket.

Laboratory Developed Tests (LDTs):

In 2014, FDA issued draft guidance documents describing how FDA would apply its oversight authorities to LDTs. The draft oversight framework guidance proposes to phase in enforcement of premarket review requirements for higher-risk LDTs, such as those used to guide treatment decisions, including the many LDTs with the same intended use as cleared or approved companion diagnostics and proposes to delay enforcement of the Quality System regulation until the time of enforcement of pre-market requirements. Additionally under the draft framework guidance, the FDA would continue to exercise enforcement discretion with respect to premarket review requirements for low-risk LDTs and LDTs for rare diseases. Enforcement would be phased in to accommodate lab preparation and FDA resource levels. The draft guidance regarding notification and medical device reporting describes the proposed process for clinical laboratories to notify the FDA of the LDTs that they manufacture, and describes the Medical Device Reporting (MDR) requirements, for clinical laboratories manufacturing LDTs. FDA believes the flexibility built into its proposed approach to LDT oversight is a critical feature of any LDT oversight model, and intends to retain and expand areas of flexibility in its final guidance documents where appropriate.

FDA is currently reviewing public comments on the draft guidance documents that it received through an open public docket and a two-day public meeting. In response to feedback from stakeholders, FDA is taking several other actions including:

- engaging in a series of discussions with CMS to ensure each agency understands the other agency's program for oversight of laboratories so the agencies can better educate their stakeholders. This collaboration will also produce a draft guidance document on how FDA's quality system requirements relate to requirements under CLIA;
- meeting with each of the third parties that conduct inspections under CLIA to better understand the CLIA program and to facilitate guidance on streamlined FDA oversight of quality system requirements in labs; and
- continuing to meet with stakeholders, including laboratories, patients, traditional IVD manufacturers, and medical practitioners.

FDA is committed to develop a final policy for oversight of LDTs that encourages innovation, improves patient outcomes, strengthens patient confidence in the reliability of these products, and helps reduce healthcare costs. FDA is carefully reviewing comments received on the draft

guidance document and will ensure its final document is narrowly tailored to address the greatest risks posed by these devices without imposing excessive regulation.

As FDA works to finalize these guidance documents, the Agency continues to monitor and engage in discussions with stakeholders and Congressional staff concerning proposals for legislation that would affect FDA's oversight of LDTs and, in some cases, IVDs. The terms of these proposals are in flux and at this time, FDA cannot take a position in support of any one of them. FDA can, however, describe the basic features that must be present in any legislative proposal for FDA to provide its support in general terms. Any proposal for legislation must:

- maintain appropriate scientific rigor in FDA's review and evidentiary standards;
- promote innovation by incorporating a flexible, risk-based approach to oversight;
- be appropriately responsive to the unique circumstances of the many stakeholders whose interests are in play; and,
- serve the interests of American patients in the availability of tests that are accurate and reliable. It is their health and well-being that will be impacted by a new regulatory framework for diagnostic tests.

Any statutory framework must have support from manufacturers, laboratories, patients, and the FDA and it may be difficult to satisfy all stakeholders. Most importantly, it must be a framework that ensures these tests are accurate, reliable, and clinically meaningful for patients – including when these tests are modified. FDA encourages all stakeholders to evaluate these proposals against their ability to fulfill these criteria.

AdvaMed CEO Survey:

In early 2013, AdvaMed informed CDRH of their intent to conduct a MDUFA III regulatory survey that was to be completed by the medical device industry. CDRH was informed that the survey would be administered to two audiences within the medical device industry—the CEOs and the regulatory affairs directors. AdvaMed shared their proposed questions, initially totaling 46, with CDRH. The survey was broken down into the following sections: demographics, pre-submission process, 510(k) submissions, premarket applications, CLIA waiver applications, general feedback, and FDA resources for sponsors.

During the spring of 2013, FDA/CDRH met with AdvaMed and provided feedback on their proposed questions. In March 2013, CDRH provided input on AdvaMed's final set of survey questions. In June 2013, AdvaMed administered the survey, which did not include some of the CDRH feedback. Also in June 2013, AdvaMed held several meetings with CDRH leadership and FDA/Office of the Commissioner leadership to discuss the survey results. CDRH has not seen the raw data from the survey results.

Attachment(s):

Tab A –AdvaMed's 21st Century Cures: Myth vs. Fact on Medical Technology Regulation & Proposed Legislative Changes

Tab B – Biographies of External Participants

Executive Secretariat Contact: Josephine Tropea, 301-796-5698

AdvaMed
Advanced Medical Technology Association

21st Century Cures: Myth vs. Fact on Medical Technology Regulation & Proposed Legislative Changes

General

Myth: Current device regulation is not rigorous.

FACT: FDA's oversight of medical technology is a rigorous regulatory framework, based on risk, which provides reasonable assurance of the safety and effectiveness of medical devices and diagnostics. FDA has the authority to require whatever evidence is necessary to assure a product's safety and effectiveness – including clinical studies – when it deems this data to be necessary to assess the product's risks and benefits.

Most medical technologies are evaluated by FDA through the 510(k) process, which has an excellent safety record:

- A study conducted the Battelle Memorial Institute found that of the nearly 47,000 medical devices cleared by FDA through the 510(k) process and on the market since 1998, only 0.16 percent were involved in a class I recall, the most serious level. The Battelle study further noted that only 0.08 percent of devices cleared via 510(k) since 1998 were recalled for design reasons, the type of issue likely to be observed during premarket review.

- Another study by Professor Ralph Hall of the University of Minnesota found that class I recalls accounted for just 0.45 percent of cleared 510(k) products over the five years studied.

- A third study by Dr. William Maisel of Beth Israel Deaconess Medical looked at all classes of recalls – the vast majority of which have no impact on patient care – and also found the 510(k) recall rate to be very low--in the range of 1.0 to 1.5 percent.

Myth: Devices cleared via 510(k) cannot have their approval rescinded.

FACT: FDA has ample authority to remove products from the market, including mandatory recall authority for medical devices. Other authorities include issuing

warning letters, ordering detention of a device, imposing civil monetary penalties, and banning a device.

Breakthrough

Myth: "Breakthrough" is defined loosely, creating a perverse incentive for manufacturers to use this term to take advantage of the faster approval process and as a marketing gimmick.

FACT: The breakthrough device proposal builds on existing law which allows for priority review of devices used in the treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions and meet one of four criteria (is a breakthrough technology; there is no approved alternative; it offers a significant advantage over existing alternatives; or is in the best interest of patients.) The proposed legislation clarifies those already-existing criteria and codifies the process for priority review. FDA alone would determine which products meet the criteria to qualify as "breakthrough." This complements FDA's EAP guidance (Expedited Access for Pre Market Approval) by establishing this priority review process for breakthrough technologies in statute.

Valid Scientific Evidence

Myth: Highest-risk medical devices could be approved on low-quality evidence, like the experiences of just one or two patients (anecdotal evidence), rather than on clinical trials.

FACT: Nothing in this proposal changes FDA's current rigorous approval standard, or directs the agency to take any particular action or make any decisions based on specific evidence. Instead, the proposal clarifies that – if appropriate – FDA *may* take certain data sources into account when evaluating a submission. These data sources include well-documented case studies (including registry data), studies published in peer-reviewed journals, or data collected OUS. This data is not intended to replace other forms of data, but to supplement them. Access to more forms of data and research advances scientific rigor and understanding, which benefits patient care. Ultimately, FDA will continue to use its scientific judgement and discretion to decide what data sources are appropriate for each particular product.

Third-Party QSR

Myth: Manufacturers can make substantial changes to products that might threaten the safety of patients without any outside scientific review of those changes by FDA or anyone else.

FACT: Medical device company quality systems are put in place to ensure good manufacturing practices are followed. This proposal would create a voluntary program where companies would have their quality system certified by an FDA-authorized third party. The certification would allow companies to self-certify certain low-risk changes to 510(k) and PMA products. For PMA products, allowable changes would include those captured currently by 30-day notices, which involve only manufacturing changes. For 510(k) products, allowable changes would include those currently covered as "special 510(k)s," which do not involve major technology changes or changes in the product's intended use. This very limited set of allowable changes represent minor alterations to an existing product or manufacturing process.

Creating this process helps to ensure that companies are accountable while lessening the burden on FDA, allowing the agency to focus on higher-priority activities. It would also represent a significant cost and time saving for companies. Both special 510(k)s and 30-day notices have a 30-day deadline attached to them, meaning that FDA is forced to prioritize these items to consider them in the specified time-frame, even though by definition they do not have a significant impact on patient safety. Additionally, companies participating in this program would be required to document the testing and validation steps taken before making an allowed change, and FDA could inspect these records at any time. Lastly, FDA would not only have access to annual reports accounting for the changes made, but could also access this information through audits and inspections.

Myth: Companies would select and pay the third party involved in their certification, creating a conflict of interest.

FACT: Third parties are an integral part of device regulation throughout the world and in the U.S. are currently used to augment FDA's device review and inspection processes. While companies participating in the third-party QSR program would select a third party from a list of those approved by the FDA, this happens routinely throughout the world and there is no conflict of interest. Third-party organizations consist of highly skilled technicians who cannot operate as a business if there is any appearance of impropriety. FDA would authorize the third parties participating in this proposed program and would have sole control of ensuring that only responsible, well-known, and above-board third parties are included.

Advanced Medical Technology Association (AdvaMed)

Stephen J. Ubl is President and CEO of AdvaMed. Mr. Ubl joined AdvaMed in 1998 as Executive Vice President of federal government relations. He left the organization in 2004 to open his own health care consulting firm, which served clients including Fortune 500 health care companies and leading investment banks. In July 2005, Ubl was chosen to lead AdvaMed as its President and CEO. Prior to AdvaMed, Ubl was Vice President of legislation for the Federation of American Hospitals. Ubl began his Washington career on Capitol Hill, where he worked for U.S. Senator Charles E. Grassley (R-IA).

Janet E. Trunzo is Senior Executive Vice President, Technology and Regulatory Affairs for AdvaMed and leads a team of regulatory experts. During her tenure at AdvaMed, she focused her efforts on the passage of the Medical Device User Fee and Modernization Act of 2002 (MDUFMA), its reauthorization in 2007 and most recently the negotiation for MDUFA III which was enacted into law as part of the 2012 FDA Safety and Innovation Act. She also concentrates on global regulatory harmonization and represented the U. S. device industry on the Global Harmonization Task Force. She currently chairs the international Board of Trustees for the Global Medical Device Nomenclature Agency. Prior to joining AdvaMed, Trunzo held positions at Hybritech, Inc., a medical device and diagnostics manufacturer and Scripps Clinic and Research Foundation, a hospital, diagnostic clinic and research institute.

Nadim Yared is the President and Chief Executive Officer at CVRx Inc. since 2006. Mr. Yared previously had served as Vice President and General Manager of Medtronic Navigation, the leading supplier of integrated image-guided surgery products in the world, from 2002 – 2006. He also worked at GE Medical for 10 years, where he held both engineering and marketing management positions. He had been Vice President of Global Marketing for the OEC Medical Systems and Vice President and General Manager of GE's European X-ray business based in Paris.

Gary Pruden is the Chairman of Johnson & Johnson's Medical Devices group, a role he assumed in May 2015. Prior to this, Mr. Pruden led the Global Surgery Group from 2012, and before that, he was the Worldwide Franchise Chairman for ETHICON and a member of the Medical Device and Diagnostics Group Operating Committee. Under his leadership, the Global Surgery businesses accelerated growth and advanced the innovation agenda, including signing landmark collaboration with Google to bring new robotic solutions to market. Gary joined Johnson & Johnson in 1985 with Janssen Pharmaceutica in New Jersey and held a number of senior positions in sales, marketing, and strategic account management. In 2003, he assumed the role of VP of Sales and Marketing, helping to successfully launch new brands and establish significant new growth.

Michael Rousseau is chief operating officer for St. Jude Medical. He oversees global sales, marketing, research and development, clinical, regulatory, supply chain and quality functions. He joined the company in 1999 as a senior vice president of marketing and since that time has taken on progressive leadership positions across the company. Mr. Rousseau has worked in the medical device industry for about 30 years. Before joining St. Jude Medical, he spent 11 years at Sulzer Intermedics, Inc., as a vice president of several functional areas and as director of risk management. He earned a bachelor's degree in business administration with an emphasis on risk management and insurance from the University of Georgia.