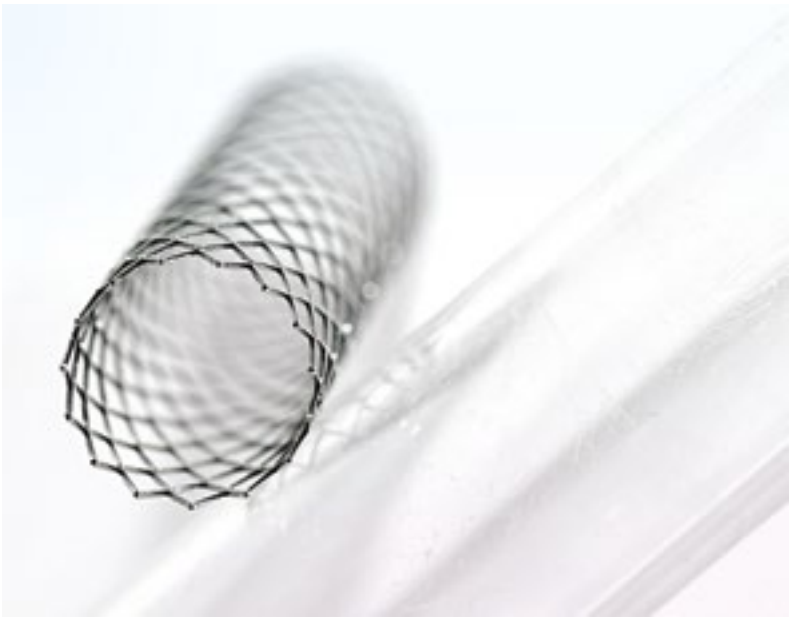
2017 – A YEAR IN REVIEW OF MEDICAL DEVICES

Regulatory affairs professionals work in a dynamic environment and 2017 was no exception. While the job rewards the detail-oriented, it is also critical to observe regulatory trends at a higher level. At the close of the calendar year, **NSF's medical devices consulting** regulatory team highlights some key guidance documents, changes in regulation, and medical device clearances and approvals in the United States.



FDA continues to balance the need for bringing new innovative technologies to market with efficiency, while also ensuring public health. While the changes in 2017 have not been as dramatic as those taking place in the EU under the new Medical Device Regulations, the U.S. executive and legislative environment, and recent user fee negotiations, continue to impact FDA and regulated industry.

21ST CENTURY CURES ACT UNFOLDS

This significant piece of legislation, enacted in December 2016, drove development/revision and issuance of new guidance documents and changes in regulatory requirements, as follows:

Guidance Documents

- Breakthrough Devices Program (October 25, 2017): This draft guidance describes a new program to facilitate more timely review and market introduction for "breakthrough technologies" intended to prevent, diagnose or treat life-threatening or debilitating conditions. This new program supersedes the Expedited Access (EAP) and Priority Review programs, and now includes 510(k) submissions (in addition to de novo and PMA submissions).
- De Novo Guidances (October 30, 2017): FDA also issued final guidance on the de novo process, which no longer includes the timeframe for submitting a de novo within 30 days of a receiving a not-substantially-equivalent (NSE) letter for a 510(k) submission. Additionally, similar to FDA's refuse-to-accept (RTA) guidance for 510(k) submissions, FDA developed a draft guidance pertaining to acceptance of de novo requests to ensure administrative completeness prior to substantive review. Of note, the 21st Century Cures Act also clarified that combination products may be eligible for the de novo pathway; however, policy development for these particular products is ongoing.
- Digital Health-Related Guidances (December 7, 2017): Two draft guidances (Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act and Clinical and Patient Decision Support Software) were released at the end of 2017 to clarify FDA's position on digital health in light of the 21st Century Cures Act.

- The first, "Changes to Existing Medical Software Policies…," updates previously published guidances (e.g., General Wellness; Mobile Medical Applications; Off-the-Shelf Software Use in Medical Devices; and Medical Device Data Systems, Medical Image Storage Devices, Medical Image Communications Devices) by further discussing what products might meet the "device" definition under this new legislation.
- The second, "Clinical and Patient Decision Support Software," helps to provide clarity on FDA's oversight of clinical decision support software intended for healthcare professionals -- and also those software functions intended for patients or caregivers -- by clarifying "clinical decision support" in the context of the 21st Century Cures Act.

Federal Register Notices

> April 13 and July 11, 2017 - FDA issued notices of class I and II devices that it has exempted from premarket notification requirements (subject to certain limitations).

> June 7, 2017 - FDA issued a final rule that changed the definition for a humanitarian use device (HUD) to "a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year." The number of affected patients was previously "fewer than 4,000."

> June 9, 2017 – FDA issued notice of reusable devices that require validated instructions for use and cleaning validation data in their 510(k) (based on 2015 public health issues with endoscopes and duodenoscopes).

MEDICAL DEVICE USER FEE AMENDMENTS 2017 (MDUFA IV)

MDUFA was reauthorized through passage of the FDA Reauthorization Act of 2017 (FDARA).

User fees and review timelines were renegotiated for FY 2018-2022 as follows:

> Fees increased significantly, with 510(k)s and PMAs costing $10,566 and $310,764, respectively, and de novo requests requiring a user fee of $93,229 in FY 2018.

> FDA's review clock goals improved, reducing decision-making timeframes for 510(k)s and PMAs (targeting 95 and 90 percent of 510(k) and original PMA submissions within 90 and 180 days, respectively).

> FDA set a review goal for de novo requests of 150 days, with 50 percent of submissions anticipated to meet this goal in FY 2018.

Guidance Documents

> Deficiency Response Guidance (September 29, 2017): This guidance is primarily intended to support FDA reviewers in issuing deficiencies to submitters of marketing applications, taking into account a least burdensome approach, whereby deficiencies are issued to request sufficient information to the reach a substantial equivalence or market approval decision. The guidance also provides examples of deficiencies and deficiency responses.

- Pre-submissions Guidance (September 29, 2017): This was a revision to the guidance originally issued in 2014. The two most significant changes include the FDA response timeframe for general pre-subs that now aligns with MDUFA III and IV commitments (target is 60-75 days with written feedback within 70 days of receipt or five calendar days, whichever is sooner) and formalization of the meeting scheduling process (a meeting date is to be set after acceptance and within 30 days of submission receipt).

OTHER REGULATORY DEVELOPMENTS

The following notable guidance documents were also released in 2017:

- "Deciding When To Submit a 510(k) for a Change to an Existing Device" (October 25, 2017): This long-awaited guidance, which is a revision to the K-97 guidance and similar to the draft guidance issued in 2016, is intended to clarify scenarios in which a 510(k) should be submitted for a change to a cleared device. FDA also issued accompanying guidance specific to software changes to 510(k) cleared devices. Importantly, FDA continues to emphasize that the threshold for submitting a 510(k) is whether a change "could" (not does) significantly affect safety and effectiveness.
- "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices" (August 31, 2017): The final version of this guidance was released earlier this year with minor modifications to the draft released in mid-2016. The main intent remains the same, with FDA communicating its recognition of real-world data (RWD) and how it may be used as evidence for the purposes of regulatory decision-making. One important note is that this consideration does not lower the bar set for valid scientific evidence, but rather acknowledges that RWD of sufficient quality could potentially be used to support regulatory decisions based on "existing evidentiary standards."
- "Classification of Products as Drugs and Devices & Additional Product Classification Issues" (September 2017): This guidance describes the request for designation (RFD) process and considerations for FDA's determination of whether a product is a drug or a device, including an explanation of the key parts of the definition of a medical device in the Federal Food, Drug, and Cosmetic Act (FD&C Act).

NOTABLE APPROVALS AND CLEARANCES

2017 produced many notable 510(k) clearances and PMA or HDE approvals, including the following:

- KardiaBand (AliveCor, Inc.), the Apple Watch's first medical device accessory, was cleared for recording EKG to detect atrial fibrillation and abnormal rhythms of the heart.
- Carbon Monoxide Breath Sensor System (Carrot Sense, Inc.), the first OTC mobile sensor and application for detecting carbon monoxide levels in breath-in smokers in cessation programs, was cleared by FDA.
- MAGNETOM Terra (Siemens Medical Solutions, Inc.), the first 7 Tesla MRI machine, was cleared by FDA.
- FDA cleared the Embrace® Neonatal MRI System, the first of its kind designed specifically for imaging the neonatal brain and head imaging in neonatal intensive care units (NICUs).
- With the U.S. opioid epidemic at the forefront, FDA cleared a new indication for the NSS-2 BRIDGE device (Innovative Health Solutions), an electrical nerve stimulation device, for use in reducing opioid withdrawal symptoms.
- Cianna Medical announced that its SAVI SCOUT® reflector is the world's first non-radioactive breast tumor location system for long-term implant to be cleared by the FDA.

- FDA approved the FreeStyle Libre Flash Glucose Monitoring System (Abbott Diabetes Care Inc.), which is the first CGM system for use in diabetic adults that does not require a fingerstick.
- The Cochlear™ Nucleus® Implant System (Cochlear Americas) was granted FDA approval as the first telehealth option to allow for remote adjustments to cochlear implants.
- The Neuroform Atlas™ Stent System (Stryker Corporation) received FDA approval under a humanitarian device exemption for the treatment of wide neck, intracranial and saccular aneurysms.

The de novo pathway also gained popularity in 2017, with the following notable de novos being granted this year:

- FDA granted market authorization through the de novo pathway for 23andMe's Personal Genome Service Genetic Health Risk (GHR) tests, the first direct-to-consumer tests by which DNA in saliva is evaluated for genetic markers associated with celiac, Alzheimer's, and Parkinson's disease.
- FDA granted marketing authorization via the de novo pathway to Beckman Coulter, Inc for its ClearLLab Reagents (T1, T2, B1, B2, M) that use flow cytometry to aid in the detection of several leukemias and lymphomas, including chronic leukemia, acute leukemia, non-Hodgkin lymphoma, myeloma, myelodysplastic syndrome (MDS) and myeloproliferative neoplasms (MPN).

Finally, manufacturers have been utilizing some of FDA's various pathways to foster a more efficient premarket review process:

- FDA granted ExThera Medical an expedited access pathway (EAP) designation for its Seraph® 100 Blood Filter in an effort to find improved treatments for drug-resistant infections.
- Second Sight also received FDA EAP designation for its Orion Cortical Visual Prosthesis System that is intended to create an artificial form of useful vision to blind patients.

For more information, or support with your regulatory strategy, 510(k), IDE, or PMA needs, contact: **medicaldevices@nsf.org** or visit **www.nsfmedicaldevices.org**

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