Accelerating Medical Device Development in the United States

New FDA Authorities and 21st Century Cures Impact on Future Innovation

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FDA is the Sole Agency for Regulating U.S. Medical Devices

Since 1976, the Food and Drug Administration (FDA) has regulated medical devices to ensure safety and effectiveness

- Medical Device Amendments of 1976
  - Defined medical device
  - Established device classes based on risk (I, II, and III)
  - Identified pathway to market for both new (post-1976) and "pre-amendment" devices
    - Premarket approval (PMA)
    - 510(k) (SE)
  - Established Advisory Panels for the review of new medical device applications

Congress Has Strengthened FDA's Regulatory Authority Over Devices

- **Safe Medical Devices Act of 1990**
  - Established post-market surveillance of medical devices
  - Required manufacturers to adopt device tracking
  - Allowed Secretary and/or manufacturer to initiate device reclassification
- **FDA Modernization Act of 1997**
  - *De novo* process for evaluating devices automatically designated as Class III
  - Class I premarket exemption
- **Medical Device User Fee and Modernization Act of 2002**
  - User fees for premarket review
  - Established the Office of Combination Products at FDA
- **FDA Administration Amendments Act of 2007**
  - Unique identifiers
  - Required study of the appropriate use and effectiveness of the 510(k) process
- **FDA Safety and Innovation Act of 2012**
  - Harmonization of regulatory requirements
  - Creates "direct *de novo*" for direct classification without prior 510(k) NSE

21st Century Cures Act (P.L. 114-255)

- House of Representatives and Senate developed separate legislative processes to promote new “innovations” in drug and device development
- Legislation originally passed House of Representatives (H.R. 6) on July 10, 2015 by vote of 344 – 77
- *21st Century Cures Act* signed into law on Dec. 13, 2016 by President Obama
- Contains several device provisions meant to accelerate new device development

H. R. 34

One Hundred Fourteenth Congress
of the
United States of America

AT THE SECOND SESSION

Begun and held at the City of Washington on Monday, the fourth day of January, two thousand and sixteen

An Act

To accelerate the discovery, development, and delivery of 21st century cures, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "21st Century Cures Act".

(b) TABLE OF CONTENTS.—The table of contents for this Act is as follows:

Sec. 1. Short title; table of contents.

DIVISION A—21ST CENTURY CURES

Sec. 1000. Short title.

TITLE I—INNOVATION PROJECTS AND STATE RESPONSES TO OPIOID ABUSE

Sec. 1001. Beau Biden Cancer Moonshot and NIH innovation projects.
Sec. 1002. FDA innovation projects.
Sec. 1003. Account for the state response to the opioid abuse crisis.
Sec. 1004. Budgetary treatment.

TITLE II—DISCOVERY

Subtitle A—National Institutes of Health Reauthorization

Sec. 2001. National Institutes of Health Reauthorization.
Sec. 2002. EUREKA prize competitions.

Subtitle B—Advancing Precision Medicine

Sec. 2011. Precision Medicine Initiative.
Sec. 2012. Privacy protection for human research subjects.
Sec. 2013. Protection of identifiable and sensitive information.
Sec. 2014. Data sharing.

Subtitle C—Supporting Young Emerging Scientists

Sec. 2021. Investing in the next generation of researchers.
Sec. 2022. Improvement of loan repayment programs.

Subtitle D—National Institutes of Health Planning and Administration

Sec. 2031. National Institutes of Health strategic plan.
Sec. 2032. Triennial reports.
Sec. 2033. Improving flexibility at the National Institutes of Health.
Sec. 2034. Reducing administrative burden for researchers.
Sec. 2035. Exemption for the National Institutes of Health from the Paperwork Reduction Act requirements.
Sec. 2036. High-risk, high-reward research.
Sec. 2037. National Center for Advancing Translational Sciences.
Sec. 2038. Collaboration and coordination to enhance research.
Sec. 2039. Enhancing the rigor and reproducibility of scientific research.
Sec. 2040. Improving medical rehabilitation research at the National Institutes of Health.

Streamlining the Use of Devices with Other Therapies

Regenerative Therapies

- Sec. 3034 requires draft guidance to be published detailing how the agency will streamline regulatory requirements for devices used with cell or tissue products (i.e. regenerative therapies)
  - Within the guidance, the Secretary must also identify specific instances where a device used with a regenerative therapy would be classified as Class III, est. preference for Class II classification by default
  - Ex. novel catheters with suction for transendocardial injection of cell-based therapies; laproscopic devices for delivering microencapsulated cells or islets.

Combination (Drug/Device/Biologic) Products

- Sec. 3038 improves the regulation of combination products by:
  - Requiring FDA offer meeting dates to combo product sponsor within 75 days of receipt of a meeting request
  - Accelerating data submissions by requiring only data or information that supplements prior finding of safety and effectiveness or SE for the prior approval of a constituent part of a combo product (Hatch-Waxman Act standards)
  - Principal reviewer clarification
    - Codified 2005 guidance establishing “primary mode of action” as determining factor for agency review
    - Sponsor may appeal initial FDA decision

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Establishing Pathways for Streamlined Review

Breakthrough Devices

- Devices that
  - Provide more effective treatment for life-threatening and debilitating human conditions
  - Represent breakthrough technologies for which cleared alternatives do not exist
  - Offer significant advantages over existing approved alternatives

- Sec. 3051 expands the existing FDA expedited access pathway (EAP) for breakthrough devices to all classes of devices rather than only Class III devices, thus opening the program to 510(k) applications
  - EAP is a voluntary program for certain medical devices subject to pre-market or *de novo* requests and demonstrating the potential to address unmet medical need for serious/life-threatening conditions
  - Expects interactive communications early and often between FDA and sponsor
  - Allows for accelerated approval of a PMA with less certainty in the risk-benefit profile compared with non-EAP devices by balancing pre- and post-market studies
  - EAP program entrants include CVRx Barostim neo neuromodulator for treatment of heart disease and Blood Purification Technologies' wearable artificial kidney

Establishing Pathways for Streamlined Review Cont.

- Pre-Cures FDA Device Guidance:
  - Real world data (RWD) is defined as "data regarding the usage, or the potential benefits or risks, of a device derived from sources other than randomized clinical trials
    - Ex. data from electronic health records, payer administrative claims, and patient registries
  - Real world evidence (RWE) is evidence derived from the analysis of RWD
  - Idea has gained popularity following the passage of FDASIA in 2012
  - FDA draft guidance published July 27, 2016; RWE may be used to understand device performance in several ways, including as a historical control, for public health surveillance efforts, etc.
  - RWD collection may also work in tandem with investigational device exemption (IDE) regulations to investigate the potential uses of new devices under existing regulations
- Sec. 3022 requires the FDA to evaluate the use of real world evidence to support the approval of a new indication for a previously approved *drug*
  - The Secretary of HHS is required to develop a framework for taking real world evidence into account within two years
  - Could be extended to device approvals

Enhancing Least Burdensome Standard for Device Review

- Sec. 3053 establishes a timeline of 60 days for FDA to review and then accept or reject all or part of a request from a sponsor to rely upon an identified national or international standard to support a pre-market submission

- Sec. 3058 requires the FDA to ensure review division employees undergo training on implementing the least burdensome requirements in their review and to periodically assess such training and implementation.

Reducing Regulatory Burden for Device Review (Cont.)

- Sec. 3057 modifies existing CLIA waiver guidance to lower the standard for CLIA facility regulation from high complexity to moderate complexity testing capability

- Sec. 3060 expands the categories of medical software that will be exempted from the definition of a "medical device," and thus the rigors of medical device regulation, due to their low levels of risk
  - Examples:
    - Administrative support software
    - Software used to transfer, store, or format certain EHRs
    - MDDS: Software used to transfer, store, or display laboratory test or device data as long as the software does not interpret results of such tests

Humanitarian Device Exemption (HDE)

- Sec. 3052 provides FDA with the authority to apply the HDE to devices that treat disease and conditions that affect up to 8,000 individuals nationwide, up from 4,000.
- Brief History of the HDE
  - Established under the Safe Medical Devices Act of 1990 to provide incentives for development of devices in small populations
  - Regulations implementing the HDE pathway were issued in June 1996
  - HDEs were originally not allowed to recoup costs beyond research and development costs
    - Pediatric profit restriction lifted in 2007 as part of FDAAA
    - Non-pediatric profit restriction lifted in 2012 as part of FDASIA
- Devices approved under HDE need only demonstrate safety and "probable benefit" rather than the higher bar of efficacy under a PMA
- HDE may only be utilized once FDA's Office of Orphan Product Development (OOPD) designates the device as a humanitarian use device to treat a disease that manifests itself in 4,000 individuals or fewer per year

Humanitarian Device Exemption (HDE) Cont.

- Incentives for use
  - HDEs eligible for orphan product grants
  - HDEs are able to waive filing fees normally required under MDUFA
  - HDEs are now allowed to be sold for a profit
- Ex. of HDE Approval
  - Vertical Expandable Prosthetic Titanium Rib (VEPTR) to preserve breath in children with thoracic insufficiency syndrome. Initial implantation on an in-patient basis and can be adjusted in an outpatient setting as a child grows
  - Approved in 2004 through the HDE pathway after years of clinical studies supported by the orphan products clinical trials grants program, which were established under the Orphan Drug Act of 1983 and provide funding for the development of drug and device products for rare diseases

Ensuring Expertise for Review of New Devices

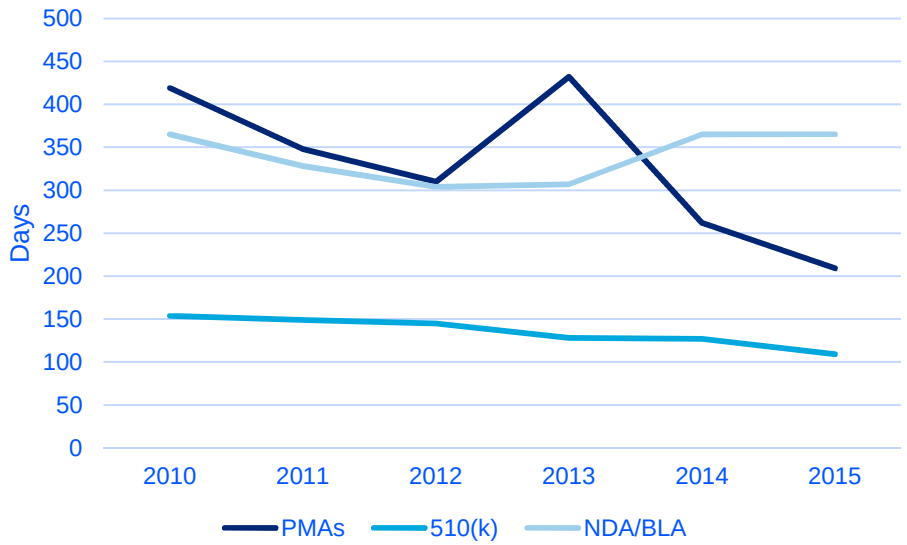
- Sec. 3055 ensures that FDA classification panels reviewing new medical device applications have adequate expertise to properly assess new devices. Also ensures that device sponsors are allowed to present their data before the panel

- Sec. 3072 emphasizes the importance of hiring scientific and professional personnel to review and regulate medical products, including devices

Improvements in FDA Application Approval Times

Average Approval Time (Days)

Year	PMA	510(k)	NDA/BLA[1]
2010	419	154	365
2011	348	149	328
2012	310	145	304
2013	432	128	307
2014	262	127	365
2015	209*	109†	365



» *Average time with 45% of cohort closed..

» †Average time with 74% of cohort closed.

» [1]Median time.

Sources: FDA: CDER Approval Times for Priority and Standard NDAs and BLAs
FDA: MDUFA III FY 2016 Performance Packet

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New Administration

- Executive Order on Jan. 23 establishing a hiring freeze affecting all federal agencies, including FDA
- Additional Executive Order issued on Feb. 24 requires each agency to develop a regulatory reform task force to identify regulations to repeal or modify that are outdated, impose costs greater than benefits, or that eliminate jobs
- 800 FDA vacancies prior to hiring freeze
- FDA's Center for Devices and Radiological Health (CDRH) and other divisions are having difficulty hiring and retaining experts
- Concern that lack of staff and other resources will preclude implementation of Cures law
- Trump Administration released FY 2018 budget outline, which referenced a doubling of medical product user fees.

Confirmation of New HHS Secretary

- Tom Price, MD confirmed on Feb. 10 as Secretary of Health and Human Services by a vote of 52-47
- Price served as a former chair of the House Budget Committee and is an orthopedic surgeon

Opportunities	Threats
Ultimately voted to sign the 21st Century Cures Act into law	Ardent opponent of the Affordable Care Act
Former orthopedic surgeon with extensive experience in the use of medical devices and related policies	Budget hawk who has advocated against additional funding for HHS agencies, including FDA
Stance on many biomedical issues is unknown, opening potential for positive influence from medical device stakeholders	Has been active in opposing FDA's regulatory authority that may stifle implementation of innovations provisions

- Price voted against 21st Century Cures in 2015 when the bill included $8.75 billion in new money for NIH and FDA citing the figure as overspending

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Leadership Changes at FDA May Affect Device Regulation

- Robert Califf, MD resigned as the 22nd Commissioner of Food and Drugs on Jan. 19. Stephen Ostroff, MD is acting Commissioner
- On March 10, President Trump named Scott Gottlieb, MD as his selection for FDA Commissioner
- Scott Gottlieb, MD
  - Partner, New Enterprise Associates
  - Former Deputy Commissioner, FDA
  - Former senior policy advisor to CMS Administrator
  - Resident Fellow at American Enterprise Institute
- Relevant Views
  - Devices
    - Supportive of shifting device oversight requirements to post- rather than pre-market using UDIs for tracking as an example
    - Emphasizes the importance of tying data requirements for device applications to the level of risk those devices pose; concerned low-risk devices are being regulated like complex drugs
  - On the record supporting reorganization of FDA around diseases rather than drug/device types
    - Could significantly impact how CDRH operates
  - Very supportive of utilizing new statistical approaches, including the use of Bayesian statistics and multi-faceted review standards

»Questions?

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