Trends seen from the perspective of a US physician

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FDA/Center for Devices and Radiological Health: Classification of devices and associated pathways

Class I               Class II               Class III
Lower risk                                    Highest risk

510(k) clearance w/wo data

Pre-market approval study

Main Line Health
Lankenau Heart Institute
What is the status of FDA device approval as compared to CE mark?

• The Boston Consulting Group (BCG) issued a report of an analysis in 2012
  – The average delay for FDA approval was 43 months (ranging to greater than 60 months/5 years)
  – Out of 89 comparable devices, there was little difference in the rates of EU and US serious recalls
    • Only 2 CE mark recalls during the delay period to FDA approval
Patient-related ramifications of these findings

• The potential for a significant impact on US patients who do not have access to the potential health benefits of the device and may suffer increased disability, reduced quality of life, and less patient choice

  – CE mark for Edwards Sapien TAVR 2007, but was still not approved as of the report in 2012. res ipsa loquitur

  – CE mark for MRI compatible pacer approved 29 months ahead of US. MRI is critical for the early detection, diagnosis and treatment of many conditions
Financial ramifications of these findings

• Modeling suggests FDA uncertainty and regulatory delays:
  – Significantly reduced the returns on investment for R&D
  – Increased the uncertainty as to the necessary funding required to bring a product to market
  – Larger companies may have multiple products/revenue streams may have capacity to better manage these issues
  – Smaller companies---and their potential investors---can’t manage as easily threatening innovation and US status
So what’s being done?
Updated CDRH initiatives

In 2014-2015 Strategic Priorities, CDRH committed to reducing the time and cost of regulatory and non-regulatory aspects of the U.S. clinical trial enterprise, while assuring the protection of human subjects and the generation of robust data.

Also FDA will encourage the use of adaptive designs for clinical trials.
Review staff were trained on the practical challenges related to conducting a successful trial. As part of this training, more than 100 review staffers visited sponsors of clinical trials to better understand the context and challenges of initiating and conducting clinical trials in the U.S.
Results thus far?

• From 2011 to 2014, the median number of days to full IDE approval decreased from 442 days to 101 days.
  – During 2015, the median number of days to full IDE approval has decreased to 30 days.

• Full approval entailed fewer review cycles.
  – In 2011, only 15% of IDEs were approved within two review cycles.
  – In 2015, 74% of IDEs were approved in two review cycles.
Introduction of Early Feasibility Studies (EFS)

• EFS are small clinical studies designed to gain early insights into an innovative technology during the development process before a larger clinical trial.

• EFS are a critical step in device innovation, but they are frequently conducted in other countries rather than the U.S.

  – Device developers tend to conduct subsequent feasibility and pivotal clinical studies, bringing their products to market earlier in those countries, where through an EFS clinicians gain experience with their technologies.
EFS (continued)

- As part of 2014-2015 Strategic Priority to Strengthen the Clinical Trials Enterprise, CDRH established a goal of increasing the number of EFS IDEs submitted to each review division

  - 50% increase in the number of EFS submissions during the first nine months of 2015, compared with the same period in 2013.

  - A comprehensive education module was developed to help industry navigate the EFS process, with the expectation that FDA will continue to see more EFS conducted in the U.S.
Introduction of the Expedited Access Pathway

- The Expedited Access Pathway (EAP) program
  - A voluntary program for certain medical devices that demonstrate the potential to address unmet medical needs for life threatening or irreversibly debilitating diseases or conditions that are subject to premarket approval applications (PMA) or are eligible for *de novo* requests.
EAP (continued)

- The FDA works with device sponsors to try to reduce the time and cost from development to marketing decision without changing the FDA's PMA approval standard of reasonable assurance of safety and effectiveness.

- Components of the program include:
  - priority review, more interactive review, senior management involvement, and assignment of a case manager.
EAP requirements

• The device is intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition AND

• The device meets at least one of the following criteria:
  – No appropriate alternative treatment exists.
  – The device represents a breakthrough technology that provides a clinically meaningful advantage over existing legally marketed technology.
  – The availability of the device is in the best interest of patients.
What else?

- More research subjects allowed from OUS
- Greater post-market approval mandated data collection
- Compassionate-use opportunities
Summary

• A recognition of the delays in devices approval by the FDA has prompted internal assessments and a host of proactive changes, innovative programs, and an even closer working relationship with industry and researchers.
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