Revamping 510(k):

Out with the Old

In with the New

Zvi Ladin, Ph.D.
Principal
Boston MedTech Advisors

1976

- US celebrated 200

- Toyota introduced Cressida

- Boeing introduced E-3 Sentry (AWACS)

1976: Medical Device Amendments to the FD&C Act

- Paradigm shift compared to review of drugs
- Intended to provide reasonable assurance of the safety and effectiveness of medical devices
- Created a three-class, risk-based classification system for all medical devices
- Established the regulatory pathways for new medical devices (devices that were not on the market prior to May 28, 1976, or had been significantly modified) to get to market: Premarket Approval (PMA) and premarket notification (510(k))
- Created the regulatory pathway for new investigational medical devices to be studied in patients (Investigational Device Exemption (IDE))
- Established several key postmarket requirements: registration of establishments and listing of devices with the FDA, Good Manufacturing Practices (GMPs), and reporting of adverse events involving medical devices
- Authorized the FDA to ban devices

1976: Medical Device Amendments to the FD&C Act

No Authority to Rescind Approval/Clearance

Medical Technology Inventions 1976 - 2016

- 1976 – First commercial PET scanner
- 1980 – Raymond Damadian builds first commercial MRI scanner
- 1980 – Lithotripter – Dornier Research Group
- 1981 – Artificial skin – John F. Burke and Ioannis V Yannas
- 1985 – Automated DNA sequencer – Leroy Hood and Lloyd Smith
- 1985 – Polymerase chain reaction (PCR) – Kary Mullis
- 1985 – Surgical robot – Yik San Kwoh
- 1985 – DNA fingerprinting – Alec Jeffreys
- 1985 – Capsule endoscopy – Tarun Mullick
- 1987 – Tissue engineering – Joseph Vacanti & Robert Langer
- 1988 – Intravascular stent – Julio Palmaz
- 1988 – Laser cataract surgery – Patricia Bath
- 1989 – Pre-implantation genetic diagnosis (PGD) – Alan Handyside
- 1989 – DNA microarray – Stephen Fodor
- 1992 – First vaccine for hepatitis A available
- 1992 – Electroactive polymers (artificial muscle) – SRI International
- 1996 – Dolly the Sheep cloned
- 1998 – Stem cell therapy – James Thomson
- 2000 26 June – The Human Genome Project draft was completed.
- 2001 The first telesurgery was performed by Jacques Marescaux.
- 2006 – First HPV vaccine approved.
- 2007 – The visual prosthetic (bionic eye) Argus II.
- 2013 – The first kidney was grown in vitro in the U.S.
- 2013 – The first human liver was grown from stem cells in Japan.
- 2014 - A 3D printer is used for first ever skull transplant.
- 2016 - The first ever artificial pancreas was created

Medical Technology Inventions 1976 - 2016

1976 – 15,000 Distinct Devices

2019 – FDA Regulates
>190,000 Distinct Devices
>18,000 Manufacturers
>21,000 Manufacturing Sites

Revamping 510(k) Program

- 510(k) Program
  - Born: May 28, 1976 – 510(k) program was born
  - Status: Most regulatory submissions for medical devices
    - 2017 – FDA cleared 3,173 devices through 510(k) pathway
      - 82% of all devices cleared/approved
  - Challenge: "Keep pace with increasing complexity of rapidly evolving technology"
  - Goal: Efficiently advancing beneficial technology to patients, while solidifying FDA's gold standard for safety
    - New Devices
      - Account for advances in technology or
      - Demonstrate meeting more modern safety and performance criteria
    - Old Devices
      - Retire outdated predicates
        - Especially where safer/more effective technology emerges

Principles of 510(k) Review

Regulatory Review

- Reflects continuum
  - Device complexity
  - Risk
- Scientific resources
  - Limited
  - Prioritization
- New frontiers
  - Material science
  - Digital health
  - 3D printing
- Focus on risk/benefit analysis

Recent Innovative Policies

- Use of real world evidence
- Modernize *de Novo* pathway
- Use of rigorous, consensus, objective criteria to serve as predicates for future clearances
- Build national patient safety net
- Re-envision regulatory paradigm for digital health products and IVD
- Pathways to enable patient access to new, innovative devices
  - Dx cancer

Upcoming Changes

- Problem – ~20% of current 510(k) cleared based on predicates that > 10 years old
- Key change – foster/encourage innovation
  - Reliance on more modern predicate devices or
  - Objective performance criteria
- Older predicates
  - Might not reflect modern technology embedded in new devices or
  - More current understanding of device benefits and risks
- FDA intends to make public devices that use ‘old’ predicates
  - Will seek public feedback
  - Does not think that older devices need to be removed from market
  - Does not think that devices relying on ‘old’ predicates are unsafe

Upcoming Changes

Sunset certain older predicates?

The Future of 510(k) – Looking Forward (Not Backward)

New Technologies

- Interconnectivity
- Interoperability
- Miniaturization
- Portability
- Mobile
- Automation
- Robotics
- Advanced materials
- Software-based
- Cybersecurity

Alternative 510(k) – Safety and Performance Based Pathway

- Well-understood devices
- Demonstrate substantial equivalence through objective criteria
  - Safety
  - Performance
- Allows adoption of modern criteria
- Will be used as new predicates for future devices
- Expand use across 510(k) program
- Make it primary pathway for eligible devices

Dynamic Baseline for Safety/Effectiveness

510(k) Program Pilots

- New programs to help improve consistency and efficiency in 510(k) review
- Intended to aid industry and FDA staff in using resources effectively
- FDA reasoning
  - Allows FDA direct more effort on the review of higher risk devices
  - Helps reduce total time to decision
  - Promotes consistency in 510(k) reviews
  - No change in statutory threshold or data requirements for determination of substantial equivalence
- Two programs pilots announced
  - Quality in 510(k) Review
  - Special 510(k)

Quality in 510(k) Review Program Pilot

- Launched September 6, 2018
- First step towards electronic submission
- Uses eSubmitter software
- Interactive review
- Limitations
  - Products considered to be well-understood by FDA
  - Covers only 39 specific Product Codes
  - Not available for combination products and IVD devices
  - CDRH is lead Center for review
- Goals
  - Make final regulatory decision within 60 days of receipt
  - Use of eSubmitter will lead to well-organized submissions
  - More efficient review
  - Improve timely access to safe, effective and high-quality devices

Special 510(k) Program Pilot

- Launched October 1, 2018
- All Special 510(k)s eligible for the program
- Goals
  - Improve efficiency of 510(k) review
  - Expand scope of allowed changes
    - Design
    - Labeling
- Reliance on design control requirements
- Eligibility requirements
  - Proposed change is made and submitted by the manufacturer authorized to market the device
  - Performance data
    - Unnecessary or well-established methods available for evaluation
    - All performance data necessary for substantial equivalence (SE) can be reviewed in summary or risk analysis format

Breakthrough Device Program (2018)

- **Protect** and **Promote** Public Health
- Finalized December 18, 2018
- 110 devices granted designation
- 8 devices received marketing authorization
  - Blood test for Dx concussion
  - AI to detect diabetes-related eye problems
- Applies to certain devices and combination products
- Products provide more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions
- Goal – provide timely access by speeding up development, assessment and review
- Close manufacturer/FDA interaction
  - Prioritized review
- Eligibility criteria – meet both:
  - **First** - The device provides for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions
  - **Second** – meet at least one:
    - Represents Breakthrough Technology
    - No Approved or Cleared Alternative Exist
    - Offers Significant Advantages over Existing Approved or Cleared Alternatives
    - Device Availability is in the Best Interest of Patients
- **First step – Designation (Q-Sub)**
  - 30 day response by FDA
- Available webinar – January 17, 2019

Safer Technologies Program (STeP)

- Support important safety advancements:
  - Improve patient quality of life
  - Advance public health mission (protect and promote)
- Available for devices that:
  - Do not meet criteria for Breakthrough Devices
  - Have potential to be significantly safer than currently available alternatives
- Apply Breakthrough principles and features to treat/diagnose **Non-Life-Threatening** diseases or conditions
- Products offer significant safety innovations that
  - Reduce occurrence of serious adverse events (SAE) or other safety issue or
  - Address known device failure mode or common user error or
  - Provide significant safety advantages for users