Device Post-Market Surveillance Under CDRH & §522

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Postmarket Surveillance

- Postmarket surveillance is a collection of processes and activities the FDA uses to monitor the safety and effectiveness of medical devices once they are on the market.

  - Establish UDI system
  - Promote development of device registries
  - Modernize adverse event reporting
  - Develop NEST
  - Calibrate risk-benefit evaluation in pre- and post-market setting
  - Develop and use new methods for evidence generation and analysis; improve clarity around real world evidence
Postmarket Safety Mechanisms

- Medical Device Reporting
- Recalls (corrections and removals)
- Postmarket surveillance under 522
- Safety communications and emerging signals
2018 Medical Device Safety Action Plan

- FDA goal to be “first” regulator
  - Active surveillance of real world evidence
  - FDA research
  - Early public communications
- Specific initiatives
  - Women’s health
  - Surgical tools
  - Materials in implantable devices
  - Cybersecurity
Example: Women’s Health

- **April 2019:** FDA ordered all manufacturers of surgical mesh intended for transvaginal repair of anterior compartment prolapse to stop selling and distributing their products
  - Required to continue follow-up in 522 studies
- **February 2019:** Safety Communication warning against use of thermography devices in place of mammography
  - Warning Letter issued to firm for marketing device as a sole screening device for breast cancer and other diseases
- **February 2019:** Safety Communication cautioning against use of robotically-assisted devices in women’s health procedures
- **July 2018:** Safety Communication warning against use of Use of Energy-Based Devices to Perform Vaginal ‘Rejuvenation’ or Vaginal Cosmetic Procedures
  - Seven (7) “It’s Come to Our Attention Letters” issued to manufacturers of these devices
- **April 2018:** Restrictions imposed by FDA on sale of Essure, a permanently implanted birth control device for women
Implantable Device Materials

- FDA has recognized a growing body of evidence suggesting that a small number of patients may have biological responses to certain materials in implantable or insertable devices (e.g., inflammatory reactions and tissue changes)
  - Some symptoms may not show up until several years following implantation and thus may not be detected in clinical studies
  - Currently available tests don’t do enough to identify which people might be at risk of reaction to the material in a certain device
- Materials of interest:
  - Metals (2019 priority)
  - Animal materials
  - Innovative materials (e.g., nanoparticles, graphene)
FDA Activities on Metals/Potential Outcomes

- FDA Scientists Conducting Research
- “State-of-the-Science” White Paper
- Advisory Panel Meeting Fall 2019

- FDA safety communications
- Up-classification
- Recalls
- New boxed warnings
- More pre-market research
- More post-market studies
MDR Reportable Event

Event that reporter becomes aware of information that reasonably suggests that the device:

- **User facilities:**
  - has or may have caused or contributed to a death or serious injury

- **Manufacturers and importers:**
  - may have caused or contributed to a death or serious injury
  - has malfunctioned and that device or a similar device marketed by the manufacturer or importer would be likely to cause or contributed to a death or serious injury if the malfunction were to recur
## Reporting Requirements

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<td>Events that require remedial action to prevent an unreasonable risk of substantial harm</td>
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<td>Annual Reports</td>
<td>FDA</td>
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Potential Pitfalls

- Not documenting and reporting MDRs from any source, including:
  - Social media
  - Literature
  - Servicing
  - Trade shows
  - Clinical trials
  - OUS
- Failure to report in timely manner, due to, e.g., employees failing to report internally
- MDR reportability decision making, including:
  - User error
  - Off-label use
  - Labeled adverse events
# Regulatory and Policy Framework Governing Recalls

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*Although published in the C.F.R, Part 7 is agency guidance*
Recalls

- Voluntary recall: Firm’s removal or correction of a marketed product that the FDA considers to be in violation of FDA and against which FDA would initiate legal action.

- Mandatory recall: If FDA finds that there is a reasonable probability that a device would cause serious, adverse health consequences or death, FDA may require company to:
  - Cease distribution of device
  - Notify health professionals and user facilities to cease use of device
  - Recall device
Recall Classification

- **Class I**: there is a reasonable probability that the use of or exposure to a violative product will cause serious adverse health consequences or death

- **Class II**: the use of, or exposure to, a violative product:
  - may cause temporary or medically reversible adverse health consequences, or
  - the probability of serious adverse health consequences is remote

- **Class III**: the use of, or exposure to, a violative product is not likely to cause adverse health consequences
Reports of Corrections or Removals

Must report any correction or removal of a device if action was initiated to:
- Reduce a risk to health posed by the device, or
- Remedy a violation of the FDCA caused by the device which may present a risk to health

Risk to health:
- A reasonable probability that use of, or exposure to, the product will cause serious adverse health consequences or death, or
- That use of, or exposure to, the product may cause:
  - temporary or medically reversible adverse health consequences, or
  - an outcome where the probability of serious adverse health consequences is remote

Reports are required for Class I and II recalls
Common Pitfalls

- Allowing too much time to elapse between identifying a systemic issue and initiating a recall
- Lack of justification for why the recall was not initiated to reduce a risk to health
- Undertaking actions in the field without realizing these actions are “corrections” or “removals” that must be analyzed for reportability under Part 806
  - Distributing a “market bulletin” or “technical advisory”
  - Applying corrections, including inspection of product, during routine maintenance services
Conditions of PMA Approval

- FDA may impose postapproval requirements in approval order, including:
  - restriction of sale, distribution or use
  - continuing evaluation and periodic reporting on safety, effectiveness, and reliability of device for intended use (e.g., post-approval studies)
  - prominent display in the labeling of a device and in the advertising of any restricted device of warnings, hazards or precautions important for the device’s safe and effective use
  - at specified intervals, submission of periodic reports

- Postapproval (Annual) Reports:
  - Identification of certain changes
  - Bibliography and summary of information not previously submitted, including unpublished reports of data involving device or related devices and reports in scientific literature concerning device
Postmarket Surveillance Studies

- FDCA § 522; 21 C.F.R. Part 822
- Postmarket surveillance can be ordered at time of approval or anytime thereafter if following conditions are met:
  - failure of the device would be reasonably likely to have serious adverse health consequences; or
  - the device is intended to be implanted in the human body for more than one year; or
  - the device is expected to have significant use in pediatric populations; or
  - the device is intended to be a life sustaining or life supporting device used outside a device user facility.
Postmarket Surveillance Studies

Manufacturers must:

- Submit a postmarket surveillance plan for approval within 30 days of receiving an order to conduct a postmarket surveillance study from FDA,
- Commence surveillance no later than 15 months from date of order
- Device is misbranded under FDCA § 502(t) if requirements are not met
Warning Letters

- 2011 – 1 Letter to manufacturer of spinal system
- 2015 – 3 Letters to: manufacturer of exoskeleton device, manufacturer of skull prosthesis, and manufacturer of multiple hip implants
- 2018 – 3 Letters to 3 manufacturers of duodenoscopes all subject to same 522 study requirement
Safety Communications and Related Notices

- Safety issues communications through “Safety Communications” and recall notices published on FDA’s website
  - Previously, called Public Health Notifications
- Safety signals:
  - 2009-2010 Signal Escalation Pilot Program
  - Posting of drug potential safety signals pursuant to section 921 of FDAAA
  - Draft guidance “Public Notification of Emerging Postmarket Medical Device Signals” published Dec. 2015
What is an Emerging Signal?

- “Public Notification of Emerging Postmarket Medical Device Signals” guidance (Dec. 2016)

- New information:
  - that supports a new causal association or new aspect of a known association between a device and an adverse event
  - for which the agency has conducted an initial evaluation and determined that the information has the potential to impact patient management decisions and/or the known benefit-risk profile of the device
When is an Emerging Signal Published?

Factors include:
- Likelihood of the event
- Severity, duration and reversibility of the event
- Magnitude of the benefit of the device
- Quality of data and strength of evidence of a causal relationship
- Extent of patient exposure
- Impact on vulnerable populations
- Potential for preventing, monitoring or mitigating risk
- Availability of alternative therapies
- Implications for similar or related devices
Emerging Signals: Open Issues

- Data sources and methodologies
- Impact on prescribing and use
- Extrapolation across multiple products
- Speed and nature of FDA investigation
- FDA follow-up and corrections
- Industry notice and involvement
- Off-label information
- Expected manufacturer response
- Potential for products liability lawsuits
- Appropriateness of acting through guidance
Office of Product Evaluation and Quality

- Office of Health Technology 1 (Ophthalmic, Anesthesia, Respiratory, ENT and Dental Devices)
- Office of Health Technology 2 (Cardiovascular Devices)
- Office of Health Technology 3 (Reproductive, Gastro-Renal, Urological, General Hospital Device)
- Office of Health Technology 4 (Surgical and Infection Control Devices)
- Office of Health Technology 5 (Neurological and Physical Medicine Devices)
- Office of Health Technology 6 (Orthopedic Devices)
- Office of Health Technology 7 (In Vitro Diagnostics and Radiological Health)