FDLI Introduction to Medical Device Law & Regulation

Post Marketing Issues

Allyson B. Mullen
Hyman, Phelps & McNamara, P.C.
202-737-9639

www.hpm.com • amullen@hpm.com

What We Will Cover

- **Complaint Handling**
- Medical Device Reporting
- Unique Device Identifier (UDI)
- Recalls
- Notices of Corrections and Removals
- Ongoing Monitoring of Device Performance
- Best Practices

Complaint Handling

- A complaint is a communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution
- Manufacturers must establish and maintain procedures for a formally designated unit to receive, review, and evaluate complaints
- Complaint procedures must ensure:
  - Timely and uniform processing of complaints
  - Documentation of oral complaints upon receipt
  - Evaluation of complaints to determine whether they represent MDR reportable events

Complaint Handling

- Complaints must be evaluated to determine whether an investigation is necessary
- Any complaint involving possible failure of a device to meet required specifications must be investigated, unless an investigation has been performed for a similar complaint and another investigation is unnecessary
- Manufacturers must document decisions to not investigate, including the name of the individual responsible for the decision

Complaint Handling

- Investigations must be documented to include:
  - name of the device
  - date complaint was received
  - any device identification(s) and control number(s) used
  - name, address, and phone number of complainant
  - nature and details of complaint
  - dates and results of investigation
  - any corrective action taken
  - any reply to the complainant
- Any MDR reportable events must maintained in a separate portion of the complaint files or otherwise clearly identified

Servicing

- When servicing is a specified requirement, manufacturers must analyze service reports to identify existing and potential causes of nonconforming product or other quality problems, and determine the need for corrective or preventive action
- Service reports describing MDR reportable events must be treated as complaints and processed in accordance with complaint handling requirements

What We Will Cover

- Complaint Handling
- **Medical Device Reporting**
- Unique Device Identifier (UDI)
- Recalls
- Notices of Corrections and Removals
- Ongoing Monitoring of Device Performance
- Best Practices

What is a Medical Device Report (MDR)?

- MDRs are intended to alert FDA to potential product issues
- MDRs are required when (i) a user facilities become aware of an event that reasonably suggests that a device has or may have caused or contributed to a death or serious injury; or (ii) a manufacturer or importer receives or otherwise becomes aware of information, from any source, that reasonably suggests that one of its marketed devices may have:
  - Caused or contributed to a death or serious injury
  - Malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to death or serious injury, if the malfunction were to recur
- A “serious injury” is one that:
  - Is life-threatening;
  - Results in permanent impairment of a body function or permanent damage to body structure; or
  - Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure

What is an MDR?

- MDRs do not necessarily reflect a conclusion by the reporting entity or by FDA that the device, the reporting entity, or its employees, caused or contributed to the reportable event
- The reporting entity need not admit and may deny that the report submitted constitutes an admission that the device caused or contributed to a reportable event

Public Disclosure of MDRs

- MDRs are publicly disclosed under the Freedom of Information Act and elsewhere
- Before disclosing, FDA should delete:
  - trade secrets
  - confidential commercial or financial information
  - any personal, medical, or other information that would constitute an invasion of personal privacy
  - and other identifying information of a third party voluntarily submitting an adverse event report

Who Must File MDRs?

- MDR requirements apply to manufacturers, importers and device user facilities
- Persons subject to “manufacturer” MDR requirements include those who:
  - Manufacture, prepare, propagate, compound, assemble, or process a device
  - Repackage or otherwise change the container, wrapper, or labeling of a device in the furtherance of its distribution from the original place of manufacture to the person who makes final delivery or sale to the ultimate user
  - Initiate specifications for devices that are manufactured by a second party for subsequent distribution
  - Manufacture components or accessories that are ready to be used and are intended for commercial distribution
- User facilities have the option of reporting to FDA or to the manufacturer

When is MDR Reporting Required?

- A manufacturer or importer is considered to have become aware of a reportable event when any of its employees becomes aware of the event
- Information giving rise to MDRs may come from a variety of sources
- A death or serious injury need not be reported as an MDR if:
  - It is determined that the information received is erroneous in that a device-related adverse event did not occur
  - A person qualified to make a medical judgment (e.g., a physician, nurse, risk manager, or biomedical engineer) reasonably concludes that the device did not cause or contribute to a death or serious injury or that a malfunction would not be likely to do so if it were to recur
  - It is determined that the device was manufactured by another manufacturer (although the information must still be forwarded to FDA with a letter explaining that the device was not manufactured by the firm)

MDR Reporting Requirements

- MDRs must include specified information “reasonably known” about the patient, adverse event or product problem, device manufacturer, and initial reporter
- Reporting entity must attempt to obtain any missing information or explain why it could not do so
- Any required information obtained after the MDR is submitted must be filed within one month of receipt of the information

Electronic MDR Reporting Requirements

- February 14, 2014 – Final rule amending 21 C.F.R. Part 803 to incorporate requirements for electronic MDR Reporting (eMDR)
  - Changes the method of reporting for Manufacturers and Imports, but does not materially change the underlying requirements for reporting MDRs
  - User Facilities may report MDRs electronically, but it is not required
- Rule took effect on August 14, 2015

eMDR Reporting Requirements

Reporting Requirements: Manufacturers to FDA		
30 day reports of death, serious injuries and malfunctions	Electronically through FDA Electronic Submission Gateway (ESG)	Report within 30 days of becoming “aware”
5 day reports on events that require remedial action to prevent unreasonable risk of harm to public health or as designated by FDA	Electronically through ESG	Report within 5 working days of becoming aware

eMDR Reporting Requirements

Reporting Requirements: User Facilities		
Death	Use Form FDA 3500A or electronically (to FDA and manufacturer)	Within 10 working days of becoming "aware"
Serious injury	Use Form 3500A or electronically (to FDA* or manufacturer)	Within 10 working days of becoming "aware"
Annual report of death and serious injury	Use Form 3419	January 1

* If manufacturer is unknown

eMDR Reporting Requirements

Reporting Requirements: Importers		
Death	To FDA electronically through ESG To Manufacturer electronically or paper	Report within 30 days of becoming "aware"
Serious injury	To FDA electronically through ESG To Manufacturer electronically or paper	Report within 30 days of becoming "aware"
Malfunction	To FDA electronically through ESG To Manufacturer electronically or paper	Report within 30 days of becoming "aware"

MDR Procedures

- MDR reportable events must be reviewed, evaluated, and investigated in accordance with the QSR complaint handling requirements
- Manufacturers must have written procedures to ensure:
  - Timely identification and evaluation of potential MDR events
  - Standardized review process
  - Timely transmission to FDA
- Recordkeeping
  - Documentation of decision-making process to determine whether MDR was required
  - Retained for 2 years from date of event or life of device, whichever is greater

MDR Procedures – eMDR

- Timely transmission of MDRs
  - The “receipt date” for purposes of a company’s timely reporting of MDRs will be the date that Acknowledgement 1 is received, but only if the eMDR is ultimately successfully loaded at CDRH (thus, a successful Acknowledgement 3 is received)
  - Acknowledgement 1 indicates that the submission was received at the ESG
  - Acknowledgement 2 indicates that the submission reached CDRH
  - Acknowledgement 3 notifies the submitter that the submission was either successfully loaded into CDRH’s adverse event database
    - If a submitter receives a notice that there were errors, the submitter will need to correct the file and re-submit

MDR Procedures – eMDR

- The MDR recordkeeping requirements for Manufacturers and Importers also includes maintaining the three acknowledgement messages from FDA (received after the eMDR is submitted) as part of the MDR file
  - new 21 C.F.R. § 803.18(b)(1)(iii)
  - Three new Acknowledgement notices will be sent if the eMDR is not successfully loaded in the first attempt.

Voluntary Malfunction Summary Reporting Program

- On August 17, 2018, FDA published a final rule for the Voluntary Malfunction Summary Program.
- This program permits manufacturers to report certain device malfunctions for low-risk products in summary form on a quarterly basis, as an alternative to individual MDR reports.
- Eligible products are identified in FDA's product code database.
- Format
  - Same electronic submission form used to submit individual MDRs.
    - Must identify the number of reportable malfunctions that each report represents.
    - Separate summary malfunction reports must be submitted for each unique combination of brand name, device model, and problem code(s).

Limitations of the Program

- Does not apply to deaths or serious injuries.
- Does not apply to importers or distributors.
- Does not replace the requirement to submit a 5-day report on events that require remedial action to prevent unreasonable risk of harm to public health or as designated by FDA.
- Does not apply to “new” product codes that have not been in existence for two years.
  - Manufacturers can requests that a product code be added to the list of eligible product codes
- Does not apply to devices subject to a recall.

Summary Malfunction Reporting Schedule

Reportable malfunctions or supplemental information that you become aware of during these timeframes:	*Must be submitted to FDA by:*
January 1–March 31	April 30
April 1 – June 30	July 31
July 1 – September 30	October 31
October 1 – December 31	January 31

MDR Reporting Example

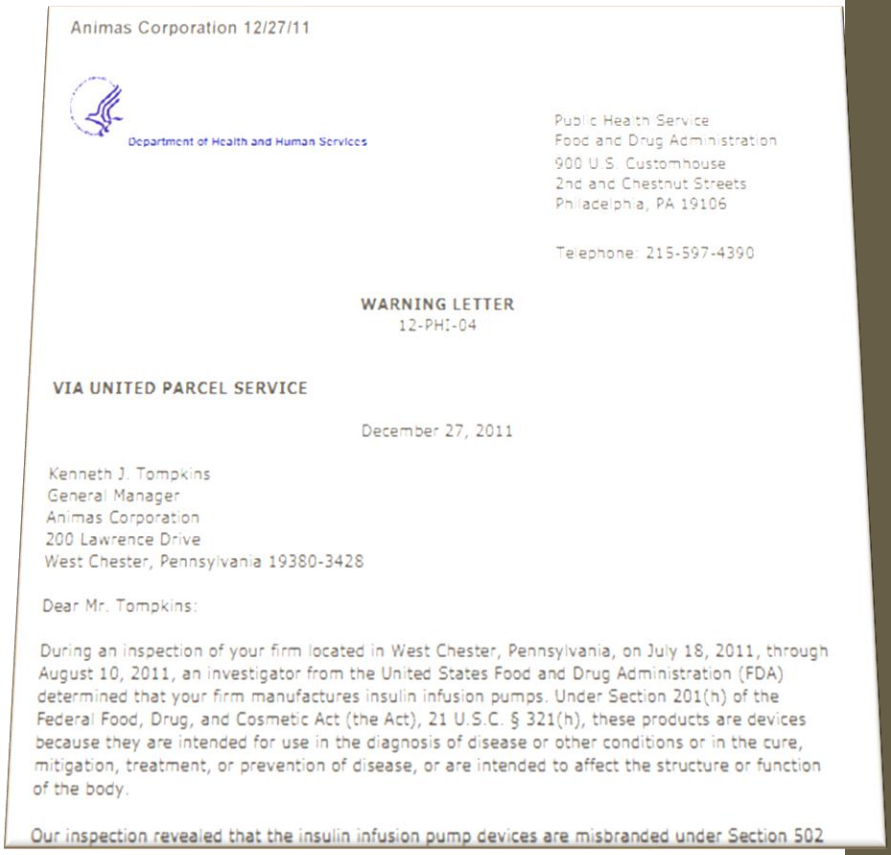
- Company A manufactures insulin pumps. Hospital reports to Company A that Company A's pump was a factor in a patient's diabetic ketoacidosis, but the hospital determined that it was due to user error.

  Reportable?

MDR Reporting Example

Reportable.

"Complaint # (b)(4) references an event where the subject device may have been a factor in a serious injury (Diabetic Ketoacidosis) as a result of user error. This event should have been reported to FDA."



Animas Corporation 12/27/11

Department of Health and Human Services

Public Health Service
Food and Drug Administration
900 U.S. Customhouse
2nd and Chestnut Streets
Philadelphia, PA 19106

Telephone: 215-597-4390

WARNING LETTER
12-PHI-04

VIA UNITED PARCEL SERVICE

December 27, 2011

Kenneth J. Tompkins
General Manager
Animas Corporation
200 Lawrence Drive
West Chester, Pennsylvania 19380-3428

Dear Mr. Tompkins:

During an inspection of your firm located in West Chester, Pennsylvania, on July 18, 2011, through August 10, 2011, an investigator from the United States Food and Drug Administration (FDA) determined that your firm manufactures insulin infusion pumps. Under Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 321(h), these products are devices because they are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or are intended to affect the structure or function of the body.

Our inspection revealed that the insulin infusion pump devices are misbranded under Section 502

What We Will Cover

- Complaint Handling
- Medical Device Reporting
- **Unique Device Identifier (UDI)**
- Recalls
- Notices of Corrections and Removals
- Ongoing Monitoring of Device Performance
- Best Practices

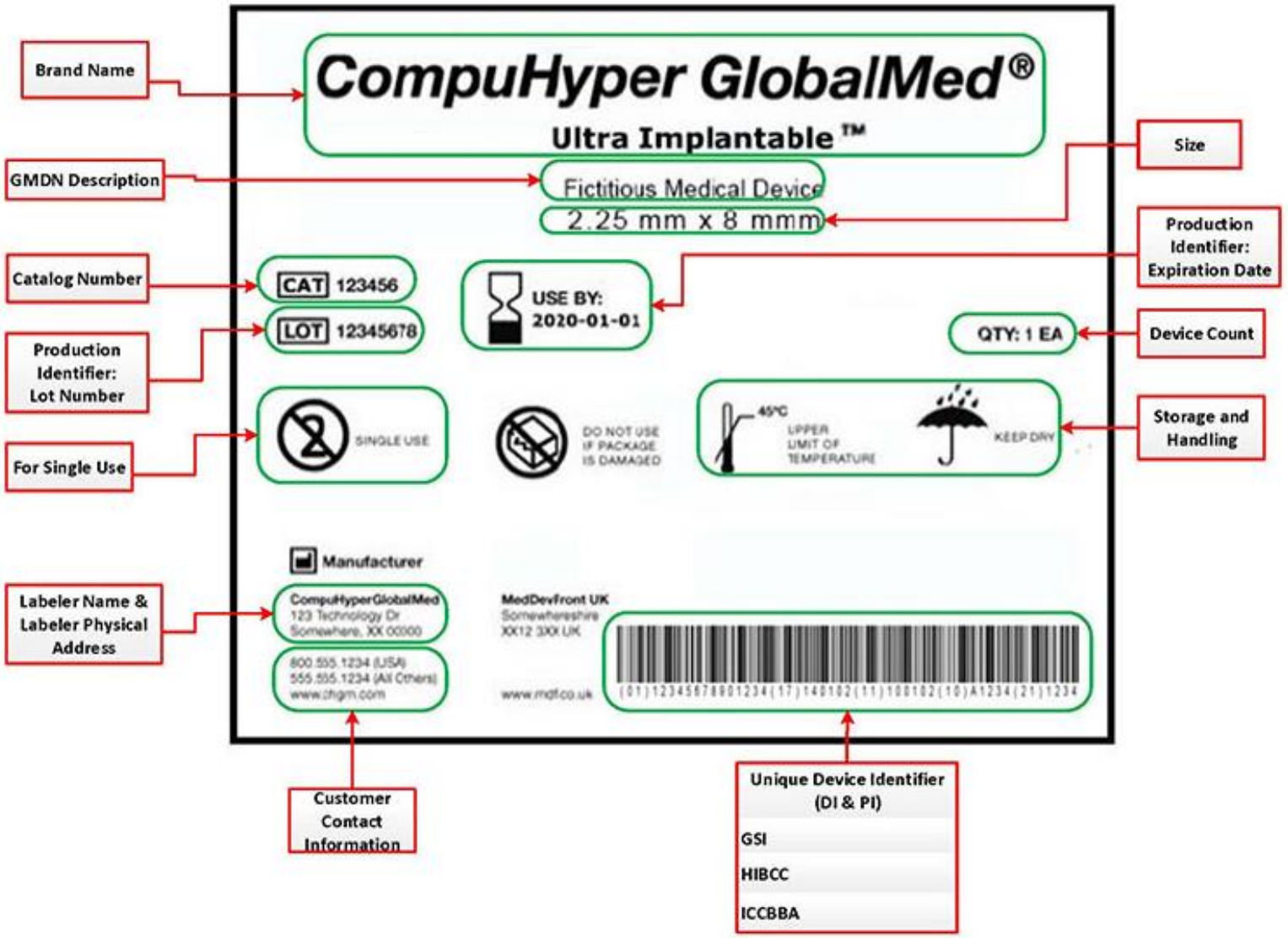
History

- Section 226 of the FDA Amendments Act of 2007 (FDAAA) and section 216 of the FDA Safety and Innovation Act of 2012 (FDASIA)
  - Amended the Federal Food, Drug, and Cosmetic Act to add section 519(f)
  - Directs FDA to publish regulations establishing a unique device identification (UDI) system for medical devices
- **September 2013 – UDI regulations published**

What is a UDI?

- Code on the device label, packaging or product, in both plain text and machine readable format
- Two parts : UDI = DI+PI
  - Device Identifier (DI) (static) – specific to a device version or model
  - Production Identifier(s) (PI) (dynamic) – one or more currently used control/production information, such as lot/batch, serial number, manufacturing date, expiration date
- Global Unique Device Identification Database (GUDID): FDA database containing DI portion of the UDI

Example Device Label



Intended Benefits of UDI System

- More accurate reporting, reviewing and analyzing of adverse event reports so that problem devices can be identified and corrected more quickly
- Reducing medical errors by enabling health care professionals and others to more rapidly/precisely identify a device and obtain important information concerning the characteristics of the device
- Standard and clear way to document device use in electronic health records, clinical information systems, claims data sources and registries.
- More robust postmarket surveillance system can also be used to support premarket approval/clearance of new devices and new uses of currently marketed devices

Benefits, cont.

- Providing a standardized identifier that will allow manufacturers, distributors and healthcare facilities to more effectively manage medical device recalls.
- Foundation for a global, secure distribution chain, helping to address counterfeiting and diversion and prepare for medical emergencies.
- Leading to the development of a medical device identification system that is recognized around the world.

From FDA, Benefits of a UDI System, http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/UniqueDeviceIdentification/BenefitsofaUDIsystem/default.htm

UDI Application

- Unique UDI applied to “base package” AND higher levels of packaging
- Default location is the label
- Human readable and encoded in a form of automatic identification technology
- No specific technology (technology neutral)
- ALSO Direct Marking (DM) for device intended to be used more than once and reprocessed before each use
- Stand-alone software - means of displaying its UDI
  - Start-up screen, if software not packaged (only downloaded)
  - On label and package, same as other devices, if packaged

General Exemptions

- Class I Devices do not need to include Production Identifiers in UDI
  - A UPC can satisfy the requirement for a UDI for a Class I device
- GMP-exempt Class I devices
- Individual single-use devices, distributed together in a single device package, intended to be stored in that device package until removed for use, and which are not intended for individual commercial distribution or sale.
  - Examples: individual contact lenses, individual condoms, etc.

Compliance Dates

- Explains when a labeler is required to comply with a regulatory requirement
- Implementation (compliance) timeframes:
  - September 24, 2014: Class III medical devices
  - September 24, 2016: Class II medical devices
  - September 24, 2018: Class I and unclassified medical devices
    - FDA established enforcement discretion for class I and unclassified devices until September 24, 2022
- For direct marking, compliance dates are extended by two years

Exception to Compliance Dates

- FDA may grant an extension to the compliance date when it is in the best interest of the public health.
  - E.g., FDA has granted several extensions to the contact lens industry
- Provides an exception for a **finished device** that is manufactured ***and labeled*** **prior to the compliance** date – exception expires 3 years after the compliance date (existing inventory).

Stand-Alone Software

- New section – explains how stand-alone software can meet UDI labeling requirements when it is not distributed in package form
  - Must bear a UDI on its start-up screen or through a menu command
- All stand-alone software to include means of displaying its UDI
- Stand-alone software that is distributed in both packaged form and in a form that is not packaged may be use same UDI
- Compliance dates are the same as class compliance dates

Exceptions and Alternatives

- FDA may initiate and grant an exception or alternative – on its own or in response to a request
- FDA may rescind an exception or alternative
- FDA will make all decisions available on its website
- Any labeler may use a granted exception or alternative

Exception/Alternative Process

- Identify the device(s) subject to exception/ alternative
- Identify the provisions subject to the request
- If exception – explain why the requirements are not technologically feasible.
- If an alternative, describe the alternative and
  - why it would provide for more accurate, precise, or rapid device identification – or
  - how it would better ensure the safety or effectiveness of the device
- Estimate the number of affected labelers and devices

Alternatives granted

- FDA granted a general alternative for a number of retail products, including:
  - Thermometers
  - Condoms
  - Pregnancy tests
  - Personal lubricants
  - Dental cements
  - Denture repair kits
  - Tampons
- Alternative allows UPC code to serve as UDI on the package for products sold in retail establishments
- Information still required to be entered into GUDID

GUDID information

- The proprietary/trade/brand name of the device
- Previous DI if a new version or model
- The version or model number
- If direct marked, DI if different than label
- The size of the version or model
- The type of production identifiers on the label
- FDA premarket submission and listing number(s)
- Global Medical Device Nomenclature (GMDN) term
  - System of generic descriptors used to identify all medical device products
- FDA product code
- The number of individual devices in each package

Complexity

- UDI implementation far more complex than anticipated
- Many manufacturers of devices likely still not compliant even though compliance dates have now passed
- Remains to be seen how FDA will enforce failure to comply with UDI

What We Will Cover

- Complaint Handling
- Medical Device Reporting
- Unique Device Identifier (UDI)
- **Recalls**
- Notices of Corrections and Removals
- Ongoing Monitoring of Device Performance
- Best Practices

Recalls

- There are two types of recalls: mandatory and voluntary
  - Mandatory recalls are initiated when FDA determines that agency action is necessary to "protect the public health and welfare" because "a distributed product presents a risk of illness or injury or gross consumer deception" and the firm has not initiated a recall. 21 CFR Part 7.45.
  - Voluntary recalls are defined as a "firm's removal or correction of a marketed product that FDA considers to be in violation of the laws it administers and against which the agency would initiate legal action." 21 CFR Part 7.3(g).
- Most recalls are voluntary

Recall Classifications

- 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

Opposite of medical device classification scheme

Health Hazard Evaluation

- FDA determines a recall's classification based on the relative degree of health hazard presented by the product being recalled
- Health hazard evaluation includes an analysis of:
  - Whether injury has occurred from product use
  - Whether existing conditions could contribute to a situation that exposes humans or animals to a health hazard
  - Assessment of hazard to various segments of the population that would be exposed, with focus on high risk populations
  - Assessment of the degree of seriousness of the hazard to which populations would be exposed
  - Assessment of likelihood of occurrence of the hazard
  - Assessment of the consequences of the occurrence of the hazard

Top 10 List for Effective Recalls

1) Adequate information from the field
2) Comprehensive investigations and trending
3) Appropriate Health Hazard Evaluations
4) Timely and accurate reporting to FDA
5) Appropriate and timely containment action
6) Effective recall communication; process & content
7) Appropriate and timely corrective action
8) Accurate device distribution records
9) Effective system for device reconciliation
10) Sufficient company resources

FDA has an office that analyzes post-market safety data (Office of Surveillance and Biometrics)

- What can they do?
  - Send follow up letters for information on MDRs
  - Order post-market studies (Section 522 of FDCA)
  - Communication to the public
- Premarket: "Statistical analyses of premarket clinical studies are a critical part of the Center's premarket approval process and provide the empirical basis for expected post-market device performance."
- Post-market: "OSB conducts statistical analyses, designs and performs targeted epidemiological studies, directs a nation-wide surveillance system designed to monitor the performance of marketed medical devices, and facilitates cross-Center response when a problem is identified."

Public Notification of a Recall

2014 Recalls

Device Name	Date
CareFusion 203, Inc., EnVe and ReVel ventilators - Power Connection Failure	10/17/14
ICU Medical, Inc., ConMed Stat2 Flow Controller – Delivers Higher Flow Rate than Intended	10/09/14
Teleflex Medical, Hudson RCI Pediatric Anesthesia Breathing Circuits - Circuit Ends May Crack or Break	10/07/14
Customed Inc., Surgical Convenience Packs - Damaged Packaging	09/05/14
Cook CloverSnare 4-Loop Vascular Retrieval Snare - Snare Tip May Break During Use	09/04/14
DePuy Synthes Craniomaxillofacial Distraction System - May Reverse Directions After Surgery	08/26/14
Children's Medical Ventures, Gel-E Donut and Squishon 2 - Possibility of Mold	08/21/14
Cardiovascular Systems Diamondback 360 Peripheral Orbital Atherectomy System - Sheath May Fracture During Use	08/19/14

- Published on FDA website
- FDA also publishes a weekly FDA Enforcement Report (includes field corrections, seizures, injunctions)
- FDA typically publishes press releases for Class I recalls

Other FDA Communications

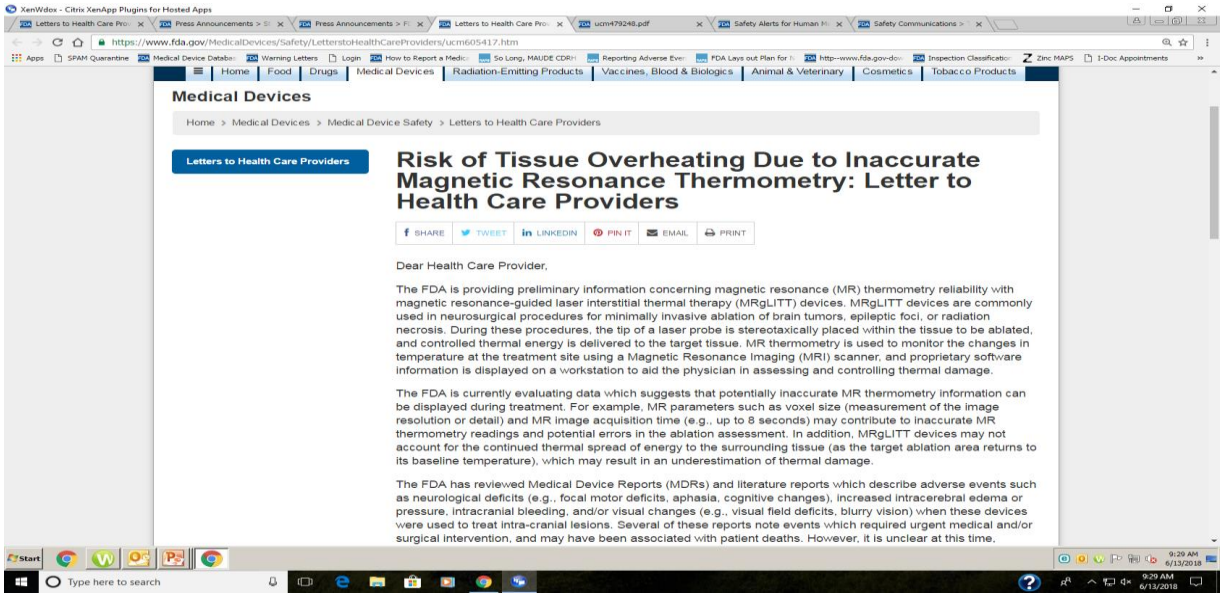
- In December 2016, FDA finalized the guidance "Public Notification of Emerging post-market Device Signals"
- An emerging signal is "new information about a marketed medical device: 1) that supports a new causal association or a new aspect of a known association between a device and an adverse event or set of adverse events, and 2) 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."
  - Information that is unconfirmed, unreliable, or lacks sufficient strength of evidence is not an emerging signal.

Other FDA Communications

- FDA can (and has) issue Safety Alerts regarding apparent product problems
  - Magellan Diagnostics Lead Testing Systems
    - FDA press release and safety communication – May 17, 2017
    - Company recall May 25 and June 5, 2017
    - Updated statement from FDA regarding Agency's investigation – July 13, 2017
    - FDA issues warning letter to Becton Dickenson regarding blood collection tubes as part of investigation – January 11, 2018
    - FDA updates investigation and BD recalls blood collection tubes – March 22, 2018
  - Ovarian Cancer Screening Tests – September 7, 2016
    - FDA issues communications directed at patients and physicians to recommend against using such tests

Other FDA Communications

- Healthcare provider letters



What We Will Cover

- Complaint Handling
- Medical Device Reporting
- Unique Device Identifier (UDI)
- Recalls
- **Notices of Corrections and Removals**
- Ongoing Monitoring of Device Performance
- Best Practices

Corrections and Removals

- Manufacturers must report “corrections” and “removals” of devices that pose or may pose a “risk to health” to FDA within 10 days of initiating action
  - Correction: the repair, modification, adjustment, relabeling, destruction, or inspection of a product without its physical removal
  - Removal: the physical removal of a product from its point of use for repair, adjustment, relabeling, destruction, or inspection
- Recalls are corrections and removals of violative product
- Class III recalls, by definition, do not involve a “risk to health” and do not have to be reported to FDA
  - Records still must be maintained

What is Not a Recall

- Product enhancements: (1) changes to improve the performance or quality of a device, that (2) are not intended to remedy an FDCA violation
  - E.g., changes designed to better meet the needs of the user, changes to make the product easier to manufacture, changes to the appearance that do not affect the device's use
- Product enhancements must be reported under Part 806 if they are intended to reduce a "risk to health"
- FDA has taken enforcement action against "silent recalls," i.e., where a manufacturer makes a product correction without reporting a recall

What is Not a Correction or Removal

- Market withdrawal: correction or removal of a product that involves a minor violation or no violation of the FDCA (e.g., normal stock rotation practices)
- Routine servicing: regularly scheduled maintenance of a medical device
- Stock recovery: correction or removal of a product that has not been marketed or that has not left the direct control of the manufacturer

Notices of Correction or Removal

- Among other things, report must include:
  - Name, address and telephone number of manufacturer and reporting individual
  - Brand, common, and classification name of device and its marketing status
  - Description of event causing removal or correction and remedial action taken
  - Any injuries or illnesses that have occurred
  - Total number of devices subject to the correction or removal
  - Date of manufacture or distribution and expiration date or expected life
  - Name, address and phone number of all domestic and foreign consignees, and dates and numbers of devices distributed to each
  - Copy of all communications regarding correction or removal

Other Part 806 Requirements

- Manufacturer must maintain an internal record of a correction or removal even when a written report to FDA is not required
- Internal record must be maintained for 2 years beyond the expected life of the device
- Required records may be inspected upon request by FDA
- Records submitted to FDA are publicly disclosed, with redaction of any protected information
- Report of correction or removal does not necessarily reflect a conclusion by the reporter or FDA that the device caused or contributed to a death or serious injury
- Reporter need not admit, and may deny, that the device caused or contributed to a death or serious injury

What We Will Cover

- Complaint Handling
- Medical Device Reporting
- Unique Device Identifier (UDI)
- Recalls
- Notices of Corrections and Removals
- **Ongoing Monitoring of Device Performance**
- Best Practices

Post-market Conditions of Approval

- Device Tracking: orders that require a manufacturer to track a device if the 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 is life-sustaining or life supporting and used outside a device user facility. *(FDCA §519(e)(1))*
  - From manufacturer to patient *(21 CFR §821)*

PMA Conditions of Approval / Post-marketing Requirements

- **Adverse Reaction or Device Defect Reporting**
  - Required to submit an "Adverse Reaction Report" or "Device Defect Report" within 10 days after receipt or knowledge of information concerning:
    - Mix up of the device or labeling with another article
    - Adverse reaction attributable to the device and is not addressed in labeling or is occurring with unexpected severity or frequency
    - Any significant change or deterioration in the device, or any failure of device to meet specification, that could not cause a death or serious injury, but are correctable by processes identified in the labeling

PMA Conditions of Approval / Post-marketing Requirements

- **Post Approval Studies**
  - Section 513(a)(3)(C) provides:
    - In making a determination of a reasonable assurance of the effectiveness of a device for which an application under section 515 has been submitted, the Secretary shall consider whether the extent of data that otherwise would be required for approval of the application with respect to effectiveness can be reduced through reliance on post-market controls.
  - May be required under 21 CFR § 814.82(a)(2)
    - Post-approval requirements may include as a condition to approval of the device: continuing evaluation and periodic reporting on the safety, effectiveness, and reliability of the device for its intended use.
    - FDA will state in the PMA approval order the reason or purpose for such requirement and the number of patients to be evaluated and the reports required to be submitted.

PMA Conditions of Approval / Post-marketing Requirements

Post Approval Studies (cont'd)

- Possible results of failure to comply with post approval study requirements:
  - Post-market surveillance under § 522 (21 CFR Part 822)
  - Withdraw approval of the PMA under § 515(e) (21 CFR 814.46(a))
  - Civil money penalties
    - A significant or knowing failure to report information about a post-approval study; or
    - Such failure constitutes a risk to public health

Post-market Surveillance (Statutory)

- Specified in 21 CFR §822 (FDCA §522) for any Class II or Class III device:
  - Failure would be reasonably likely to have serious adverse health consequences; or
  - Expected to have significant use in pediatric population; or
  - Intended to be implanted in human body for more than one year; or
  - Intended to be life sustaining or life supporting device used outside device user facility

Post-market Surveillance (cont.)

- Purpose:
  - Implement surveillance
  - Maximize plans that collect useful data
    - Unforeseen adverse events
    - Rate of anticipated events
    - Information to protect public health
- Ordered by FDA
  - Post-market surveillance order: 522 Studies
  - Before or after marketing

Post-market Surveillance (cont.)

- May be condition of PMA approval

OR

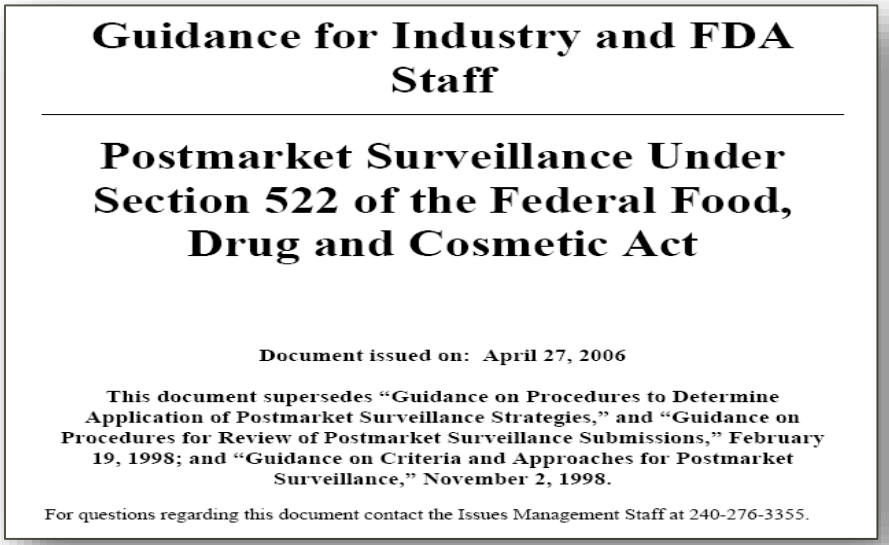
- May stem from:
  - Product complaints; adverse event reports
  - Recall or corrective action
  - Published literature
  - New or expanded uses for existing devices
  - Significant changes in device characteristics
  - Long-term follow-up for rare events

Post-market Surveillance (cont.)

- FDA will provide information about post-market concerns
- FDA will identify specific surveillance methods that may be appropriate
  - Complaint history and literature review
  - Non-clinical device testing
  - Follow-up with defined patient sample
  - Clinical studies

Post-market Surveillance (cont.)

- Manufacturers must submit plan for approval within 30 days of receiving order
- FDA has 60 days to approve plan
- Guidance document available



Guidance for Industry and FDA Staff

Postmarket Surveillance Under Section 522 of the Federal Food, Drug and Cosmetic Act

Document issued on: April 27, 2006

This document supersedes "Guidance on Procedures to Determine Application of Postmarket Surveillance Strategies," and "Guidance on Procedures for Review of Postmarket Surveillance Submissions," February 19, 1998; and "Guidance on Criteria and Approaches for Postmarket Surveillance," November 2, 1998.

For questions regarding this document contact the Issues Management Staff at 240-276-3355.

Post-market Surveillance

- FDA has public listing of studies
  - Applicant name
  - Device
  - Specialty
  - 510(k) or PMA number
  - 522 order date
  - Status

§522 PS Studies Page

Active Orders

Suggest Enhancement / Report Issue | Export to Excel

522 Order Number	Manufacturer	Device Name	Medical Specialty	Date 522 Order	Study Name	Study Status
PS160002	Vermillion, Inc	Ova1 Next Generation test	Immunology	03/21/2016	PSS	Plan Pending
PS160001	Bayer Healthcare, LLC	Essure system for permanent birth control		02/29/2016	PSS	Plan Pending
PS150002	Fujifilm Medical Systems USA, Inc.	Fujifilm Duodenoscopes	Gastroenterology/ Urology	10/05/2015	Human Factors Study	Plan Pending
					Sampling and Culturing Study	Plan Pending
PS150003	Olympus Medical Systems Corporation (OMSC.	Duodenoscopes	Gastroenterology/ Urology	10/05/2015	Human Factors Study	Plan Pending
					Sampling and Culturing Study	Plan Pending
PS150004	Pentax Medical	Duodenoscopes	Gastroenterology/ Urology	10/05/2015	Human Factors Study	Plan Pending
					Sampling and Culturing Study	Plan Pending
PS150001	Preceptis	Hummingbird tympanostomy tube system	Ear Nose & Throat	04/23/2015	Post-market Surveillance Study (PSS)	Study Pending
PS140001	Argo Medical Technologies, Inc	Rewalk	Physical Medicine	06/26/2014	ReWalk Registry	Plan Overdue
PS130046	St. Jude Medical, Inc.	Amplatzer	Cardiovascular	09/30/2013	ADVANCE ASO	Progress Inadequate
PS130044	Boston Scientific Corporation	Pinnacle LITE Pelvic Floor Repair Kits - Uphold Lite Posterior and Uphold	Obstetrics/ Gynecology	07/03/2013	POP AE and Effectiveness rates, registry	Progress Inadequate
PS130041	Halt Medical Inc.	Acessa system	Obstetrics/ Gynecology	06/17/2013	Newly Enrolled	Progress Adequate
PS130039	Coloplast Corp	Altis single incision sling system	Obstetrics/ Gynecology	03/13/2013	AE and effectiveness rates	Progress Adequate
PS120111	St. Jude Medical, Inc.	Riata, quicksite, quickflex, durata	Cardiovascular	08/16/2012	Lead Externalization and Abrasion	Progress Inadequate
PS120110	Stryker Neurovascular	Wingspan stent system and gateway pta balloon catheter	Neurology	08/08/2012	Rates of Stroke and Death	Progress Adequate
PS120106	Coloplast Corp.	Restorelle polypropylene mesh	Obstetrics/ Gynecology	04/09/2012	POP AE and Effectiveness rates,	Progress Adequate

Updated monthly

What We Will Cover

- Complaint Handling
- Medical Device Reporting
- Unique Device Identifier (UDI)
- Recalls
- Notices of Corrections and Removals
- Ongoing Monitoring of Device Performance
- **Best Practices**

QSR/ISO 13485 Harmonization

- February 23, 2022, FDA published in the Federal Register a proposed rule that would replace the Quality System Regulation (QSR), at 21 C.F.R. Part 820, with a newly named Quality Management System Regulation (QMSR)
- QMSR omits many of the specific QSR requirements and instead incorporates by reference ISO 13485:2016
  - QMSR retains definitions of some terms that do not appear in ISO 13485 (e.g., component, finished device, design validation, remanufacturer, and nonconformity)
  - Some existing terms have also been revised for better alignment with ISO 13485 (e.g., replacing the defined term “management with executive responsibility” with “top management”)
- Some FDA-specific requirements retained (e.g., control of records and device labeling and packaging controls)
- Risk management is a key component of ISO 13485
- Includes a proposed one-year transition period
- FDA is accepting comments until May 24, 2022

Risk Management

- Risk management is implicitly required by FDA as part of Design Control under the QSR
- FMEA is used preferentially but is not the only approach
  - Complexity and impact of changes may dictate another approach
- Risk analyses are controlled documentation
  - Post-market feedback
- Risk analyses are “living” documents—updated upon identification of new complaints/failure modes
- Risk analyses should be updated with every design change

Questions?