FDLI/CDRH Virtual Course
Introduction to Medical Device Law and Regulation

Post Marketing Issues

November 17, 2022

FDLI

Agenda

- Complaint Handling
- Medical Device Reporting (MDR) (21 CFR § 803)
- Unique Device Identifiers – Regulations and Implementation (21 CFR § 830)
- Product Recalls, Part 7 (Enforcement Policy) / Reports of Corrections and Removals Under Part 806
- Ongoing Monitoring of Device Performance
- Best Practices

Complaint – Definition

- Any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution
- 21 CFR § 820.3(b)

General Requirements

- Establish and maintain procedures for receiving, reviewing, and evaluating complaints by a formally designated unit to ensure:
  - Uniform and timely processing of complaints;
  - Documentation of oral complaints upon receipt; and
  - Evaluation of complaints to determine whether they represent MDR reportable events
- 21 CFR § 820.198(a)

Service Report as Input to Complaint

- 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
- 21 CFR § 820.200

Adverse Events/Product Problems

- Any undesirable experience associated with the use of a medical product in a patient
- Serious adverse event:
  - Death
  - Life-threatening
  - Hospitalization
  - Disability or permanent damage
  - Disability or permanent damage
  - Congenital anomaly/birth defect
  - Required intervention to prevent permanent impairment or damage
  - Other

Complaint Investigation

- 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
- Document decisions to not investigate, including the name of the individual responsible for the decision

Complaint Records

- 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 be maintained in a separate portion of the complaint files or otherwise clearly identified

Medical Device Reporting – Purpose

- Post-market surveillance tool used to monitor device performance, detect potential device-related safety issues, and contribute to benefit-risk assessments

What types of events must be reported to FDA?

- 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

What types of events must be reported to FDA? (cont.)

- 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.

Who needs to report MDRs?

- Manufacturer – manufactures, prepares, propagates, compounds, assembles, or processes a device by chemical, physical, biological, or other procedure. The term includes any person who either:
  - Repackages or otherwise changes the container, wrapper, or labeling of a device in furtherance of the distribution of the device from the original place of manufacture
  - Initiates specifications for devices that are manufactured by a second party for subsequent distribution by the person initiating the specifications

Who needs to report MDRs? (cont.)

- Importer – imports a device into the US and markets device from original place of manufacture to person who makes final delivery or sale to ultimate user
- Device User Facility – refers to hospital, ambulatory surgical facility, nursing home, outpatient diagnostic facility, or outpatient treatment facility; not a physician's office:
  - Option of reporting to FDA or to manufacturer

Summary of Mandatory Reporting Requirements for Manufacturers and Importers

REPORTER	WHAT TO REPORT	REPORT FORM #	TO WHOM	WHEN
Manufacturers	30 day reports of deaths, serious injuries and malfunctions	Form FDA 3500A *	FDA	Within 30 calendar days of becoming aware of an event
	5-day reports for an event designated by FDA or an event that requires remedial action to prevent an unreasonable risk of substantial harm to the public health	Form FDA 3500A *	FDA	Within 5 work days of becoming aware of an event
Importers	Reports of deaths and serious injuries	Form FDA 3500A *	FDA and the manufacturer	Within 30 calendar days of becoming aware of an event
	Reports of malfunctions	Form FDA 3500A *	Manufacturer	Within 30 calendar days of becoming aware of an event

* Or electronic equivalent

Summary of Mandatory Reporting Requirements for User Facilities

REPORTER	WHAT TO REPORT	REPORT FORM #	TO WHOM	WHEN
User Facility	Device-related Death	Form FDA 3500A	FDA & Manufacturer	Within 10 work days of becoming aware
User Facility	Device-related Serious injury	Form FDA 3500A	Manufacturer. FDA only if manufacturer unknown	Within 10 work days of becoming aware
User Facility	Annual summary of death & serious injury reports	Form FDA 3419	FDA	January 1 for the preceding year

Electronic Submission of MDRs in Electronic Submissions Gateway (ESG)

- 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

ESG Acknowledgements

- 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)

ESG Acknowledgements (cont.)

- 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

Voluntary Malfunction Summary Reporting 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

Voluntary Malfunction Summary Reporting Program (cont.)

- 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

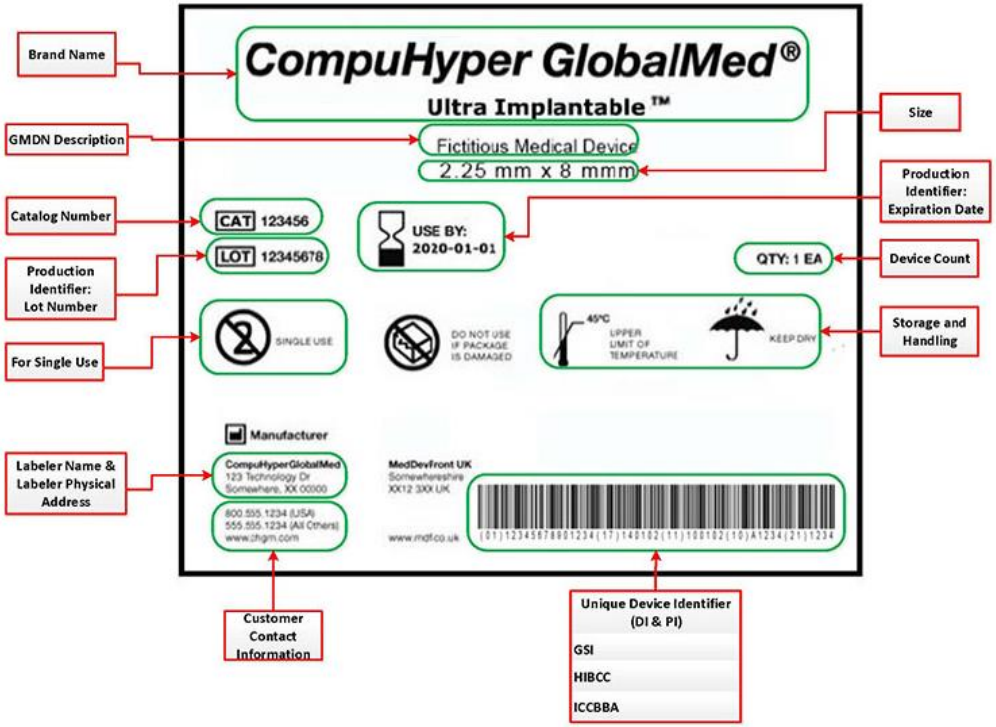
Summary Malfunction Reporting Schedule

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

Unique Device Identifiers (UDI) - Definition

- 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

Device Label Example



Purpose – Traceability

- 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 post-market surveillance system can also be used to support pre-market approval/clearance of new devices and new uses of currently marketed devices

Purpose – Traceability (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

Global Unique Device Identification Database

- 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

Enforcement Policy and Draft Guidance, "Select Updates for Unique Device Identification: Policy Regarding Global Unique Device Identification Database Requirements for Certain Devices"

- Developed to revise policy on standard date formatting, UDI labeling, and GUDID submission requirements for Class I and unclassified devices
- Explained there are certain class I devices for which FDA does not intend to enforce GUGI requirements
- Not for implementation at this time

Reports and Records

- 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

Reports and Records (cont.)

- 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
- §§ 806.10 – 806.40

Mandatory Medical Device Recall Procedures

- Cease distribution and notification order
- Regulatory hearing
- Written request for review of cease distribution and notification order
- Mandatory recall order
- Cease distribution and notification or mandatory recall strategy

Mandatory Medical Device Recall Procedures (cont.)

- Communications concerning a cease distribution and notification recall order
- Cease distribution and notification or mandatory recall order status reports
- Termination of a cease distribution and notification or mandatory recall order
- Public notice
- §§ 810.10 – 810.18

Safety Alerts Communication to Users, Health Institutions, Public Health Notification

- FDA can (and has) issued 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

Post-approval Study as Conditions of Approval

- Continuing evaluation and periodic reporting on the safety, effectiveness, and reliability of the device for its intended use

Potential Consequences of Non-adherence to Post-market Study Conditions

- 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
  - Such failure constitutes a risk to public health

Post-market Surveillance (PMS) (21 CFR § 822)

- Intended to maximize likelihood that post-market surveillance plans will result in collection of 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
- Methods
  - Complaint history and literature review
  - Non-clinical device testing
  - Follow-up with defined patient sample
  - Clinical studies

FDCA Section 522

- 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

Use of Post-market Data

522 Order Number	Manufacturer	Device Name	Medical Specialty	Date 522 Order	Study Name	Study Status
PS220001	Canary Medical, Inc.	Canary health implanted reporting processor	Orthopedic	01/24/2022	Study of Subjects with the CTE Tibial Extension	Study Pending
PS210002	Pentax	Pentax ed32-i10 duodenoscope	Gastroenterology/ Urology	04/01/2021	Postmarket Surveillance (PS) Study	Progress Adequate
PS210001	Abbott Diabetes Care Inc.	Freestyle libre 2 flash glucose monitoring system	Clinical Chemistry	02/18/2021	Postmarket Surveillance	Progress Inadequate
PS200008	Tandem Diabetes Co.	Control-iq technology	Clinical Chemistry	06/23/2020	Postmarket Surveillance	Progress Adequate
PS200006	Medtronic, Inc.	Carpediem	Gastroenterology/ Urology	04/29/2020	CARPEDIEM 522	Progress Inadequate
PS200005	Caldera Medical, Inc.	Desara One Single Incision Sling System	Gastroenterology/ Urology	02/11/2020	Postmarket Surveillance Study	Progress Inadequate
PS200004	Bluegrass Vascular Technologies, Incorporated	Surfacer inside-out access catheter system	Cardiovascular	02/10/2020	Postmarket Surveillance Study	Progress Adequate
PS200003	Olympus America, Inc.	Evis exera iii duodenovideoscope tjf-q190v	Gastroenterology/ Urology	01/17/2020	Sampling and Culturing Study	Progress Inadequate
PS200001	Avenu Medical, Inc.	Ellipsys vascular access system	Cardiovascular	01/10/2020	Ellipsys Vascular Access System PS Study	Progress Adequate
PS190006	Tandem Diabetes Co.	Control-iq, algorithm	Clinical Chemistry	12/13/2019	Postmarket Surveillance Study	Progress Adequate
PS190005	Pentax of America, Inc.	Pentax duodenoscope model ed34-il0t2	Gastroenterology/ Urology	11/15/2019	Sampling and Culturing Study	Progress Inadequate
PS190001	Rapid-Medical, Ltd.	Comaneci embolization assist device	Neurology	05/22/2019	Success in Comaneci-assist Coils Embolization Surv	Progress Adequate
PS180002	TVA Medical, Inc.	Everlinq endoavf system	Cardiovascular	06/22/2018	EverlinQ endoAVF	Progress Adequate

21 CFR Part 820 & EN 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 CFR 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”)

21 CFR Part 820 & EN ISO 13485 Harmonization (cont.)

- 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 accepted comments until May 24, 2022

Integration of Risk Management Into Quality System

- 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

Post-market Surveillance per European Union Regulation (EU) 2017/745 on Medical Devices (MDR)

- Applies to medical devices for human use on market and in clinical investigations
- Does not apply to *in vitro* diagnostics
- Post-market surveillance refers to systematic procedure to collect and review experience from devices on the market

Post-market Surveillance System Uses

- Update the benefit-risk determination and to improve the risk management,
- Update the design and manufacturing information, the instructions for use and the labelling,
- Update the clinical evaluation,
- Update the summary of safety and clinical performance (if applicable),
- Detect reportable trends,

Post-market Surveillance System Uses (cont.)

- Update the technical documentation,
- Identify necessary preventive, corrective or field safety corrective action,
- Identify opportunities to improve the usability, performance and safety of the device, and/or
- If applicable, to contribute to the post-market surveillance of other devices.

Questions?