Introduction to Medical Device Law and Regulation

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POST MARKET SURVEILANCE(PMS) (21 CFR § 822)

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FDLI

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Michael Chellson has over 30 years of experience in the field of medical devices as a laboratory scientist, an operational quality assurance leader and a global quality and regulatory leader. He has focused on assisting organizations with Quality System integration and automation .

Through practical executions of operations, regulatory affairs and quality systems, he has developed and implemented risk-based solutions to integrate business functions and improve operational and quality performance. He's led technically-oriented projects focusing on design controls, verification and validation, process improvement, regulatory market clearance, risk management and implementation of corrective actions.

In earlier roles, he served as Global Director RA with Sunrise Medical and VP RA/QA with ConMed Corporation. He also served on several U.S. FDA working groups, both as an industry partner in development of published FDA product safety guidance (SHBWG) and as a member of initial U.S. FDA "case for quality" initiatives.

Mr. Chellson began his career working with QA, microbiological and sterility testing for processed food. He then held increasingly senior positions in QA/RA leadership and consulting at small and large medical device manufacturers.

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Dhanmati Rupnarine brings more than 30 years of Quality, Compliance and Regulatory experience to this forum, having served in regulated industries covering medical products, drug-device combination products, pharmaceuticals and *in vitro* diagnostic (IVD) products in markets world wide. In addition to her work in quality and regulatory affairs, Ms. Rupnarine has experience in company acquisitions, integrations and divestitures.

In her career of increasing technical responsibilities, Ms. Rupnarine has served key industrial leaders such as Baxter, Boston Scientific, J&J and Cardinal Health. Capitalizing on her personal industry experiences, Dhanmati has served as a principal consultant to a wide array of industry leaders, providing pragmatic leadership and cultural sensitivity to global teams.

Ms. Rupnarine earned her Bachelor of Science in Food Science at the University of Manitoba, her Master of Science in Quality Management with Honors from the University of Miami, and her Doctorate in Business Administration in Quality Systems Management from the National Graduate School of Quality Management in Boston, MA.

Agenda

- Learning objectives
- Complaint handling
- Medical Device Reporting (MDR)
- Unique Device Identifiers (UDI) - Regulations and Implementation
- Product Recalls, Part 7(Enforcement policy)/Reports of Corrections and Removals under Part 806
- Ongoing Monitoring of Device Performance
- Best Practices in Post market Surveillance
- Questions

Learning Objectives

- Learn how medical device manufacturers are required to evaluate and report post-market complaints, adverse events and product problems
- Understand what types of events are reportable and who needs to report the event to the FDA
- Recognize when to conduct a recall and how corrections and removals are reported to the FDA
- Understand how medical device manufacturers are required to monitor device performance
- Learn best practices for post market surveillance, vigilance and market surveillance

Complaint Handling

Complaint handling (21 CFR § 820.198)

Complaint is 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)

Sources for Complaints include:

- Customers by letter, credit memo, phone, fax, email, Service Requests, returned goods form, Employees
- Distributor, Importer, User facilities
- Servicing Reports (21 CFR 820.200)
- Literature
- Regulatory Authorities (agencies and Notified Bodies etc)
- Clinical trials, marketing evaluations etc

Examples of Complaints

- Death
- Injury
- Any product problems/malfunctions which require any medical/surgical intervention to prevent any death, serious injury or serious adverse event to the patient
- Actual/Potential Cross Contamination between patients
- Out of Box Failure (OBF)
- Product misuse or use error
- Issues found with product in the field (by field service technician or customer)
- Product fails to meet documented specifications or to perform as intended
- Notice of Litigation involving medical products
- Replacement of parts earlier than their documented normal life expectancy
- Identical repairs of multiple units of a device; each unit repair is a separate complaint
- Product has incorrect/unclear labeling or inadequate instructions for use

Complaint handling (21 CFR § 820.198)

Process:

a) General Requirement b) Initial Review and Evaluation c) Investigation of Failures d) Medical Device Reporting e) Records f) Off-Site Accessibility g) Outside U.S. Accessibility

❑ **General Requirements**

Establish and **maintain** procedures for receiving, reviewing, and evaluating complaints by a **formally Designated Unit** to ensure:

- o Processing of complaints in a uniform and timely manner
- o Documentation of oral complaints upon receipt
- o Evaluation to determine if failure investigation and/or a medical device report (MDR) is required

❑ **Initial Review and Evaluation 21 CFR 820.198(b)**

- ○ Review and evaluate complaints to determine whether an investigation is required
- ○ If no Investigation is required then document the reason and the name of responsible individual responsible for the decision not to investigate

Complaint Requirements

- **Investigation of Failures 21 CFR 820.198(c)**
  - Any alleged complaint involving possible failure of a device or labeling/packaging to meet any of its specifications must be reviewed, evaluated, and investigated.

  Exceptions:

  1. When an investigation has already been performed on a similar complaint

  - 2. Recurring similar complaints may not require investigation under complaint file handling but may require CAPA.

Investigation – Why?

- All medical devices will eventually have a failure or MDR- reportable event.
- May impact everything from design to manufacturing
- Robust system ensures responses/reactions are: o Accurate o Appropriate o Timely
- Result is a better, safer and more effective product.

Complaint Requirements cont'd

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  1. When an investigation has already been performed on a similar complaint
  - 2. Recurring similar complaints may not require investigation under complaint file handling but may require CAPA.

- **Medical Device Reporting (MDR) 21 CFR 820.198(d)**
  - Complaints that are also Medical Device Reports (MDRs) must be promptly reviewed, evaluated, and investigated by designated individual(s).
  - Maintain in a separate portion of the complaint files or be otherwise clearly identified.

Complaint handling (21 CFR § 820.198)

How to Report a Complaint in a company?

- Electronically enter data in a complaint handling system or omplete the Complaint Notification Form within ***2 business days*** of becoming aware of a complaint.
- *In* case of a death or serious public health threat, the complaint must be immediately forwarded to the Manufacturer's **Complaint Handling Unit (CHU)** *within* ***1 working day****.*

How To Document a Complaint

- An adequate description of the event and alleged deficiency
  - Who was involved?
  - What happened?
  - When did the problem happen (i.e. date and time)
  - With what circumstances (such as prior, during, or after procedure? What procedure was being performed? Occurred/identified during reprocessing?)
- Patient impact such as any adverse consequences (injury, hospitalization, observation) or explicitly states there was no impact to patient
- Patient/User signs and symptoms and final diagnosis are documented
- Details of the product(s) involved (i.e. name, catalog number, serial number(S/N) or lot number(L/N))
- Will the product be returned?
- Documents any action taken, including servicing, if applicable.

Complaint Files - Records

Records 21 CFR 820.198(e)
Manufacturer Responsibilities

❑ Records of investigations must be maintained:
o Device name
o Date complaint received
o Unique Device Identifier (UDI), Universal Product Code (UPC), and other device identification(s) (e.g., control/batch/lot number(s))
o Name, address, and phone number of complainant
o Nature/details of the complaint o Results and dates of investigation
o Corrective action taken
o Reply/response to complainant

Complaint Files – Records cont'd

Records 21 CFR 820.198(e)

Manufacturer Responsibilities continued

Manufacturers must understand their own product, risks, conditions and context for its use, and apply the regulatory requirements to make their Complaint Files System work

• Result: Manufacturers must decide upon their own details
- Details • Definitions o Failure (device, labeling/packaging)
o Medical Device Report o Other ("non complaints")
• Actions
o Investigate ("investigable")
o Other ("non complaints," "similar" complaint)
• Investigation Thresholds
o Handle within Complaint Files System
o Refer to Corrective and Prevent Action Subsystem

Complaint Files – Records cont'd

❑ **Off-Site Accessibility**

If the manufacturer's formally designated complaint unit is located at a site separate from the manufacturing establishment, the investigated complaint(s) and the record(s) of investigation shall be reasonably accessible to the manufacturing establishment

❑ **Outside U.S. Accessibility**

If a manufacturer's formally designated complaint unit is located outside of the United States, records shall be reasonably accessible in the United States at either:

(1) A location in the United States where the manufacturer's records are regularly kept; or

(2) The location of the initial distributor

Minimum content for complaint investigation documentations:

- Who performed investigation and when (start and end)
- What activities were performed, for example:
  - Device evaluation/ testing performed
  - Documents reviewed (e.g. Instruction For Use (IFU), DHR, service manuals, manufacturing /service procedures, etc.)
  - Data analysis performed (i.e. historical complaint or service data) if applicable
- What were the results of each activity
- What are the conclusions of the investigation
- For a Reportable Complaint, also provide (including evidence to support results):
  - Whether the device failed to meet specifications
  - Whether the device was being used for treatment or diagnosis
  - The relationship, if any, of the device to the reported incident / AE

  The investigation information will be used to review and potentially any related regulatory submissions

Circumstances to consider when there is a need to contain product:

Containment shall be considered for product complaints involving the following circumstances

- Product identify problem –Labels, labelling, Instruction For Use (IFU)
- Report of death or serious injury involved with reported event
- Upon examination of returned product, manufacturing defect is obvious (i.e. missing/incorrect component)
- Containment is appropriate for the complaint device IF the device was involved and is suspected to have caused or contributed to a serious injury or death
- Containment may also be considered for similar/same devices involved in the received complaint.
- All containment decisions shall be made by management

Medical Device Reporting (MDR) (21 CFR § 803)

Medical Device Reporting (MDR) (21 CFR § 803)

- Establishes regulatory pathway for collecting reportable adverse event data
- Defines critical reporting roles, responsibilities, and deadlines
- Section 519 of the Food, Drug, and Cosmetic Act grants FDA the authority to require mandatory medical device reports from **Manufacturers, Importers and Device User Facilities**

What is a Reportable Event For The USA FDA?

- Information in a complaint that reasonably suggests: **death** or s**erious Injury** 21 CFR 803.3(o)

OR

- A malfunction of the device has occurred and, if it were to recur, could cause or contribute to a death or serious injury 21 CFR 803.3(o)

An MDR reportable event reasonably suggests that a marketed device:

- Malfunctioned, and
- Likely to cause or contribute to death or serious injury were it to recur

Medical Device Reporting (MDR) (21 CFR § 803)

- ***Non-reportable*** **rationale shall address two things:**

1) clear and unambiguous complaint documentation stating the patient did not experience an adverse event or medical intervention to prevent a serious injury

AND

2) why the device problem would not result in an adverse event if it were to happen again under the same or different circumstances

- Decision to not report (rationale) must be supported by:

  1) Risk Documentation

  2) Known Field Experience

  3) Clinical Hazard Assessment

Who is Required To Report MDRs To The FDA?

Mandatory Reporters:

- Manufacturers • 21 CFR 803.3(l)
- Importers • 21 CFR 803.3(j)
- Device User Facilities - Example: Hospitals and Nursing Homes 21 CFR 803.3(d)

Voluntary Reporters:

- Patients
- Health care Professionals
- Caregivers

What Do Mandatory Reporters Report To The USA FDA ?

Events	Manufacturers	Importers	User Facilities
Deaths			
Serious injuries/illness			
Certain malfunctions			

How to Report?

❑ **Manufacturers and Importers:**

- Electronic submission only
- Electronic Medical Device Reporting (eMDR) Final Rule effective August 14, 2015
- Use Electronic Submissions Gateway (ESG) – eMDR Guidance

❑ **User Facilities:**

- Electronic submission is encouraged
- eMDR Final Rule permits written reports – Use Form 3500A
- Guidance: Medical Device Reporting For User Facilities

❑ **Voluntary Reporters:**

- Online through MedWatch; By postal mail;
- Voluntary Reports – Form 3500
- Consumer-friendly version – Form 3500B

USA Medical Device Reporting Requirements21 CFR Part 803

REPORTER	WHAT TO REPORT	TO WHOM	WHEN
Manufacturer	Deaths, serious injuries and malfunctions	FDA	Within 30 calendar days of becoming aware of an event
Manufacturer	An event designated by FDA or an event that requires remedial action to prevent an unreasonable risk of substantial harm to the public health	FDA	Within 5 working days of becoming aware of an event
Importer	Deaths and serious injuries	FDA and the manufacturer	Within 30 calendar days of becoming aware of an event
Importer	Malfunctions	Manufacturer	Within 30 calendar days of becoming aware of an event

What Does FDA do with the report?

- FDA submits 3 acknowledgements to which must be kept in the MDR event file
- FDA processes the device report into the Manufacturer and User Device Experience (MAUDE) database
- FDA makes non-confidential information available to the public
- FDA analysts review the MedWatch 3500A
- Completeness of the report (they want the entire story of the event)
- Event including patient and device outcomes
- Investigations by the manufacturer
- Review across similar or same devices within the company
- Review across similar devices with other manufacturers
- Review the labeling
- Review compliance history
- Review pre and post market activities surrounding this device

What Does FDA Do with the report?

- Evaluate new, modified, or additional information received
- Assess if a supplemental MDR is required
- Ensure information in the MDR file and the complaint file are the same
- Verify the two files does not contradict each other
- MDR file is part of the complaint file

Benefits and Use of MDR data

Consumers and Industry:

- Understand device safety and performance
- Design improvement

Benefits for the FDA:

- Monitor device safety and performance
- Assess need for regulatory action

MDRs are Used to:

- Identify Trends, Identify Possible Actions
- FDA inspection of manufacturer, Changes to device labeling
- Notices to the public. Example: Safety Communications, Device recall

MAUDE

Manufacturer and User Facility Device Experience (MAUDE)

- Publicly searchable database of adverse event reports

– User facility reports since 1991

– Voluntary reports since 1993

– Manufacturer reports since August 1996

Maude

Allows a person to search the database using a variety of criteria

Unique Device Identifiers (UDI) - (21 CFR §830)

Unique Device Identifiers (UDI) - (21 CFR §830)

What is UDI?

- A Unique Device Identification (UDI) system is intended to provide single, globally harmonized positive identification of medical devices through distribution and use, requiring the label of devices to bear a globally unique device identifier (to be conveyed by using Automatic Identification and Data Capture and, if applicable, its Human Readable Interpretation) based upon standard, with the UDI-DI (Device Identifier) of that unique identifier being also linked to a jurisdiction-specific public UDI database (source: International Medical Device Regulators Forum (IMDRF): http://www.imdrf.org/).

Unique Device Identifiers (UDI) - (21 CFR §830)

- A unique device identifier (UDI) is a unique numeric or alphanumeric code. It generally consists of the following:
  - **Device identifier (DI)**, a mandatory, fixed portion of a UDI that identifies the labeler and the specific version or model of a device.
  - **Production identifier (PI)**, a conditional, variable portion of a UDI that identifies one or more of the following when included on the label of a device:
    - Lot or batch number within which a device was manufactured
    - Serial number of a specific device
    - Expiration date of a specific device
    - Date a specific device was manufactured;
    - Distinct identification code required by §1271.290(c) for a human cell, tissue, or cellular and tissue-based product (HCT/P) regulated as a device.

Unique Device Identifiers (UDI)

Device Labelers: Comply with UDI Requirements

- Requires device labelers (typically, the manufacturer) to:
  - Include a unique device identifier (UDI), issued under an FDA-accredited issuing agency's UDI system, on device labels, device packages, and in some instances, directly on the device.
  - Submit device information to the Global Unique Device Identification Database (GUDID)

Unique Device Identifiers (UDI) - (21 CFR §830)

- The device labeler must provide the UDI in **two forms** on labels and packages:
  - Easily human readable plain-text
  - Machine-readable form that uses automatic identification and data capture (AIDC) technology.
- **Automatic identification and data capture (AIDC):** Any technology that conveys the UDI or the device identifier of a device in a form that can be entered into an electronic patient record or other computer system via an automated process.
- Device labeler must present dates on device labels and packages in a standard format that is consistent with international standards and international practice (YYYY-MM-DD)

Benefits of Unique Device Identifiers (UDI)

- Providing a standardized identifier that will allow manufacturers, distributors and healthcare facilities to more effectively manage medical device recalls.
- Allowing 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 and precisely identify a device and obtain important information concerning the characteristics of the device.
- Enhancing analysis of devices on the market by providing a standard and clear way to document device use in electronic health records, clinical information systems, claim data sources and registries. A more robust post-market surveillance system can also be leveraged to support premarket approval or clearance of new devices and new uses of currently marketed devices.
- Provides a foundation for a global, secure distribution chain, helping to address counterfeiting and diversion and prepare for medical emergencies.
- A medical device identification system that is recognized around the world

UDI Timeline

Device Risk Class	Requirements	Compliance Date
Class III	Labels and packages Stand-alone software Data must be entered into GUDID	September 24, 2014
Class II	Labels and packages Stand-alone software Data must be entered into GUDID	September 24, 2016
Class II	Devices intended to be used more than once and reprocessed before each use	September 24, 2018
Class I and unclassified	Labels and packages Stand-alone software Data must be entered into GUDID	September 24, 2018
Class I and unclassified	Devices intended to be used more than once and reprocessed before each use	September 24, 2020

Product Recalls, Enforcement policy, Corrections and Removals

Product Recalls, Enforcement policy, Corrections and Removals

What is a recall?

- A recall is a method of removing or correcting products that are in violation of Food and Drug Administration law. Recalls occur when a medical device is defective, when it could be a risk to health, or when it is both defective and a risk to health.
- Recall is a voluntary action that takes place because manufacturers and distributors carry out their responsibility to protect the public health and well-being from products that present a risk of injury or gross deception or are otherwise defective
- A manufacturer conducts voluntarily Medical device recalls **21 CFR 7**
- Guidance for firms to conduct an effective recall -**21 CFR 7** – Enforcement Policy

Product Recalls, Part 7(Enforcement policy)/Reports of Corrections and Removals under Part 806

- In rare instances, where the manufacturer or a USA importer fails to voluntarily recall a device that is a risk to health, FDA may issue a recall order to the manufacturer under 21 CFR 810, – Medical Device Recall Authority
- Per 21 CFR 810 ,Medical Device Recall Authority FDA can issue a medical device recall authority under section 518(e) of the Federal Food, Drug, and Cosmetic Act (Act).

Classification of Product Recalls

Recalls are classified into a numerical designation (I, II, or III) by the FDA to indicate the relative degree of health hazard presented by the product being recalled.

- **Class I** - a situation in which 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** - a situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.
- **Class III** - a situation in which use of, or exposure to, a violative product is not likely to cause adverse health consequences

Reports of Corrections and Removals

Who must report

- Manufacturers and importers are required to report a correction or removal of a product if it involves a risk to health. Only the person that initiates the correction or removal is required to report.
- Manufacturers and importers are required to submit a report to FDA of any correction or removal of a medical device(s) if the correction or removal was initiated to reduce a risk to health posed by the device or to remedy a violation of the Act caused by the device which may present a risk to health Under 21 CFR 806, Medical Device Correction and Removals
- A report must be made even if the event was caused by use error. A report is not required if the information has already been provided to FDA under Medical Device Reporting (21 CFR 803) or Repurchase, Repairs or Replacement of Electronic Products (21 CFR 1004) or if the corrective or removal action was initiated by an FDA order under Medical Device Recall Authority (21 CFR 810)

When to report

- The report must be submitted to FDA within 10 working days from the time the firm initiates the correction or removal . If there is no "risk to health" involved, a report to FDA is not

Reports of Corrections and Removals

What to Report - §806.10(c)

- Registration number, date the report is made, sequence number (001, 002, etc.), "C" for Correction or "R" for Removal.
- Name, address, phone number, and contact person of the firm responsible for conducting the correction or removal.
- Brand name and common name of the device and intended use.
- FDA marketing status, i.e., 510(k), PMA, pre-amendment status and device listing number.
- Model/catalog number, lot/serial number
- Manufacturer's contact information (name, address, phone number, contact person) if different from item #2 above.
- Description of event(s) and the corrective and removal actions that have been, and are expected to be taken.
- Any illness or injuries that have occurred with the use of the device. If applicable, include any Medical Device Report (MDR) numbers submitted under 21 CFR 803.
- The number of devices subject to the Correction or Removal.
- Date of manufacture or distribution; expiration date or expected life.

Reports of Corrections and Removals

What to Report - §806.10(c)con't

- Name, address, and telephone number of all consignees (domestic and foreign) and the dates and number of devices distributed to each consignee.
- A copy of all communications regarding the correction or removal.
- A statement as to why any required information is not available and a date when it will be submitted.

Where to report?

- **1. eSubmitter -**FDA Electronic Submission Software (eSubmitter)
- FDA encourages personnel to to submit the report via eSubmitter. Once created, the report is sent to CDRH through the FDA Electronic Submission Gateway (ESG). Instructions on how to use the eSubmitter tool to electronically report corrections and removals may be found using this link: Electronic Submission of 806 Reports of Corrections and Removals
- **2. E-mail:** e-mail it to your FDA's Office of Regulatory Affairs (ORA) Division Recall Coordinator (DRC) by state or region (look for Product Type "Medical Device").
- Foreign manufacturers and importers must e-mail the report to the DRC where their US agent is located.

Examples of major product recalls

- Medical device failures can have adverse consequences for healthcare professionals, as well as patients, in certain cases

2020 worst recall

- Medtronic MiniMed insulin pumps.
- Becton Dickinson CareFusion 303 Inc. Alaris system infusion pumps
- Stryker Neurovascular Trevo XP ProVue Retriever.
- Medtronic StealthStation auto-registration feature
- Medtronic Pipeline Flex embolization device
- Medtronic Rashkind balloon septostomy catheters

Recalls listing can be found in FDA site
https://www.fda.gov/medical-devices/medical-device-recalls

Ongoing Monitoring of Device Performance

USA Post-market Surveillance

- Limited scope-Only required when “notified” by FDA
- FDA has authorization to require post-market surveillance for class II and class III medical devices that meet one of four criteria:
  - Failure of the device would be reasonably likely to have a serious adverse health consequence
  - The device is intended to be implanted in the human body for over one year
  - The device is intended to be a life-sustaining of life-supporting device used outside of a user facility
- Requires PMS plan & regulatory submission/approval
- PMS can be a condition of device approval

US FDA 21CFR 822

Sec. 822.5

We will send you a letter (the postmarket surveillance order) notifying you of the requirement to conduct postmarket surveillance. Before we send the order, or as part of the order, we may require that you submit information about your device that will allow us better to define the scope of a surveillance order. We will specify the device(s) subject to the surveillance order and the reason that we are requiring postmarket surveillance of the device under section 522 of the act. We will also provide you with any general or specific guidance that is available to help you develop your plan for conducting postmarket surveillance.

Sec. 822.8

You must submit your plan to conduct postmarket surveillance within 30 days of the date you receive the postmarket surveillance order..

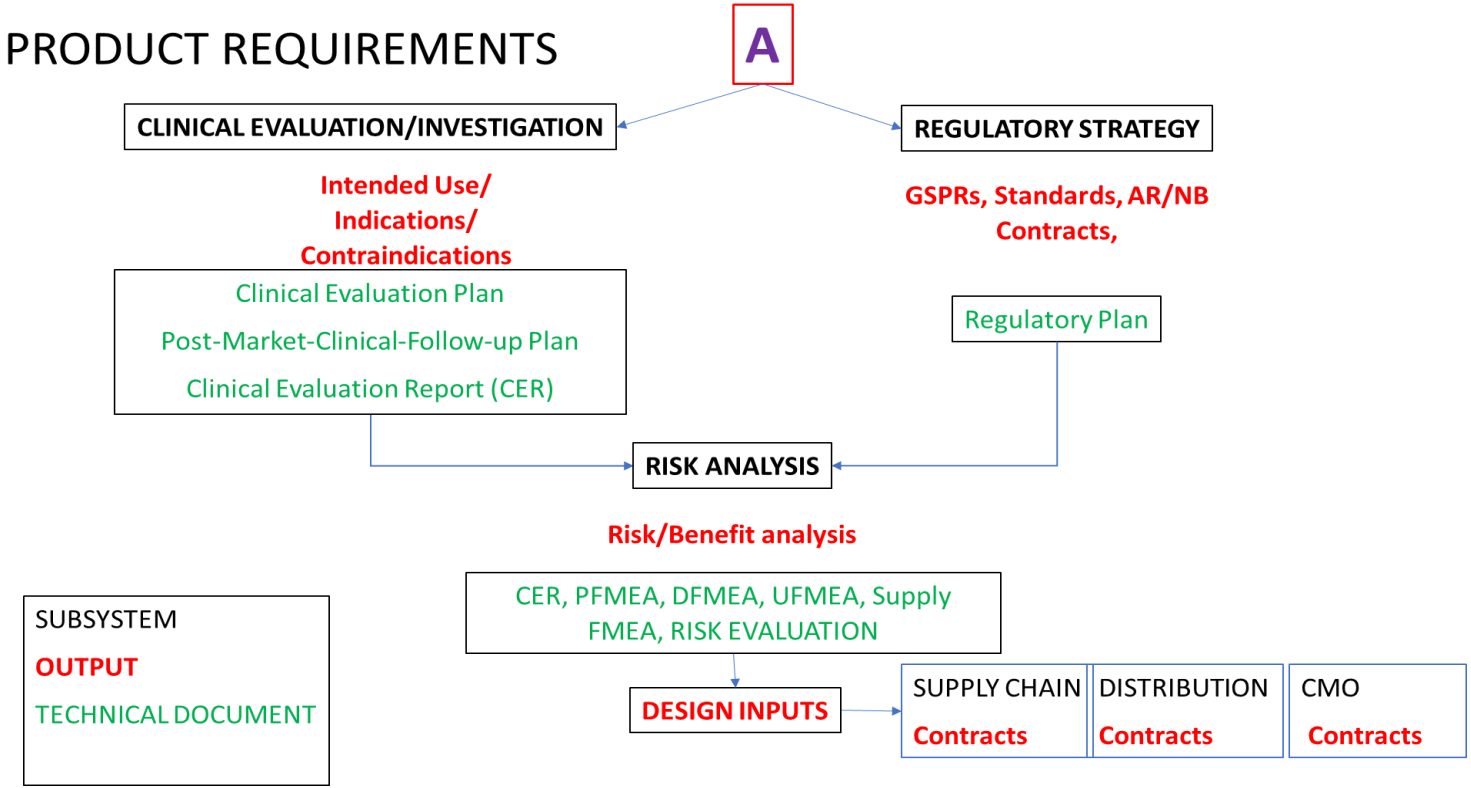
Best Practices/Future State

PMS System

- PMS is not a single process but a comprehensive integrated lifetime product performance surveillance and data analysis subsystem.
- International regulatory and industry recognition of the criticality of planning for complete and accurate analysis of all sources of post production data for determination of potential changes in clinical risk profile throughout the product lifecycle.
- NB & QMS certification auditors are focusing with increased specificity on PMS QMS integration

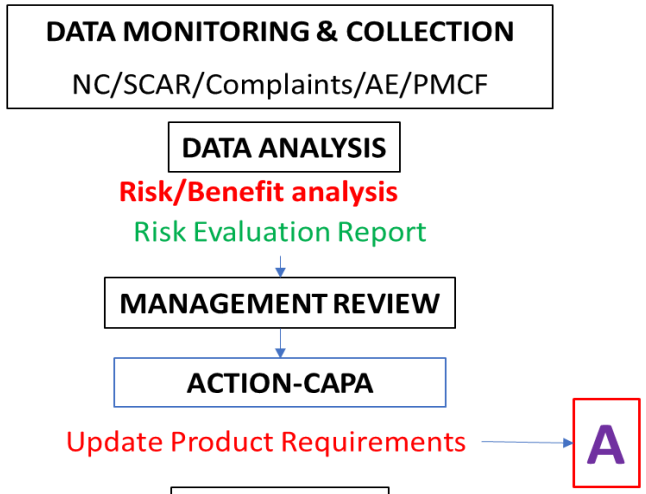
PMS Planning & Integration

Product & System Requirements



PMS Execution and Integration

POST MARKET SURVEILANCE



SUBSYSTEM

TECHNICAL DOCUMENT

OUTPUT

USA FDA 21CFR 820 & EN/ISO 13485 HARMONIZATION

- Release planned for 2019 but delayed due to COVID, but should be released ***shortly***
- Increased emphasis on Risk Management integration into QMS & post market surveillance
    - 13485 currently in harmonization revision with EU MDR requirements

EN ISO 13485 - Risk Based QMS

4.1.2 The organization shall:

determine the processes needed for the quality management system and the application of these processes throughout the organization taking into account the roles undertaken by the organization;

apply a risk-based approach to the control of the appropriate processes needed for the quality management system;

determine the sequence and interaction of these processes.

13485-Post Production Data Analysis

- Increased emphasis on data collection & analysis of data streams, (Feedback, Internal NC, Supply chain, Clinical review)

  8.4 Analysis of data

  The organization shall document procedures to determine, collect and analyse appropriate data to demonstrate the suitability, adequacy and effectiveness of the quality management system. The procedures shall include determination of appropriate methods, including statistical techniques and the extent of their use.

  The analysis of data shall include data generated as a result of monitoring and measurement and from other relevant sources and include, at a minimum, input from:

  feedback; conformity to product requirements; characteristics and trends of processes and product, including opportunities for improvement,; suppliers; audits; service reports, as appropriate.

  If the analysis of data shows that the quality management system is not suitable, adequate or effective, the organization shall use this analysis as input for improvement as required in 8.5.

POST-MARKET SURVEILLANCE PER EUROPEAN UNION

REGULATION (EU) 2017/745

ON MEDICAL DEVICES (MDR

FDLI

2017/745-PMS

- Requires a PMS “subsystem (graphic)
- Requires full integration of Risk management and Clinical data planning and documentation as a part of PMS
- MDR requires a PMS plan as part of technical documentation. The plan must be implemented to produce PMS reports (PMSRs) or Periodic Safety Update Report (PSURs) depending on the class of the device.
  - PMSRs apply to class I medical devices under the MDR, PMSRs should present results and conclusions of data gathered from the post-market surveillance plans, alongside the rationale and description of any corrective and preventive actions taken.
  - PSURs apply to class IIa, IIb and III medical devices under the MDR PSURs are identical to PMSRs with a few additions - manufacturers must publish the conclusion of the Benefit/Risk determination, main findings of the post-market clinical or performance follow-up, sales volume, and estimated user population characteristics and usage frequency.

2017/745-PMS Article 83

Post-market surveillance system of the manufacturer

For each device, manufacturers shall plan, establish, document, implement, maintain and update a post-market surveillance system in a manner that is proportionate to the risk class and appropriate for the type of device. ***That system shall be an integral part of the manufacturer's quality management system referred to in Article 10(9).***

The post-market surveillance system shall be suited to actively and systematically gathering, recording and analyzing relevant data on the quality, performance and safety of a device throughout its entire lifetime, and to drawing the necessary conclusions and to determining, implementing and monitoring any preventive and corrective actions.

Data gathered by the manufacturer's post-market surveillance system shall in particular be used:

(a)to update the benefit-risk determination and to improve the risk management as referred to in Chapter I of Annex I;
(b)to update the design and manufacturing information, the instructions for use and the labelling;
(c)to update the clinical evaluation;
(d)to update the summary of safety and clinical performance referred to in Article 32;
(e)for the identification of needs for preventive, corrective or field safety corrective action;
(f)for the identification of options to improve the usability, performance and safety of the device;
(g)when relevant, to contribute to the post-market surveillance of other devices; and
(h)to detect and report trends in accordance with Article 88.

The technical documentation shall be updated accordingly.

Post-Market Clinical Follow-up (PMCF)

- Requires Clinical data periodic review
- The PMCF must be detailed in a specific plan and addressed in the PMS plan. Post market clinical follow-up is always applicable, and is not to be conflated with a PMCF study/investigation or specific PMCF studies.
- MDR is very specific on the PMCF being part of the quality management system and part of the technical file included in the clinical evaluation report.

2017/745-ANNEX XIV PART B
POST-MARKET CLINICAL FOLLOW-UP

5. PMCF shall be understood to be a ***continuous process that updates the clinical evaluation*** referred to in Article 61 and Part A of this Annex and shall be ***addressed in the manufacturer's post-market surveillance plan.*** When conducting PMCF, the manufacturer shall ***proactively collect and evaluate clinical data from the use in or on humans*** of a device which bears the CE marking and is placed on the market or put into service within its intended purpose as referred to in the relevant conformity assessment procedure, with the aim of confirming the safety and performance throughout the expected lifetime of the device, of ensuring the continued acceptability of identified risks and of detecting emerging risks on the basis of factual evidence.

6. PMCF shall be performed pursuant to a ***documented method laid down in a PMCF plan***.

6.1. The PMCF plan shall specify the methods and procedures for proactively collecting and evaluating clinical data with the aim of:

(a)confirming the safety and performance of the device throughout its expected lifetime,

(b)identifying previously unknown side-effects and monitoring the identified side-effects and contraindications,

(c)identifying and analysing emergent risks on the basis of factual evidence,

(d)ensuring the continued acceptability of the benefit-risk ratio referred to in Sections 1 and 9 of Annex I, and

(e)identifying possible systematic misuse or off-label use of the device, with a view to verifying that the intended purpose is correct.

6.2. The PMCF plan shall include at least:

(a)the general methods and procedures of the PMCF to be applied, such as gathering of clinical experience gained, feedback from users, screening of scientific literature and of other sources of clinical data;

(b)the specific methods and procedures of PMCF to be applied, such as evaluation of suitable registers or PMCF studies;

(c)a rationale for the appropriateness of the methods and procedures referred to in points (a) and (b);

(d)a reference to the relevant parts of the clinical evaluation report referred to in Section 4 and to the risk management referred to in Section 3 of Annex I;

(e)the specific objectives to be addressed by the PMCF;

(f)an evaluation of the clinical data relating to equivalent or similar devices;

(g)reference to any relevant CS, harmonised standards when used by the manufacturer, and relevant guidance on PMCF; and

(h)a detailed and adequately justified time schedule for PMCF activities (e.g. analysis of PMCF data and reporting) to be undertaken by the manufacturer.

7. The manufacturer ***shall analyse the findings of the PMCF and document the results in a PMCF evaluation report that shall be part of the clinical evaluation report and the technical documentation.***

8. The ***conclusions of the PMCF evaluation report shall be taken into account for the clinical evaluation referred to in Article 61 and Part A of this Annex and in the risk management referred to in Section 3 of Annex I. If, through the PMCF, the need for preventive and/or corrective measures has been identified, the manufacturer shall implement them.***

Thank You!

Questions?

REFERENCES

USA FDA
GHTF/IMDRF
EUROPEAN UNION (EU)
MDCG

FDLI

USA FDA REGULATION

- 21 Code of Federal Regulations Part 803

- Medical Device Reporting for Manufacturers: Guidance for Industry and Food and Drug Administration Staff, Issued November 8, 2016
  https://www.fda.gov/media/73972/download

- Electronic reporting:
  https://www.fda.gov/emdr-electronic-medical-device-reporting

- Form 3500A and Instructions:
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USA FDA REGULATION

- PART 803 MEDICAL DEVICE REPORTING https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=803&showFR=1
- PART 820 QUALITY SYSTEM REGULATION https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=820&showFR=1
- PART 822 POSTMARKET SURVEILLANCE https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=822&showFR=1

USA FDA GUIDANCE

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Postmarket Management of Cybersecurity in Medical Devices: Guidance for Industry and Food and Drug Administration Staff https://www.fda.gov/regulatory-information/search-fda-guidance-documents/postmarket-management-cybersecurity-medical-devices

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Balancing Premarket and Postmarket Data Collection for Devices Subject to Premarket Approval: Guidance for Industry and Food and Drug Administration Staff https://www.fda.gov/regulatory-information/search-fda-guidance-documents/balancing-premarket-and-postmarket-data-collection-devices-subject-premarket-approval

GLOBAL HARMONIZATION TASK FORCE (GHTF) & INTERNATIONAL MEDICAL DEVICE REGULATOR FORUM (IMDRF)

IMDRF Post-Market Clinical Follow-Up Studies http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-210325-wng65.pdf

GHTF SG2 - Medical Devices Post Market Surveillance - February 2009 http://www.imdrf.org/docs/ghtf/final/sg2/technical-docs/ghtf-sg2-n79r11-medical-devices-post-market-surveillance-090217.pdf

GHTF SG2 - Review of Requirements on Postmarket Surveillance http://www.imdrf.org/docs/ghtf/final/sg2/technical-docs/ghtf-sg2-n47r4-2005-guidance-postmarket-surveillance.pdf

GHTF SG2 - Manufacturer's Trend Reporting of Adverse Events - January 2003 http://www.imdrf.org/docs/ghtf/final/sg2/technical-docs/ghtf-sg2-n36r7-2003-manufacturer-trend-reporting-adverse-event-030101.pdf

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IMDRF Medical Devices: Post-Market Surveillance: National Competent Authority Report Exchange Criteria and Report Form http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170921-pms-ncar-n14-r2.pdf

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European Union
Medical Device Regulation

EU MEDICAL DEVICE REGULATION 2017/745 https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32017R0745&from=EN

EU MEDICAL DEVICE COORDINATION GROUP (MDCG)

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MDCG 2020-7 Guidance on PMCF plan template
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FORTHCOMING MDCG GUIDANCE

4. Post-Market Surveillance and Vigilance (PMSV)				
MDR + IVDR	*Guidance on Periodic Safety Update Report requirements*		Q4 2021	PSUR for MDR to be later adapted for IVDR
MDR + IVDR	*Guidance on Post-Market Surveillance requirements*	MS	Q2 2022	Work to be coordinated with the Market Surveillance WG
MDR + IVDR	*Q&A document on Vigilance terms and concepts* *Q&A document on Art 87 to 90 on Vigilance requirements*		Q4 2021 Q3 2022	Task force work has been divided in 2 groups respectively on definitions and on Art 86-90 interpretation
MDR + IVDR	*Development of harmonised reporting forms for incidents*		Q1 2022	Several Task Forces on-going on the updating of the MIR form and the Trend report form