Ensure Timely, Compliant and Consistent MDR Reporting & Avoid Inspection Findings

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Objectives

• MDR Reporting Requirements
  - Regulation & Definitions
    ‣ Reporting Requirements & Timeframes
    ‣ What to Report
    ‣ How to assess Malfunctions
  - Challenging MDR Scenarios
    ‣ Servicing
    ‣ OUS Events
  - New FDA MDR Guidance
  - Case Study

• MDR Implementation
  - MDR & Post market surveillance
  - Investigation & Analysis
    ‣ Risk Assessments and Health Hazard Evaluations
    ‣ Events from Clinical Trials
  - Form 3500a & Electronic Reporting (eMDR)
  - Best Practices
  - Case Study

• Questions & Discussion
Why MDR Reporting?

“The goal of the MDR regulation is to provide **signals** to both FDA and the Manufacturer that a device may present a potential **public safety** problem that **corrective action** may need to be taken to protect the public health”

*Sharon Kapsch*
*Chief, Reporting Systems and Monitoring Branch, CDRH*

**Patient Safety** – Missed signals may result in unnecessary patient injuries

**Regulatory Sanctions** – Complaint handling and MDR are top priorities in FDA inspections.
- Non-compliance nearly always results in a 483 or warning letter

**Product Liability** – Failure to act increases liability
Federal Food, Drug and Cosmetic Act

- FDA authority for mandatory medical device reports is defined in the Federal Food, Drug and Cosmetic Act Sec 519 – Records and Reports on Devices
  - Manufacturers
  - Importers
  - Device user facilities

- 21 CFR part 803 – Medical Device Reporting
  - Establishes reporting requirements for mandatory Reporters
  - Provides a mechanism for FDA and manufacturers to monitor significant safety events involving marketed medical devices.

- 21 CFR part 820 – Quality Systems regulation QSR)- Complaint Handling
  - Definition of a complaint [21 CFR 820.3(b)]
  - Requirement to review and evaluate all device-related complaints in a timely manner to determine whether the complaint represents an MDR reportable event [21 CFR 803.18(e) and 820.198].
Evaluate All Complaints for Reportability

**Complaint**

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 C.F.R. § 820.3(b)

- Timely evaluation of all complaints to determine whether the complaint represents an event which is required to be reported to FDA under part 803 of the chapter, Medical Device Reporting 21 C.F.R. § 820.198(a)(3)

- **MDR Events**
  - Maintained in Separate Portion of Complaint Files or Clearly Identified
  - Promptly Reviewed, Evaluated and Investigated by Designated Individuals
  - Trended and appropriate actions taken
  - Escalation as required
    - Field action
    - CAPA / NCE
MDR Requirements

• Have written **MDR procedures** (21 CFR Part 803.17)

• Create a **standardized review process** for determining whether an event is MDR reportable.

• Establish and maintain **MDR event files** (21 CFR Part 803.18)
  – Ensure a system in place that allows for timely record review and follow-up/inspection by FDA.

• Provide all information reasonably known about the event on FDA **Form 3500A** (or eMDR) to FDA
  – Required information is listed in 21 CFR Part 803.52
    ➢ Any information that can be obtained by contacting the reporter
    ➢ Any information in your possession   - or-
    ➢ Any information that can be obtained by analysis, testing or other evaluation
    ➢ Explain why information is missing or incomplete

• Ensure that MDR reports are submitted to FDA in a **timely fashion**.
  – FDA frequently cites manufacturers for failure to have in place adequate written MDR procedures.

• **Investigate each event** to determine the cause of the event (21 CFR Part 803.50(b))
Describe the following:

- Conduct timely, effective identification, communication and evaluation of events that may be subject to MDR requirements

- Determine when events meet the criteria for reporting
  - Each event must be considered on its own merits
  - Decision trees, examples can promote consistent reporting

- Submit timely and complete MDRs
  - Provide all information reasonably known about the event on FDA Form 3500A to FDA
  - Send that information to FDA in a **timely fashion**.

- Document the information evaluated to determine if the event should be reported.

- Keep copies of the records submitted to FDA

**Be certain your procedure mirrors the MDR Regulation!**
- Do not mingle International reporting with MDR reporting
• **MDR Complaint Files Must Include:**
  - All information required for a Complaint file **AND**
  - Whether Device Was Being Used for **Treatment or Diagnosis**
  - Whether Device **Failed to Meet Specifications**
    ‣ Evaluate if device malfunction even when MDR determination to file as a death or serious injury
    ‣ Important for field action decisions and compliance with (21 C.F.R. § 806)
  - Relationship of Device to Incident
  - All deliberations regarding reporting decisions
  - Copies of all submitted reports
  - Must Be Reasonably Accessible to Manufacturing Establishment
“. . . You must report to us no later than 30 calendar days after the day you receive or otherwise become aware of information, from any source, that reasonably suggests that a device that you market:

(1) May have caused or contributed to a death or serious injury; or

(2) Has malfunctioned and this device or a similar device that you market would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur.”
Manufacturers – Reporting Timeframes

• **Within 30 calendar days** of receiving or otherwise becoming aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer
  - May have caused or contributed to a **death** or **serious injury**; or
  - Has **malfuctioned** and such device or similar device marketed by the manufacturer **would be likely to cause or contribute** to a death or serious injury if the malfunction were to recur.
  - This is called a 30-Day Report (21 CFR Part 803.50)
  - Submit **supplemental** reports within 30 calendar days of receipt of new/changed information (21 CFR Part 803.56)

• **Within 5 work days of:**
  - Becoming aware that a **reportable MDR event**, from any information, including any trend analysis, **necessitates remedial action** to prevent an unreasonable risk of substantial harm to the public health; or
  - Becoming aware of an MDR reportable event for which FDA has made a written request for the submission of a 5-day report.
  - This is called a 5-Day Report (21 CFR Part 803.53)
    ‣ Work Day = Monday-Friday, excluding Federal holidays
    ‣ Not all MDR reportable events requiring remedial actions need to be submitted as 5-day reports
MDR Definitions

“Become Aware”

- When any employee of the manufacturer becomes aware of information from any source that reasonably suggests that a reportable event (death, serious injury, or malfunction)
  - That is required to be reported within 30 days, or
  - That is required to be reported within 5 days pursuant to a written request from FDA; and
- When an employee, who is a person with management or supervisory responsibilities (over persons with regulatory, scientific, or technical responsibilities), or a person whose duties relate to the collection and reporting of adverse events, becomes aware that an MDR event or events, from any information, including any trend analysis, necessities remedial action to prevent an unreasonable risk of substantial harm to the public health.

“Aware Date”

- The date on which any employee (first) Becomes Aware of information from any source, that reasonably suggests that an MDR reportable event has occurred.
"From Any Source"

- User and Employee Complaints
- Servicing
- OEMs & Suppliers
- Other sources of customer feedback
  - Trade Shows, Focus groups, Demonstrations and training sessions
  - Post market clinical studies, Registries (condition of approval)
  - Medical and Popular Literature
  - Internal Product Testing
  - Lawsuits
- Consider Same and Similar Devices

"Information That Reasonably Suggests"

- Information such as professional, scientific, or medical facts and observations or opinions that would reasonably suggest that a device has Caused or may have Caused or Contributed to an MDR Reportable Event.
You must report to us no later than 30 calendar days after the day you receive or otherwise become aware of information, from any source, that reasonably suggests that a device that you market:

(1) May have caused or contributed to a death or serious injury; or

(2) Has malfunctioned and this device or a similar device that you market would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur.”
“Caused or Contributed”

• Means that a death or Serious Injury was or \textbf{may have been attributed} to a medical device, or

• A medical device was or \textbf{may have been a factor} in a death or Serious Injury, including events occurring as a result of:
  – Failure
  – Malfunction
  – Improper or inadequate design
  – Manufacture
  – Labeling or
  – User error

• Evaluate the ‘\textit{contributed}’ portion of ‘caused or contributed.’
  – Event may be reportable even if the device did not directly cause the patient's injury (if the information reasonably suggests that the device may have been a contributing factor in the death or deterioration of the condition of the patient.) e.g. procedural delay. Consider the patient condition before and after the event.
“Adverse Events”

- Those events...related to a FDA-regulated product and which have a negative or harmful effect on the user or recipient of the product’s use.
- .....The only adverse events required to be reported under this regulation, however, are ‘MDR reportable events’ as defined in section 803.3(q) of the final rule. (Preamble to MDR, comment 31)

“MDR Reportable Events”

- Death
- Serious Injury
- Or an event where the device malfunctioned and would likely to cause or contribute to a death or serious injury if the malfunction were to recur.  21 C.F.R. § 820.3(r)
MDR Reportable Events

“Serious Injury”

An injury or illness that

• is life threatening (even if temporary); or

• results in permanent impairment of a body function or permanent damage to a body structure; or

• necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

Permanent Impairment

– Irreversible impairment or damage to a body structure or function, excluding trivial damage

Medical Intervention

– If a device caused or contributed to an injury, and surgical / medical intervention was necessary to prevent the patient from suffering permanent impairment of body function or permanent damage to the body structure then the event is MDR reportable.

– What is considered Medical Intervention?

  ➢ “Anything beyond basic first aid or diagnostic testing administered by health professional”
MDR Malfunctions

No Death or Serious Injury? You must then consider:

21 C.F.R. § 803.50(a) Subpart E Manufacturer Reporting Requirements

“... You must report to us no later than 30 calendar days after the day you receive or otherwise become aware of information, from any source, that reasonably suggests that a device that you market:

(1) May have caused or contributed to a death or serious injury; or

(2) Has malfunctioned and this device or a similar device that you market would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur.”
• A **malfunction is reportable** if any one of the following is true:
  - the chance of a death or serious injury occurring as a result of a recurrence of the malfunction is **not remote**;
  - The consequences of the malfunction affect the device in a catastrophic manner that may lead to a death or serious injury;
  - The malfunction involves:
    - a long-term implant or
    - a device that is considered to be life-supporting or life-sustaining and thus is essential to maintaining human life;
Malfunctions – How To Assess?

• Does the malfunction result in the failure of the device to perform its essential function and compromise the device's therapeutic, monitoring, or diagnostic effectiveness, which could cause or contribute to a death or serious injury?

• Has there been a previous device-related death or serious injury associated with the malfunction? (presumption rule)

• Has the device malfunction led to a recall?

• Did the device fail to meet its performance specifications or otherwise perform as intended?
  - Performance specs include all claims in the labeling
  - Intended performance refers to intended use for which the device is labeled or marketed

  - Consider:
    ‣ What did the reporter tell you?
    ‣ Did you get the device back?
    ‣ What are the results of your tests on the suspect device?
    ‣ Can you rule out a device malfunction?
Has malfunctioned and this device or a similar device that you market would be **likely to** cause or contribute to a death or serious injury, if the malfunction were to recur.”

“**Likely To**”

- If there was a malfunction that did not cause or contribute to a death or serious injury, but would be likely to cause or contribute to a death or serious injury if the malfunction were to recur, then the event should be reported as a malfunction.

- Consider the following:
  - Has there been a previous device-related death or serious injury?
  - Has there been a previous “Near miss” event?
  - Is the device used on critical patients who would face life-threatening consequences if the device malfunctioned?
  - Is the device used in a setting that includes alarms and close monitoring?
  - Have previous malfunctions of this type investigated to verify that they have not lead to death or serious injury. Are the investigations documented?
MDR Reporting Challenges

- MDR reporting

- Conducting robust and timely investigations;

- MDR Reportability – Malfunctions
  ‣ FDA removal of the “2 year rule” for malfunctions
  ‣ Malfunction events that are within labeled frequency
  ‣ Discontinued product
  ‣ Product in Foreign countries that may be “similar”
  ‣ Malfunctions in Life sustaining and supporting devices
  ‣ How to cease reporting certain malfunctions

- Clear, consistent documentation
• **Events that occur outside of the U.S. ("OUS").** Such events are reportable to FDA if:

- The same product involved in the event is approved or cleared in the U.S.
- The product was manufactured in the U.S.
- A *malfunction* involves a "similar" product that is approved or cleared in the U.S.
  ‣ Death, SI on "similar" product that is approved or cleared in the U.S. not reportable
  ‣ “Similar” Devices that would be assigned the same FDA product code (procode) are considered by FDA to be similar for the purposes of the MDR requirements of 21 CFR §803.
### Service Reports

- **Field Service reports must be reviewed for complaint information and MDR reportability**

Each manufacturer who receives a service report that represents an event which must be reported to FDA under part 803 of this chapter shall automatically consider the report a complaint and shall process in accordance with the requirements of § 820.198. (21 C.F.R. § 820.200(c))

- Complaint handling and MDR process should be able to identify service events for **unusual conditions that may include complaint information vs. Routine Service**
  - A request for routine service is not always a complaint
  - Process for capturing and reviewing service records
  - Review of addition of incremental information to service records
  - Training of field service staff to recognize and report complaints
    - Distributors and 3’rd parties providing service
  - Trending of service reports - malfunctions
  - Out of Box vs. post-installation failures
MDR Reports

• **Complete event descriptions and narratives**
  – Stick to the Facts and Use factual, non-speculative language.
  – MDRs may include:
    ‣ Trending information
    ‣ Non-return of device does not mean you don’t need to investigate
    ‣ Information may vary for different devices or device families
    ‣ Human factors/use error follow up

• **Accurate event type (malfunction, injury, death)**
  – Event type “other” should not be used for device mandatory reports

• **Include Patient information and outcome**

• **Codes must mirror text**
How To Report?

- **Paper Form 3500A**
  - CDRH, Medical Device Reporting
  - P.O. Box 3002
  - Rockville, MD 20847-3002

- **Electronic reporting (eMDR)**
  - Electronic Reporting will be *mandatory* August 15, 2015!
  - eMDR guidance – Published August 21, 2009; Docket Number FDA-2008-N-0393;
    - [http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/eMDR%E2%80%93ElectronicMedicalDeviceReporting/default.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/eMDR%E2%80%93ElectronicMedicalDeviceReporting/default.htm)
    - [http://www.fda.gov/ForIndustry/FDAeSubmitter/ucm107903.htm](http://www.fda.gov/ForIndustry/FDAeSubmitter/ucm107903.htm)
1. **Duplicate report sequence numbers provided in the Manufacturer Report Number box and Block G-9.**
   - Each report must have its own sequence number to avoid confusion.
   - You should not use the same sequence number on more than one report in any given year.

2. **Multiple devices or events are included in the same report.**
   - Manufacturers must complete and submit a separate Form FDA 3500A for each different suspect device involved in each event.

3. **Blocks B-2 (Outcomes Attributed to Adverse Event) and B-5 (Description of Event or Problem) do not match or do not accurately represent the text contained in H-1 (Type of Reportable Event), H-10 (Additional Manufacturer Narrative), or H-11 (Corrected Data).**
   - Provide an explanation in Block H-11 for any conflicting data.

4. **Block D (Suspect Medical Device) is left blank or specific items within Block D are left blank.**
   - Good faith efforts to obtain information to properly identify the device and evaluate the event.

*Source: FDA Draft Guidance - Medical Device Reporting for Manufacturers July 9, 2013*
5. No box is marked, or more than one box is marked, in Block H-1 (Type of Reportable Event).
   • Only one of these boxes should be marked.
   • If the device malfunctioned, and the malfunction may have caused or contributed to a death or serious injury, label either “Death” or “Serious Injury” as appropriate, but do not also mark the “Malfunction” box.
   • Separate report for each outcome. e.g. a single event caused or contributed to the death of one person and the serious injury of another, separate reports.
   • Box marked “Other” should not be used.

6. Codes required to be entered in Block H-6 (Evaluation Codes) are put in boxes on the wrong row.
   • Make sure your codes are applicable and are placed in the proper space.
   • For example, an evaluation method code might be entered in the space for evaluation results codes or evaluation conclusion codes.

7. Event problem codes (patient problem codes and/or device problem codes) are not provided in Block F-10.
   • Codes either not provided or, incorrect codes used.
   • Coding manual containing instructions on the use of patient and device codes: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm106737.htm

Source: FDA Draft Guidance - Medical Device Reporting for Manufacturers
July 9, 2013
Exemptions – Part 803.19

- FDA offers alternatives to reporting individual MedWatch forms and may exempt a manufacturer from some or all of the MDR requirements

- **Alternative Summary Reporting (ASR)** – is a subset of information required by Part 803.52
    - Investigation of event still required
    - Individual reports may be required under certain circumstances
    - Manufacturers must apply in writing for an exemption. Requests must include:
      - Information identifying the firm and device
      - Statement of request for exemption
      - Justification for exemption
      - FDA may grant request or impose additional requirements to protect public health

- **Remedial Action Exemption (RAE)** - for recalled products covered by 21 CFR Part 806 (Corrections and Removals)

- **Retrospective Reports** - submission of a one-time summary report of late MDRs.

- **Single MDR** - submission of a single MDR for an event where two reporters have a reporting responsibility
• Information would cause a person qualified to make a medical judgment to reach a conclusion that a device did not cause or contribute to a death or serious injury, or that a malfunction would not be likely to cause or contribute to a death or serious injury if it were to recur.

  ‣ A person qualified to make a medical judgment: Includes physicians, nurses, risk managers, and biomedical engineers

  ‣ A device-related event did not occur.

  ‣ You receive information from multiple sources regarding same patient and same event (report only once).

  ‣ Information received in erroneous in that a device-related incident did not occur.

  ‣ You determine that the device was manufactured by another company (send reportable info to FDA with cover letter).

- Be sure to document the information used to make this decision in your MDR event / complaint file
Draft Guidance for Industry and Food and Drug Administration Staff; Medical Device Reporting for Manufacturers – July 2013

• Describes and explains the FDA regulation for MDR reporting and recordkeeping
• Question and Answer Format
• Manufacturer Reporting Requirements
• Procedures, record keeping, Public Disclosure
• Enforcement
• Terms & Definitions
Draft MDR Guidance

- Tracks to much of the advice of the 1997 Guidance intact, expands upon that guidance with a few notable changes
  - The “two year rule” has been abandoned
    - Eliminates the presumption if malfunction does not cause or contribute to a serious injury or death for two years or it is no longer reportable
    - Current guidance requires continued reporting, however a request for exemption may be submitted to FDA for further reporting if no reports have been received

- Malfunction reporting continues to apply to all devices
  - Statutory changes in FDAAA would have required only summary or quarterly reporting of malfunctions of Class I and Class II device not permanently implanted, life supporting or sustaining
    - Until FDA publishes a rule to establish malfunction reporting requirements manufacturers must continue to report
      - There is no timeline for publishing such a rule
• “Likelihood” of types of malfunctions to cause or contribute to serious injuries
  - Events where chance of serious injury or death is “not remote”
  - Malfunctions that affect the device in a catastrophic manner that “may” lead to death or serious injury
  - Failure of a device to perform its essential function which “could” cause or contribute to death or serious injury
    ‣ The terms “not remote”, “may” and “could” set a lower bar than one would interpret as ‘likely’

• Correctable malfunctions may still be reportable
  - If a malfunction may be corrected by service or maintenance it is reportable if it may contribute to serious injury or death

• Similar devices for malfunction reportability
  - Devices are similar if they have the same basic design and basic performance characteristics, intended use and function, device classification and product code
  - Factors include brand name, clearance/approval requirements
• User Error may be reportable as an MDR if causes or contributes to a death or serious injury
  - “Caused or contributed” (21CFR803.3) includes use error
  - Usually indicates issues with labeling, user interface or device design

• Delays in Surgery may or may not be reportable
  - An event is not reportable “solely” on the basis of a delay
  - It is reportable if the delay may have caused or contributed to a death or serious injury
  - If no death or serious injury occurs – may still be reportable if the device malfunctioned and the malfunction and associated delay would likely cause or contribute to serious injury or death if it were to recur

• Alarms to signal a malfunctioning device
  - When a device malfunction alarm alerts the user to intervene before harm to the patient occurs, the event is MDR reportable.
    Should be reported as a malfunction based on potential to cause or contribute to a death or serious injury
• Investigation of reported events should include good faith effort to obtain additional info with at least one written attempt, and focus less on number of attempts
  - Level of effort should be based on nature and severity of event
  - Attempts shall be documented in MDR file subject to FDA review
  - If device is *not* returned event must still be analyzed (similar events, DHR review, review of manufacturing processes, etc.)

• Expected Life of Device - the time a device is functional after placed into use including overall lifecycle of the device including all calibration and maintenance cycles
  - Warranty period can *not* be used to determine expected life
  - There is no requirement to establish an end of life of a device
  - MDR files are to be maintained for two years or the expected life of a device

• Assigning MDR responsibility between two entities
  - Exemptions are needed to eliminate duplicative reporting
CASE STUDY
Sweet Dream Device, Inc., a U.S. manufacturer of anesthesia devices is a Division of their parent holding company Sleep More Devices, located in Vietnam.

The global sales offices of Sleep More warehouse, sell, distribute and service Sweet Dream Device products.

During a routine quarterly visit to a client outside of the US a Sleep More global sales representative learned of a patient injury associated with the U.S. manufactured product. The Sleep More’s sales representative returned to her office after her two week client road trip and left immediately for a 1 week vacation.

Upon her return, she sent the injury information to Sweet Dream Device, Inc in the U.S. for their evaluation and review.
The firm’s investigation determined the following:

The clinician accidentally pressed the wrong button on the machine, putting the device into a maintenance cycle that prohibited ventilation of the patient. The clinician had to manually ventilate the patient and was able to successfully stabilize the patient. Once the anesthesia machine completed its maintenance cycle, the clinician was able to ventilate the patient normally using the machine.

Both the Hospital and the Firm’s Biomedical Engineers tested the device and found the device operated normally and that there was no system malfunction.

As part of the firm’s investigation, a complaint review identified two similar events. In one of these events, the patient expired. The firm’s investigation of this previous event was unable to conclude whether the interruption of ventilation caused the patient death.
Questions:

1. Should Sleep More Devices employees report such events to Sweet Dream Device Inc.?
2. Sweet Dream Device, Inc first learned of the injury upon receipt of the Sleep More Devices Sales rep. report. Is that the “Become Aware Date”?
3. At what point was the Become Aware Date reached?
4. Will any subsequent MDR filing, if needed, be late?
5. What steps can be taken to reduce this problem (potentially late MDR) from recurring?
6. Was there a serious injury?
7. If there was a serious injury, did the device cause or contribute to the patient injury?
8. Is the event reportable as an MDR?
9. What other actions should the firm take?
10. Does the firm have a potential recall?
Case Study – Sweet Dream Device Inc.

- Parent company sales rep waited 3 weeks before reporting incident to the firm.
- Clinician accidentally pressed the wrong button and could not exit checkout cycle delaying patient ventilation.
- Required medical intervention to preclude serious injury.
- Device operated normally; no system malfunction.
- Two previous complaints. One was a death event; firm unable to determine if interruption of ventilation caused the patient death.

Questions

1. Should Sleep More Devices employees report such events to Sleep Dream Inc.?

- Yes; Sweet Dream Device Inc., needs to be clear who is the designated complaint unit - All employees, affiliates, distributors need to be trained on identifying a complaint, required information, where to send the information and timeframes for reporting the information.
2. *Sweet Dream Device, Inc* first learned of the injury upon receipt of the *Sleep More Devices* Sales rep. report. Is that the “Become Aware Date”?

- No! The firm’s become aware date is the date when the firm first became aware of the incident; this is the date the sales representative first received the report that an injury occurred.

3. At what point was the Become Aware Date reached?

- The date the sales representatives had been present and observed the surgical procedure at which this injury occurred.
4. Will any subsequent MDR filing, if needed, be late?

- There is a potential for a late MDR. The firm has 30 days after the day the firm first became aware to report the MDR. Given the sales rep took 3 weeks to report the complaint, the firm has only a short time left to complete the investigation and file the MDR if needed.
5. What steps can be taken to reduce this problem (potentially late MDR) from recurring?

- The firm needs to ensure all company personnel – Sales reps, Service, all employees know how to identify a complaint, what information is minimally required, where to report the complaint.

- Roles, responsibilities need to be clearly documented between the parent company and its Divisions.

- The Firm needs to clarify and document:
  - Who holds the registration for the product?
  - Who manufactures the product?
  - Investigation site?
  - Designated Complaint Handling Unit?
  - Who is responsible for reporting MDRs and Vigilance reports?
6. Was there a serious injury?

Yes, medical intervention to preclude a serious injury

7. If there was a serious injury, did the device cause or contribute to the patient injury?

Device did not cause (e.g. system malfunction), however, it contributed to the serious injury.

8. Is the event reportable as an MDR?

Yes, although the serious injury was attributable to User error, this event is reportable as a MDR.
9. What other actions should the firm take?

Utilize risk assessments for determination of whether the hazardous situation has been reduced to As Low as Reasonably Practicable.

- Labeling alone or relying on training may be inadequate for this device and intended use.
- Investigate adequacy of the design to prevent user error.

10. Does the firm have a potential recall?

Potentially - depends on whether the firm intends to take any field actions to address the complaint.
MDR Implementation – Key Considerations
Objectives

• MDR Reporting Requirements
  - Regulation & Definitions
    ‣ Reporting Requirements & Timeframes
    ‣ What to Report
    ‣ Properly assess Malfunctions
  - Challenging MDR Scenarios
    ‣ Servicing; OUS Events
  - New FDA MDR Guidance

• MDR Implementation
  - MDR & Post market surveillance
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  - Form 3500a & Electronic Reporting (eMDR)
  - Best Practices

• Case Studies

• Questions & Discussion
Post market Surveillance System

**Surveillance (Information Input)**
- Complaints
- Servicing
- Customer Feedback
  - Surveys
  - Focus Groups
  - Literature
- Post market clinical studies;
- OUS events if same / similar product is marketed or manufactured in US
- Integrated data systems

**Investigation & Analysis**
- Failure Investigations
  - Good faith Efforts
  - Returned products
  - Internal testing
- Medical review
- Risk Assessment

**Action**
- MDR reporting
- Vigilance (MDV)
- CAPA
  - Process
  - Design
  - Labeling
  - Training
- Correction / removal

**Communication**
- All stakeholders
  - Management
  - Internal businesses & plants
  - R&D; Risk Mgt.
- US / OUS Regulatory Agencies
- Hospitals, Physicians, Patients
- Suppliers Distributors

**Goal of PMS system is to take appropriate action to protect public safety and improve product performance**
MDR Reporting Challenges

- **Timely reporting**

- **Conducting robust and timely investigations**;

- **MDR Reportability**
  - Providing accurate information to FDA in the way FDA wants to receive that information
  - Events from clinical trials
  - Events that are the result of user error; off-label use; abnormal use

- **Clear, consistent documentation**;
Investigation & Analysis

- **Accurate, complete, and timely information exchange**
  - Between complaint handling unit, investigating site, and local site
  - Request for follow-up information; Privacy issues
  - End users, customers, regulatory authorities

- **Make it easy for auditors to read and understand complaint files, investigations, and reporting decisions**
  - Record structure – goal is complaint file should be stand-alone;
  - Complaint summary and record closure
  - Periodic audits of complaint files
  - Reviews of source documentation e.g. service records, and outputs e.g. associated CAPAs, field actions etc.
  - Actions taken consistent and aligned with the objective data

- **Make it easy for customers and field service to return device**
  - Consistent policy on when to request device for investigation
Must be both Patient- and Product-Centric

• **Patient-Related Questions**
  - What was the patient’s condition prior, during, and after the use of the device?
  - Did or would the patient require medical or surgical intervention related to an issue associated with the use of the device?
  - What medication did the patient require prior to and subsequent to the adverse event?
  - Did the patient require return visits to a physician or health care provider to monitor healing after the adverse event?

• **Product-Related Questions**
  - How and why was Company made aware of this event?
  - What other experience has Company learned about the use of this device in the same or similar circumstances?
  - What have past Company investigations revealed about the use of this device?
  - What is the severity and frequency of reported complaints associated with this device?
  - Has there been any change to the manufacturing of, or materials used in the manufacturing of, the device, even ones meant to improve quality?
Risk Assessments

- **Risk assessments can be helpful in making MDR reporting decisions**
  - Formal evaluation of issues that may pose risk to patient safety
    - Evaluation of “potential to cause or contribute”
    - Combination of the probability of occurrence of harm and the severity of harm
  - May provide rationale on why reporting is or is not needed (Caution)
    - Medical / Clinical input required
  - Input to Escalation
    - May provide a basis for making determination of Field action
    - DFU changes
    - Manufacturing or Design changes
    - Update of product risk management file
Health Hazard Assessments

- **Health Hazard Assessments (Evaluations) key component of Risk Assessments**
  - Clear description of the issue
  - Comprehensive complaint review; include historical trends
  - Directions for Use (DFU) review; Literature
  - Review of FMEA and design risk assessments
  - Include all available qualitative and quantitative information e.g. complaint frequency; frequency of harm, severity of harm
  - Details of the non-conformance and results of failure analysis and performance testing

- **Health Risk assessments should be consistent with those used in Design or evaluation of product performance**
Events that occur during Clinical Trials e.g. new indication may be reportable under 21 CFR § 803

- Typically, events on investigational devices being studied fall under § 812 IDE regulations

- § 812 IDE regulations cover the unapproved device.

- Once the device is approved, reporting falls under § 803 regulations.

- Events with a marketed (approved or cleared) device (either control or ancillary) on patients enrolled in an IDE study must be evaluated for reporting as MDRs under § 803 regulations.
Events from Clinical Trials

- Reporting is required under MDR regulations even if IDE study is still on-going (in addition to any IDE annual report requirements e.g. if the IDE is kept open for long-term follow-up).

  - Can satisfy the IDE reporting requirements by just referencing the MDRs in the IDE annual report.

  - If study involves blinding, the company “becomes aware” when the data is un-blinded for any reason (e.g., early un-blinding for safety reasons), in accordance with the protocol for data analysis, or inadvertently for any other reason.

  - If the device is on the market in the US and is being studied under an IDE e.g. for a new indication, and the device is used outside of the IDE (either US or OUS) for the investigational indication (i.e., "off-label" use), and a complaint associated with this off-label use becomes known, then this complaint must be evaluated for reporting under § 803.

- Clinical Complaint Reporting Management Plans may be helpful to define and document reporting rationale
Electronic MDR Reporting (eMDR)

- Proposed rule (74 FR 42203 – Aug 21, 2009) to amend part 803 to require manufacturers, importers, and user facilities to submit MDRs to the agency in an electronic format (the 2009 Proposed rule).

- Final rule (FR Docket No. FDA-2008-N-0393] Feb14, 2014) requires device manufacturers and importers to submit medical device reports (MDRs), to the Agency in an electronic format that FDA can process, review, and archive.

- **Final rule is effective August 14, 2015** - Reporting entities that are unable to comply with this date should request an exemption.
1. History of the Medical Device Reporting Regulation

2. Changes to the 2009 Proposed Rule

   a) The final rule contains part 803 in its entirety for ease of reading and clarity. The 2009 proposed rule included only the amended parts of the regulation.

   b) Certain terminology has changed in the final rule. e.g. “CeSub” (CDRH eSubmitter) have been revised to “eSubmitter.”

   c) Manufacturer or importer needs to request and obtain an exemption from electronic reporting to continue to report via hardcopy past the effective date.

   d) Electronic reporting is also available to user facilities, but this rule permits user facilities to continue to submit written reports to FDA.
eMDR – Summary Final Rule

Changes to the 2009 Proposed Rule Cont’d

e) MDR 3500A. content changes to reflect re-processor information

f) Technical changes e.g.
   ‣ § 803.11 provide the updated sources for Form FDA 3500A.
   ‣ § 803.12 update the contact information for the FDA/Office of Crisis Management when reporting a public health emergency
   ‣ § 803.19 update the contact information for the FDA/CDRH/Office of Surveillance and Biometrics when submitting an MDR Exemption Request.
   ‣ § 803.21 provide the current Web site addresses for obtaining adverse event reporting codes information; also provides the current contact information for the FDA/CDRH/Division of Small Manufacturers, International, and Consumer Assistance (DSMICA).
   ‣ § 803.33 provide the updated sources for Form FDA 3419.
3. Overview of the Final Rule Cont’d
   
a) Mandatory eMDR provides FDA with more timely access to the information to improve the Agency's process for collecting and analyzing postmarket medical device adverse event information.

b) Firms have two options to report MDRs to FDA:
   - Single reports using the eSubmitter tool (Low-volume option)
   - Batch reports using the Health Level 7 Individual Case Safety Reporting (ICSR) tool. (high-volume option)

c) Other Requirements:
   - Record keeping requirements; What to do in the case of a system outage (document submission attempts).

d) Extensive Discussion & Analysis:
   - FDA Legal Authority for the rule;
   - Economic Impact of the Rule; Cost/ Benefit Analysis;
   - Regulatory alternatives to the final rule;
   - Insight to FDA’s policy-making e.g. address industry concerns rule is overly burdensome.
eMDR Submission Methods

• **Low-volume reporters:**
  - **CDRH “eSubmitter”**
    - Web-based application will create the XML 3500A HL7 ICSR
  - **“Webtrader”**
    - Electronic portal for sending .xml files to FDA and receive acknowledgements
    - Feedback loop verifying file receipt

• **High-volume reporters:**
  – **B2B connection** with FDA servers
  – Submit MDR files formatted as an **HL7 ICSR** message.
  – Ability to process electronic MDR files either individually or as a batch.
  – Requires system and infrastructure configurations
    - Convert data to HL7 format
    - Send file to FDA
    - Acknowledgments for each stage of report transmission.
eMDR Low Volume Requirements

- Download eSubmitter
- Register for Webtrader
- Test submissions
- Submit eMDR!

**Advantages:**
- Small validation / Installation effort – approx 6 weeks
- No hardware or software needed
- Purchase Digital Certificate (~$20); Sign non-repudiation forms.
- Permits attachments; Ability to “clone” MDR and quickly generate supplements
- Confirmation of receipts at various levels

**Disadvantages:**
- Cannot scale up to High Volume
- Not integrated with complaint system
1. **eMDR Vendor Application Setup**
   - Purchase eMDR vendor application
   - Install and Configure eMDR mapping utility which will convert 3500A data into HL7 format
   - Map 3500A fields from paper form to system fields for eMDR.
     - Identify fields that are missing in the current configuration which are required for eMDR.

2. **eMDR Regulatory Setup**
   - Complete Non-Repudiation Form
     http://www.fda.gov/esg/esg_sample_letters.htm
   - Obtain digital certificate

3. **eMDR Gateway Setup**
   - Select Vendor for Gateway Software and Hardware
   - Install and configure Gateway
   - Request an FDA Test Account
   - Register AS2 Test Account Information Detail with FDA:
     http://www.fda.gov/esg/Registering_for_an_AS2_test_account.htm
4. **Test Submissions**
   - Contact FDA and plan test submissions
   - Send Test Submission

5. **Move to Production**
   - Request FDA to convert Test Account to Production
   - Submit e-MDR!

6. **Monitor Performance**
   - Maintain metrics on failed submissions and take appropriate action
1. Decide on approach – **Low or High volume**
   - Two options for submission:
     - **B2B (Automated/High Volume/Batch Reporting)**
     - **WebTrader (Manual/Low Volume/Single Reports)**

2. Get a test account with the ESG
3. Get a digital certificate
4. Send a letter of non-repudiation ( authenticating your digital identity)
5. Contact CDRH ([eMDR@fda.hhs.gov](mailto:eMDR@fda.hhs.gov)) to initiate testing
6. Test sending MDRs with CDRH
7. CDRH approves production account with the ESG
UDI and MDR Reporting

- CDRH **Unique Device Identifier (UDI)** initiative will enable FDA to enhance and improve its postmarket surveillance and recall processes.
  
  ‣ Leverage the UDI # to link multiple databases including MAUDE MDR database
  
  ‣ Allow more accurate reporting, reviewing and analyzing of adverse event reports so that problem devices can be identified and corrected more quickly.
  
  ‣ In an MDR or recall, potential for electronic population of the UDI attribute information into the MAUDE and RES (Recall Enterprise System) databases.
  
  ‣ In 2013 the FDA launched a MedWatch Mobile App & new consumer friendly form
  
  ‣ The new 3500B consumer-friendly & 3500Voluntary forms collect the UDI # and the FDA has piloted the intent to capture the UDI # in the mandatory 3500A form
1. **MDR procedures must demonstrate they meet all of the applicable elements of 21 C.F.R Part 803**
   - Procedures should use FDA’s terminology and align with the regulations.
   - If company has multiple procedures, e.g. corporate and local SOP, the procedures should be consistent in content, process, and terminology.

2. **Ensure that Supplemental MDRs are filed within 30 days of becoming aware of new or additional information**
   - Exercise caution when “resetting the clock”
   - Did you really receive new information?
   - Did the investigation result in only the original complaint “confirmed”? 

3. **Ensure Medical Safety / Clinician input to aid in understanding of clinical outcomes**
   - Show that the healthcare professional rendering the opinion was provided with and understood the MDR reporting criteria.
     - Clinical impact of Adverse Events
     - Treatment/Therapy not achieved
     - Significance of delay in treatment
4. Ensure that events (regardless of the source) are handled consistently and appropriately.
   - Events in which little information was provided or is not available.
     ‣ Conservative (aggressive) reporting – When in doubt file; Supplement with additional information when it becomes available
   - Events that are the result of user error or “off-label” use may be reportable
     ‣ Events resulting from user error or off-label use **may** be the result of problems with the device labeling or training
     ‣ Off-label use cannot automatically be considered user error – may reflect accepted standard of care or medical practice
   - Events involving sterility failures or breach of packaging integrity; Labeling mix-ups; Out-of-box failures may be reportable
   - Whether malfunction failure modes have ever caused or contributed to a death or serious injury (and triggered the reporting “presumption”)

5. Deaths and serious injuries that are within the labeled frequency may be reportable
   ‣ FDA does not accept a non-reportable rationale that the event is within an expected or labeled frequency or severity. Evaluate each event individually
6. Simplify complaint and MDR process where possible
   - Show how procedures align with regulatory requirements
   - Use decision trees and examples to facilitate consistent decision-making
     ‣ What Objective Evidence supports the “non-reporting” decision?
   - Leverage Risk Documents to aid in Malfunction reporting decisions

7. Consider the use of Reporting/Non-reporting Guidelines
   ‣ Guidelines / rationales have been reviewed by cross-functional representatives (RA, Legal, Clinical, etc.) and are updated routinely.
   ‣ CAUTION – Guidelines augment decision-making but do not replace need to evaluate each complaint in totality

8. Review FDA publically available MDR databases
   ‣ MAUDE – Manufacturer and User Facility Device Experience
   ‣ Web search and downloadable MDR reports; FOI required for patient codes
     • http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/TextSearch.cfm
   ‣ MDR – MDR reports prior to 1996; Web search only
     • http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMDR/Search.cfm
9. **Provide training on the regulation to facilitate better MDR decision-making**
   - Test MDR decision-making staff to show consistent understanding
     ‣ Watch for problems caused by staff turnover!
   - Provide examples from where others have gone wrong
     ‣ Analysis of 483 and warning letters are useful

10. **Institute Independent reviews of MDR files and decision making**
    - Use both internal and outside company experts
    - Review both reportable and non-reportable decisions; queries for complaint files with high risk of incorrect MDR decision
    - Disseminate learnings and guidance around contemporary FDA thinking
Summary

- Device manufacturers need to have an effective system for:
  identifying potentially reportable MDR events
  - Analyzing in a consistent manner whether events are reportable,
  - Submitting accurate and timely MDR reports to FDA.

- An effective MDR system has a set of written procedures
  that incorporate the principles of FDA's MDR and complaint
  files regulations.
  - A manufacturer that lacks such a system may expose itself to FDA
    enforcement action, as well as increased product liability risk

- Helpful Websites:
CASE STUDY
Case Study 2 “MedRight Inc.”

• “MedRight Inc.” is conducting clinical trials under an IDE for its new intra-arterial blood pressure monitoring catheter. The catheter uses an ancillary device, the firm’s “Tail wind” pressure gauge which is marketed world-wide.

• The blinded study has been in progress for six months, and as a result of accidental un-blinding, the study coordinator noticed reports that the “Tail wind” device was showing erroneous results and having difficulty calibrating.

• At a meeting with the “MedRight Inc.” Design team, the Clinical Trials VP, and the R&D VP, it was decided these events did not compromise the study, the accidental un-blinding was documented, and the study continued.

Questions:

1. What gaps exist in the “MedRight Inc.” process and why is the firm at compliance risk?

2. What should have “MedRight Inc.” done with the information from its clinical trial?

3. How could the firm improve the process for handling clinical trials and ensure adequate linkages with post-market surveillance?
Case Study 2 “MedRight Inc.”

Questions:

1. What gaps exist in the “MedRight Inc.” process and why is the firm at compliance risk?
   - The firm did not evaluate reports on the marketed device for MDR reportability.

2. What should have “MedRight Inc.” done with the information from its clinical trial?
   - The events on the marketed device should be fed into the complaint process for investigation and evaluation for MDR reportability.

3. How could the firm improve the process for handling clinical trials and ensure adequate linkages with post-market surveillance?
   - The firm should consider instituting controls that before starting a clinical trial, an assessment is done to determine if marketed devices are to be used, and if complaint management plans are required.
   - Additionally, process, procedures established and training of Design, R&D, medical etc. that all clinical studies require review for use of marketed devices.
QUESTIONS & DISCUSSION