Global Post Market Surveillance

Effectively Manage Complaints & Meet Regulatory Challenges in International Markets

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Agenda

• Post market surveillance, MDR and vigilance reporting - how to streamline to meet global regulatory requirements
  - Regulatory requirements
  - EU and emerging markets vs. US
  - MDR Challenges
  - Vigilance Challenges

• Components of an effective Post market surveillance System
  - Surveillance information sources
  - Investigation and Analysis
    ‣ Risk Analysis
  - Action System and Outputs
    ‣ Decision Trees
  - Management Reviews & Dissemination
  - Monitoring Health of Post market surveillance system

• Best Practices
• Case Studies
• Questions & Discussion
What is Post Market Surveillance?

Definitions vary but generally defined as comprehensive set of Passive (Reactive) and Proactive post market activities.

Passive PMS – Always required
Active PMS – Required, but level and type of activity dependent upon product risk.
Post market Surveillance

Post market surveillance is more than Complaint Handling

<table>
<thead>
<tr>
<th>US</th>
<th>“The active, systematic, scientifically valid collection, analysis, and interpretation of data or other information about a marketed device.” 21 CFR 822.3(h) implementing § 522 of FDCA</th>
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<tbody>
<tr>
<td>AUS</td>
<td>The proactive activities carried out by either regulators or manufacturers to gain information about the quality, safety or performance of medical devices which have been placed in the market.*</td>
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<tr>
<td>CA</td>
<td>The proactive collection of information on marketed medical devices.*</td>
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<td>JP</td>
<td>Active investigation or survey with the specific purpose of confirming or better defining the safety or efficacy of a medical device.*</td>
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*From GHTF SG2 N47R4
Early identification and rapid response to problems with marketed products

- Missed signals may result in unnecessary patient injuries
- Failure to act increases liability /punitive damages
- Facilitates development of improved products
- Reduces loss (cost/loss revenue, damage to manufacturer’s brand)
- Good for Business
Post Market Surveillance - US Regulations

- Complaint handling (21 CFR 820.198)
- MDR reporting (21 CFR 803)
- Reports on Accidental Radiation Occurrences or Device Defects (21 CFR 1003.10 and 1002.20)
- Medical Device Tracking as ordered by FDA (21 CFR 821)
- Reports on Corrections and Removals (21 CFR 806)
- Post-Market Surveillance for Class II and Class III medical devices (21 CFR 822 – FDCA §522 – “Section 522 Studies”)
- Post-Approval Studies – conditions of PMA, HDE, PDP approval, such as participation in a registry (21 CFR 814.82)
Current FDA Post-Market Surveillance Efforts

The FDA’s Center for Devices and Radiological Health (CDRH) has traditionally relied on several approaches in its post-market surveillance program:

**Passive:**
- Medical Device Reporting (MDR)
- Medical Product Safety Network (MedSun)

**Active:**
- Post-Approval Studies (Condition of Approval for some Class III devices)
- Post-Market Surveillance Studies (“Section 522” Studies)
- Literature Searches / Systematic Reviews
- FDA Discretionary Studies (using registries, databases, etc.)

**Quality System-Based Inspections:**
- Primary Focus on Complaint Handling
FDA CDRH Post Market Surveillance Guidance

- Section 522 Guidance – April 2006
- Post-Approval Studies Guidance – June 2009
- Draft Recalls and Enhancements Guidance – February 2013
- Draft MDR Guidance – July 2013
- Balancing Premarket and Post-Market Data Collection for Devices subject to Premarket Approval – April 2014
**EU Post-Market Surveillance and Vigilance**

**Post-Market Surveillance** – preventive systems that monitor the market

**Vigilance** – reactive systems activated in case of adverse events

**Current system for medical devices defined by:**

- European Medical Device Directive 93/42/EEC (including annexes and amendments)*
  - Sets the harmonized standards to be met (e.g. ISO 14971)
- MEDDEV 2.12-1 Rev8 “Guidelines on a Medical Devices Vigilance System”
- MEDDEV 2.12-2 Rev2 “Post-Market Clinical Follow-up (PMCF) Studies”
  * IVD and AIMD have similar legislation; all are transposed to national legislation
Directives: Key Stakeholders

- **Manufacturer** - responsible for notifying Competent Authorities (CA) of incidents immediately upon learning (per MEDDEV 2.12-1: without delay – 2 / 10 / 30d) – May be done through EC Rep

- **Competent Authority (CA)** - responsible for monitoring vigilance data and taking appropriate action
  - EU Commission Home page lists Vigilance Contact Points within CAs
    (http://ec.europa.eu/health/medicaldevices/links/vigilance_contact_points_en.htm)

- **Notified Body (NB)** - responsible for reviewing QMS / Technical documentation to ensure compliance with legislation (re: vigilance)
  - Vigilance shall be forwarded in standardized format (form in MEDDEV 2.12/1/Rev. 6)
  - Vigilance data shall be stored in European Database (EUDAMED)
### EU Regulatory Requirements vs. Standards & Guidance

<table>
<thead>
<tr>
<th>Legally Binding</th>
<th>Non-Binding (Voluntary)</th>
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<tr>
<td>Regulations</td>
<td>Standards (e.g. QMS - ISO 13485)</td>
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<tr>
<td>MDD - 93/42/EEC*</td>
<td>MEDDEV</td>
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<td>AIMD – 90/385/EEC*</td>
<td>(Vigilance - MEDDEV 2.12-1 rev 7;</td>
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<td>IVDD – 98/79/EEC*</td>
<td>2.12-1 rev 8</td>
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<td>PMS – MEDDEV 2.12-2</td>
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<td>EC Reps – MEDDEV 2.5/10)</td>
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- Notified bodies look for confirmation that the MEDDEV guidance is implemented.
- Assurance that the legally binding regulations are met.
- NCA have specifically instructed Notified Bodies to focus on adequacy of the vigilance process and expect full implementation of 2.12 rev 8 requirements for post market clinical follow-up, post market plan, and review, trending.
• **ISO 13485:2012** - Medical devices -- Quality management systems -- Requirements for regulatory purposes
  - Procedures to collect information from various sources such as users, service personnel, training personnel, incident reports and customer feedback.
  - ISO 13485:2003 – Section 8.2 “gain experience from the post-production phase, the review of this experience shall form part of the feedback system”.

ISO Standards for Post-Market Surveillance
ISO Standards for Post-Market Surveillance

- **ISO 14971:2007**
  - Establish, document and maintain a PMS system to collect information in production and post-production
  - “... appropriate methods are in place to obtain relevant production and post-production information. The results for this review shall be recorded as the risk management report and included in the risk management file.”

- **ISO 14971:2009, Annex F.7**
  - “The risk management plan should include documentation of decisions, based on risk analysis, about what sort of post-market surveillance is appropriate for the device, for example, whether reactive surveillance is adequate or whether proactive studies are needed.”
ISO 14971:2012 - Medical devices — Application of risk management to medical devices

- Methods of obtaining relevant post-production information
  ‣ Established quality management system procedures (for example ISO 13485:2003)
  ‣ ISO 14971:2009, Annex F.7 “The risk management plan should include documentation of decisions, based on risk analysis, about what sort of post-market surveillance is appropriate for the device, for example, whether reactive surveillance is adequate or whether proactive studies are needed.”
  - Post market surveillance data required:
    - Correction on current products
    - Inputs to future designs

- Risk Management Plan should also define what type of post-market surveillance is appropriate for the device
  - Reactive surveillance
  - Proactive studies
MEDDEV requirements (guidance)

- **MDD 93/42 EEC; MEDDEV 2.12-2; Annexes II, IV, V, VI, VII; Annex X 1.1c**
  - Manufacturer must institute and keep up to date a systematic procedure to **review experience gained in post-production phase**; Implement appropriate means to apply any necessary corrective action.
    - Identification and investigation of residual risks associated with the use of medical devices placed on the market.
    - These residual risks should be investigated and assessed in the post-market phase through systematic **Post-Market Clinical Follow-up (PMCF) studies**.
      - PMCF studies are performed on a device within its intended use/purpose(s) according to the instructions for use.”
    - Where PMCF, as part of the **post-market surveillance plan** for the device, is not deemed necessary, this must be fully justified and documented
  - Manufacturer must have procedures to gather **clinical data post-market on all devices**, analyze the data, and take action as needed.
    - Clinical evaluation and documentation must be actively updated with data obtained from post-market surveillance.
MEDDEV requirements (guidance)

- “The Notified Body shall as part of its assessment of a specific medical device:
  
  ‣ Verify that the manufacturer has appropriately considered the need for PMCF as part of post market surveillance based on the residual risks including those identified from the results of the clinical evaluation and from the characteristics of the medical device...
  
  ‣ Assess the appropriateness of any justification presented by a manufacturer for not conducting a specific PMCF plan as part of post market surveillance...”
Definitions

**Incident**
- “Any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or the instructions for use which, directly or indirectly, might lead to or might have led to the death of a patient, or USER or of other persons or to a serious deterioration in their state of health.”

**Trend Reporting**
- A reporting type used by the MANUFACTURER when a significant increase in events not normally considered to be INCIDENTs according to section 5.1.3. occurred and for which pre-defined trigger levels are used to determine the threshold for reporting. (Per MEDDEV 2.12-1 rev 6)

**Post Market Surveillance Plan (PMSP)**
- Plan for collection of post market surveillance data collected by both active and passive monitoring.
- Plan is intended to outline the collection of experience data gained from the product/product family during the production and post production phase.

**Post Market Surveillance Review (PMSR)**
- Periodic product/product family review of information gathered as indicated in the Post Market Surveillance Plan used to assess product safety.
- Designed to encourage discussion and sharing of information across functions to actively determine product safety and identify potential additional actions that need to be taken.
MEDDEVs – How to implement

• Ensure the Product development process includes establishing Post market Surveillance Plan and a Post Market Surveillance Review

• Post Market Surveillance Plans:
  - Evaluate type of post market surveillance needed – Passive (complaints) and/or Active.
  - Passive PMS (complaints, MDR, Vigilance always required)
  - Active PMS – Required, but type of activity dependent upon product risk
  - Describe the product specific methods by which information is collected, processed, and evaluated for possible relevance to safety and efficacy.
  - May be implemented as part of the Risk Management Plan; Responsibilities typically fall with the Risk Management Documentation owners, depts. that submit for licensure to NB.

• Post Market Surveillance Review:
  - Periodic product reviews and periodic Risk-benefit reanalysis
MEDDEVs – How to implement

• **Establish Post Market Surveillance Policy**
  – Establish formal requirement for a post market surveillance plans and review.
  
  – Clearly outline linkages between business units, sales and marketing, design assurance, R&D, clinical, risk management, with clearly defined roles and responsibilities
  
  – Clearly outline passive (reactive) and active post market surveillance; sources; mechanisms for flow-down into the post market surveillance system.
  
  – Post market surveillance follow-up studies
    - Establish Process and procedures for periodic product reviews and periodic Risk-benefit reanalysis
      - Literature reviews
      - Post market surveillance
      - Clinical Evaluations
      - Other sources of information
      - Cross-functional review
      - Clear decision-making and documentation
    
    • If determination they are not needed – document rationale
Section 4.18 of (MEDDEV 2.12-1 rev 6) - Requirement to file vigilance reports on otherwise not reportable complaints, when trends exceed a pre-set level.

Current situation described in MEDDEV guidance (MEDDEV 2.12-1 rev. 7 (Guidelines on a medical devices vigilance system, published in March 2012) includes three situations where trend reporting should be considered:
- Already reportable INCIDENTs
- INCIDENTs that are usually exempt from reporting
- Events that are usually not reportable

How to Implement:
- Requirements not clearly defined; highly variable expectations of the Competent Authorities, nor with respect to the approach taken by manufacturers
- Establish thresholds; review process; clearly document rationales for reporting / not reporting MDVs.
Preparing for International Inspections

• Implement an Inspection SOP and establish an Inspection team
  – Roles/responsibilities; facility tours; how to handle documentation (paper and electronic) requests; training records; management reviews; inspection closeout procedures;
  – Ensure US-based support; time zones; dry-run data systems

• Review Agency and Notified Body guidance and learn from others’ mistakes
  – FDA's often-evolving view of industry standards, analyze past Warning Letters and available Form FDA 483s;
  – Review any prior Form FDA 483 observations or recurring issues and any Notified body NCs.

• Conduct a mock inspection
  – Provides a dry-run for employees and helps identify any weaknesses in procedures or inadequacies in records, and it prepares employees for the types of questions that will be asked by the FDA investigator.
  – Schedule far enough in advance to afford time to implement any corrective actions which become needed as a result of the mock inspection.
Procedures

- No procedure for reporting EU incidents
- Procedure does not allow ability to meet 2 day timeframe for serious public health threat (e.g. only review once a week) including situations when death or serious injury could have resulted (even if it didn’t)
- Incident procedure does not include requirement for reporting to Notified Body (if required by contract terms & conditions)

Non-reporting of reportable EU incidents Including failure to report incident outside EU that resulted in corrective action inside the EU

Delayed reporting of reportable EU incidents

Documentation not provided to show adherence to MEDDEVs
Preparing for International Inspections

• Organize documentation and dry-run pulls of complaint, MDR, MDV data
  – Update and verify product lists with registrations; reconcile with complaint, MDR, MDV records.
  – Identify and ensure appropriate actions (CAPA or NC) taken for any late Regulatory Reports and/or late entered complaints
  – Run queries on complaint records to identify records that suggest an issue with the documentation or decision-making e.g. records associated with MDR, MDV, recalls. FDA uses this approach as well in their review of the complaint listing firms are asked to provide electronically during inspections.
  – Query searching for records with certain combination of key words with no MDR and/or no investigation.
  – Query searching for the same failure mode as the recall after the recall has been executed and closed – shouldn’t have additional issues if recall or CAPA was effective.
  – Review Trending / Unfavorable Trends & associated investigations

• Conduct Independent Review of Complaint Files and Documentation
  - Review MDR / MDV reportable and non-reportable decisions
  - Use queries and filters to identify files with high risk of incorrect decision e.g. patient harm codes with non-reportable decisions; MDV with no MDR.
CASE STUDY
Case Study 1 “MedRight Inc.”

• “MedRight Inc.” is preparing for a Notified Body inspection. The firm reviewed a major nonconformance received by one of its competitors from the same Notified Body. The firm’s product risk profile and markets are similar to that of its competitor.

• The nonconformance issued by the Notified Body reads as follows:
  “Post Market surveillance does not meet the requirements of the amended MDD... the current procedure does not define relative inputs of the post market procedure including inputs to design process, risk management and clinical reviews.”

  “Documented evidence that post market surveillance plans are based on the outputs of risk management... could not be provided.”

  “Documented evidence that vigilance reports are filed on otherwise not reportable complaints, when trends exceed a pre-set level could not be provided.” (section 4.18 of MEDDEV 2.12-1 rev 6)

**Questions:**

What actions should MedRight Inc, take to avoid a similar non-conformance?
Case Study 1 “MedRight Inc.”

Firm should prepare and be ready to provide documentation (and examples) showing:

- System/process for conducting Post Market Surveillance Reviews (PMSR) (Procedures, templates; examples showing use..)

- Information on Clinical Evaluations and Post Market Surveillance Planning as part of Risk Management.

- Clearly defined linkages between business units, sales and marketing, design assurance, R&D, clinical, risk management, with clearly defined roles and responsibilities (Post market surveillance Policy)

- Process established and procedures updated to meet the MEDDEV guidance and include:
  - How to identify trends
  - How to report trends
  - How to document reported trends
  - Clearly defined roles and responsibilities
Post market Surveillance System

Post market Surveillance and Action 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
Organizational Alignment

• Consider how is the company structured?
  - Multiple manufacturing sites, businesses, divisions
  - Call centers
  - Complaint processing site vs. Investigation site
  - Distributors, affiliates, 3′rd parties
    ‣ Clear definition roles & responsibilities
• Who are the designated complaint handling units
• Reporting – Central team; Regulatory Affairs; Local Units
• Electronic systems and flow of information
  - Service Systems
  - Complaint Handling Systems; Electronic vs. paper
  - Time zones; Local language and provisions for translation
  - Record availability
Surveillance Information Sources

• Customers, Sales Force, Field Service, Affiliates, Distributors; 3rd parties
  ‣ Are roles, responsibilities, accountabilities for reporting complaints in a timely fashion, undertaking the necessary follow-up; when req’d; parts returns etc. clearly understood and documented by all parties?
  ‣ Training
    – Do all employees know where and how to report complaints?
    – Complaint handlings staff trained on the products, use, and the regulation.
    – Document complaints so that they are easy to follow and understand – internal and external uses.
    – Training records for company employees service; sales force; documenting they have been appropriately trained in complaint handling.
  ‣ Quality agreements between Manufacturing sites and Complaint handling unit; Quality agreements with Affiliates and Distributors.
Surveillance Information Sources

• Field Service reports **must** be reviewed for complaint information and MDR reportability 21 C.F.R. § 820.200(c)
  ‣ Train field service staff to recognize and report complaints
  ‣ Distributors and 3’rd parties providing service

• Establish process for capturing and reviewing service records
  ‣ Unplanned service; Corrective Repairs
    - Out of Box vs. post-installation failures
  ‣ Service reports for routine service requests (e.g. general maintenance) typically are not complaints and do not require same level of investigation.
  ‣ Open vs. closed service records; review of incremental information added to service records
  ‣ Quality of information received and required follow-up
  ‣ Trending of service records; component replacement – feeders into the complaint system.
Investigation & Analysis

• **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?
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

- Sample and Device returns
  ‣ Consistent policy on when to request device for investigation
  ‣ Make it easy for customers and field to return device
Risk Analysis

DEVELOPMENT
- Risk Analysis
  - User Needs
  - Design Input
  - Design Output
  - Design Verification
  - Design Validation
  - Process Validation

VALIDATION
- Design Validation
- Process Validation
- Medical Device
- Field Assessment
- Information Flow
  - Risk Management
  - Design Controls
  - Post-Market Surveillance

COMMERCIALIZATION
- Production
- Customer Complaints & Post-Market Surveillance

Update harms, hazards, failure modes, occurrence estimates
MDR Reporting Challenges

- Conducting robust and timely investigations

- Timely reporting

- MDR Reportability
  - Adverse Events Occurring Outside the U.S.
  - Events from clinical trials
  - Events that are the result of user error; off-label use; abnormal use
  - Events that are within labeled frequency
  - Discontinued product

- Clear, consistent documentation
Vigilance Reporting Challenges

Challenges:

- Differing global regulatory requirements
- Timeframes for reporting differ by country and / or region
- Implementing MDD / EU / MEDDEV Requirements
- Field actions - Reliance on Affiliates, distributors, 3’rd parties
- Maintaining accurate install base and product listing

Solutions:

- Be aware of current and emerging regulations
- Use country-specific Decision trees and standard forms documenting reporting decision
- Establish process for updating decision matrices and electronic systems
- Clarify authority to make reportability decisions at local / country level and ensure local / country personnel are adequately trained
- Local language and provisions for translation
- Ensure consistent record content
Australia / New Zealand Decision Tree

1. Device(s) installed in ANZ?
   - No → End - No Report
   - Yes → Event occurred in ANZ?
     - Yes → Event is a death or serious injury associated with device?
       - Yes → 10 Day Report
       - No → Evaluate for Field Action Reporting
     - No → Is field action being reported in the country where incident occurred?
       - Yes → 30 Day Report
       - No → Evaluate for Field Action Reporting
2. Could result In death or serious injury if recurred?
   - Yes → 30 Day Report
   - No → End - No Report
Action System & Outputs

• CAPA
  ‣ Process
  ‣ Design
  ‣ Labeling
  ‣ Training

• Escalation
  - Correction / removal
    ‣ Field action
    ‣ Safety notice

• Risk Management
Action System & Outputs

Complaints & Complaint Trending
PM Studies & Registries
Product Testing Inspections
Suppliers

Escalation

Product Inquiry Report

Quality Escalates Issue Investigation Root Cause Risk Management

Medical Health Hazard Evaluation

Regulatory Recommends Field Action / Recall

Field Action Committee Senior Mgmt. Decision Makers

Field Action Execution CAPA
No Field Action CAPA
Field Safety Corrective Action (FSCA)

- When medical devices are suspected of being potentially harmful to users, due to nonconformity to quality, safety and performance requirements, they may be subjected to a Field Safety Corrective Action (FSCA).
  - FSCA is synonymous with a systematic recall or withdrawal of the device from the market
  - Action taken by a manufacturer to reduce the risk of death or serious deterioration of a patient's health associated with use of a medical device on the market.
  - FSCA needs to be reported in the Field Safety Notice template form provided in Annex 4, Report Form: Field Safety Corrective Action.
  - Provided to the competent authorities in all affected countries and to the national competent authority responsible for the manufacturer along with relevant documentation: e.g. related parts of risk analysis, background, description, justification, advice to distributor and user, and affected devices (serial, lot, batch number ranges).
Dissemination & Management Reviews

Timely & Accurate information Exchange

Internal & External stakeholders

- Site, Business Unit, Regional and Exec Management Reviews
- Local, Regional & Corporate quality boards
- Businesses; Manufacturing plants; R&D; Risk Mgt.
- Hospitals, Physicians, Patients
- US & Outside US Regulatory Agencies
- Suppliers, Distributors, other 3rd parties

Typical information disseminated/discussed

- Serious AE; Reportable events; Trends
- System performance efficiency and effectiveness metrics
- Relevant CAPAs; Projects/initiatives
- Complaint investigations Status & Aging
- Industry trends and new/changing regulations
- User feedback
- Procedural changes/improvements
How to Implement:

- Institute a systematic process for reviewing post market surveillance system and provide timely feedback

**System Efficiency Metrics**
- Late Regulatory Reports & Late Entered Complaints
  - Feeder to CAPA / NCE process
- Complaint and Investigation Cycle Times vs. Targets
- Complaint and Investigation Aging
- Total Complaints & Investigations Entered and Closed

**System Effectiveness Metrics**
- Independent Review of Complaint Files and Documentation
  - Review MDR / MDV reportable and non-reportable decisions
  - Use queries and filters to identify files with high risk of incorrect decision e.g. patient harm codes with non-reportable decisions; MDV with no MDR;
  - Monitor results to identify if need for systemic fixes or additional training required

**Product Performance Metrics**
- Top 10 As Reported and As Analyzed Codes
- Top Complaint Products
- Unfavorable Trends
FDA Plans for Improving Device Post-Market Surveillance

- Establish a multi-stakeholder Medical Device Post-market Surveillance System Planning Board
- Establish a unique device identification (UDI) system and promote its incorporation into electronic health information
- Promote the development of national and international device registries for selected products
- Modernize adverse event reporting and analysis; and
- Develop and use new methods for evidence generation, synthesis, and appraisal

Vehicles

- UDI will make individual device model identifiable
- Sentinel initiative – full implementation for Medical Devices
- MDEpiNet, and collaborations with providers, academic centers
- Enhanced technology for data mining and extraction (eMDR, FAERS, access to EHRs)
Future Considerations – EU

**Updated regulations on medical devices being adopted:**

- European Commission desires better coordinated information exchange between national competent authorities
- Device traceability system in planning
- Stricter requirements for clinical evidence
- More accountability for Notified Bodies in certifying devices, and in post market follow-up
  - Heightened expectations for NB performance from EC and national Competent Authorities
  - Increase in NB scrutiny of manufacturers and devices
1. **Establish procedures and systems to assure complaint information from all sources are entered into the complaint handling system within defined timeframes**

- Establish procedures and train all company employees and agents to recognize and report complaints within a defined timeframe
  - Customers to call centers;
  - Customers to Sales Reps; Distributors; 3rd parties
  - Service
  - Customer feedback – focus groups, training sessions, social media
  - Post market clinical studies; registries (condition of approval and “marketing” studies.
  - Literature; social media
2. **Develop Tools to facilitate collection and documentation of comprehensive complaint information (e.g. product specific complaint questionnaires)**

- Balance Patient-centric vs. Product-centric information collection

- Use Complaint Notification Forms
  - What happened? When did it happen? Was the patient / user injured? Severity of Injury?
  - If injury or suspected injury, follow-up to determine patient outcome
  - Device / Lot / Batch #? Is the device available for return?
  - Is the device past shelf-life? Reprocessed?

- Take proactive steps to maximize likelihood of device return
  - Communicate to customers importance of device return
  - Provide clear instructions and processes to facilitate return
3. **Ensure MDR / MDV procedures and processes fully comply with regulatory requirements in all regions where products are marketed**

- Evaluate all complaints for MDR / MDV reportability
  - Balance information with timely decision-making; If in doubt report on-time and supplement when additional information becomes available.
  - Use decision trees and examples to facilitate consistent decision-making; What objective evidence supports the “non-reporting” decision?
  - Medical review and escalation process for safety issues and serious events & Assessment of various clinical scenarios: e.g.
    - Treatment/Therapy not achieved
    - Significance of delay in treatment
    - Medical Intervention
  - Leverage Risk Management information to aid in assessment and making reporting decisions.
CASE STUDY
“Sleep Well Inc.” received a report on one of its medical devices. A German hospital facility crossed the oxygen and nitrous oxide delivery lines to a surgical room. The firm’s anesthesia delivery device was used to perform surgery in this room where the input lines were switched. During the surgery the patient became hypoxic and died.

The firm filed an adverse event report with the German competent authority but decided upon investigation not to file an MDR.

Questions:
• Did the firm make the correct decision?
• What other actions should the firm take?
FDA requires manufacturers to report actual injury events when they “become aware of information that reasonably suggests a device you market may have caused or contributed to a death or serious injury”

“Caused or contributed” means that a death or serious injury was or may have been attributed to a medical device, or that a medical device was or may have been a factor in a death or serious injury, including events occurring as a result of:
1. Failure;
2. Malfunction;
3. Improper or inadequate design;
4. Manufacture;
5. Labeling; or
6. User error.”
2.5 What is meant by “caused or contributed” to a death or serious injury?
This means that a death or serious injury was or may have been attributed to a medical device or that a medical device was or may have been a factor in a death or serious injury, including events occurring as a result of [21 CFR 803.3]:
- Failure;
- Malfunction;
- Improper or inadequate design;
- Manufacture;
- Labeling; or
- User error.

2.6 What is device “user error” and why do you want to know about events involving user error?
We consider a device “user error” to mean a device-related error or mistake made by the person using the device. The error could be the sole cause of an MDR reportable event, or merely a contributing factor. Such errors often reflect problems with device labeling, the user interface, or other aspects of device design. Thus, FDA believes these events should be reported in the same way other adverse events a device causes or contributes to should be reported. This is especially important for devices used in non-health care facility settings.
- When is it “use error” vs. “abnormal use” vs. design/manufacturing issue?
  - If clear labeling disregarded speaks to use error or abnormal use
  - If customer notes they did not use it correctly, or if operator could have used device correctly and prevented issue, then use error.

- Always consider whether a different ‘design’ could have obviated the use error (e.g. different line colors for oxygen and nitrous oxide).

- Caused or contributed must consider the procedure required to utilize the device.

- Use error does NOT mean it is automatically not device related.

- No difference whether patient, healthcare provider, or service provider are injured. Must consider the events and risks in a similar manner.

- Differentiate intentional misuse (e.g. intentionally staring into a laser) which is not cause/contribute vs. non-intentional use error
Definitions

• ISO 14971 2007   2.27 Use error: A use error is an act or omission that results in a medical device response that is either not expected by the user or unintended by the manufacturer. Use errors include slip-ups, lapses, and mistakes.

• MEDDEV 2.12-1   4.20 Use Error: Act or omission of an act, that has a different result to that intended by the Manufacturer or expected by the Operator of the Medical Device.

            4.1 Abnormal Use: Act or omission of an act by the Operator or User of a Medical Device as a result of conduct which is beyond any means of risk control by the Manufacturer. Reference: EN IEC 60601-1-6

• MEDDEV 2.12-1rev 4   Misuse: Intentional use of a device contrary to its intended purpose according to the labeling, instructions for use and or in the promotional material related to the device.
1. Did the device malfunction?
   - No evidence device malfunctioned (did not cause), however, device contributed to patient event.

2. What actions should the firm take?
   - Evaluate for MDR reportability. The device did not cause (it functioned correctly). However, although investigation shows user error a factor, the device did contribute to the incident. Under MDR requirements, this incident may be reportable in the US as well.

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

   - Does the firm have design and risk data to show risks of crossed gas lines reduced to ALARP?
     - Investigate adequacy of the design to prevent accidental mixup of gas lines.
     - Labeling alone or relying on training may be inadequate for this device and intended use.
3. Does the firm have a potential recall?
   - Firm needs to investigate whether design change could prevent the incident from recurring.
QUESTIONS & DISCUSSION