FDA Device Inspections: CDRH

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Director, Division of Regulatory Programs 2: Establishment Support
ORP, OPEQ, CDRH
Outline

- ORP/Division of Regulatory Programs 2: Establishment Support
- Routine Inspections
- Risk-Based Work Plan
- Preapproval Inspections
- Directed Inspections
Office of Product Evaluation and Quality

- OPEQ: Immediate Office
  - Communications
  - Training and Professional Development

  - Quality & Analytics Staff
  - Clinical & Scientific Policy Staff

  - Strategic Initiatives Staff
  - Regulation, Policy & Guidance Staff
  - Operations Staff

- OHT1: Office of Ophthalmic, Anesthesia, Respiratory, ENT & Dental Devices
- OHT2: Office of Cardiovascular Devices
- OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
- OHT4: Office of Surgical and Infection Control Devices
- OHT5: Office of Neurological and Physical Medicine Devices
- OHT6: Office of Orthopedic Devices
- OHT7: Office of Invitro Diagnostics and Radiological Health
- Office of Clinical Evidence & Analysis (OCEA)
- Office of Regulatory Programs (ORP)

Super Office  Office  Division  Branch  Team  Program/Staff
Division of Regulatory Programs 2: Establishment Support

- Responsible for regulatory programs policy and provides high-level programmatic support to the device specific offices.
- Develops policy and processes for core regulatory programs.
- Provides 2nd level programmatic expertise, policy interpretation and analysis of difficult and new review issues.
- Ensures proper application of FDA and CDRH policy.
- Regulatory Inspections and Audits Team; Imports and Registration & Listing Team, Exports Team; and Quality System Team.
Division of Regulatory Programs 2: Establishment Support

Division Director
CDR Cesar Perez

Deputy Director
(Vacant)

- Regulatory Inspections and Audits Team
  LCDR Neil Mafnas

- Imports and Registration & Listing Team
  Deniz Mackey

- Exports Team
  Leila Lawrence

- Quality System Team
  (Vacant)
# Medical Devices Inspections

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Risk-Based Routine Inspections

• FDA employs a targeted, risk-based approach to address specific areas of concerns by focusing on high-risk firms and/or products.

• A risk-based approach allows the agency to focus on firms and products most likely to be violative.
Site Selection: Risk-Based Routine Inspections

FDA Analyses various data for input into site selection:

- Class of device(s)
- Regulatory/Inspection history and inspection outcomes
- Recall history and MDRs
- Product codes manufactured at the site
- Information from premarket and postmarket submissions
- Compliance history and industry compliance trends
- Public health concerns
- Participating in MDSAP and pilot programs

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Risk-Based Work Plan (RBWP) Inspections

• Initiated annually by CDRH
• Developed to focus limited resources on key public health needs
• Provides the most health promotion and protection to the public by focusing inspectional activities on medical devices and firms which pose a greater risk
• Inspectional guidance is drafted to guide FDA investigators
• RBWP inspections may be more in-depth in certain areas than a typical QSIT inspection
Site Selection: Risk-Based Work Plan (RBWP)

Initial Selection

• Preliminary list of product codes (6-10) are initially selected using the following factors:
  - MDR, Allegations, and Recall Risk Factors
  - Number of Premarket Submissions
  - Products covered in previous RBWP Assignments
  - Input from all OHTs

*Note*: FDA can use its discretion to target specific devices for the RBWP to address immediate or higher priority public health needs

Final Selection

• CDRH leadership selects the final list for the RBWP annual assignment based on the factors listed above
Site Selection: Risk-Based Work Plan (RBWP)

Reasons for Exclusion

• Recent inspection

• Participation in:
  – Medical Device Single Audit Program (MDSAP)
  – Case for Quality (CfQ) Pilot Activities (i.e. Voluntary Medical Device Manufacturing and Product Quality Pilot Program, Premarket Approval Critical-to-Quality Pilot Program)
Preapproval Inspections

- Original PMA/Modular PMA (after converted); Site Change Supplements; and Certain HDEs.
- CDRH determines that manufacturer demonstrated that the design and manufacturing processes meet QS regulation requirements and facility ready for inspection.
Site Selection: Preapproval Inspections

Submissions that could generate an inspection request:

- No inspectional history; or a violative inspectional history
- Questions regarding data quality or integrity
- Last inspection- OAI
- Last Inspection (NAI/VAI)- benefit/risk based approach: TPLC query report
For-Cause or Directed Inspections

Investigate a specific problem that has come to FDA’s attention

- Recall, MDRs, Allegations, sample analysis results, whistle-blower.
- Directed toward the identified or suspected issue.
- Inspection occurs promptly after triggering event (Public Risk)
- Inspections are not pre-announced
- Usually initiated by CDRH- drafts a “Directed Inspection Assignment”
- EIR and exhibits are reviewed by CDRH Staff
Contact Information

- DICO Director- CDR Cesar Perez- cesar.perez@fda.hhs.gov
- MDSAP Program- MDSAP@fda.hhs.gov
- Field Inspections (RIAT)- LCDR Neil Mafnas- neil.mafnas@fda.hhs.gov
Demystifying the Process of What Happens Before and After Your Inspection

Arduino Frankovic – OMDRHO Division 1 Director, Investigations Branch
Gina Brackett – OMDRHO Division 1 Director, Compliance Branch
Melissa Michurski - OMDRHO Division 2 Director, Compliance Branch
Work Planning Process Begins

- Annual Work Planning from March-September covering domestic and foreign firms
- Collaboration between CDRH and ORA
- Inspection coverage based on appropriated budget and resources available (FTE’s- Full time employees)
- CDRH provides a list of high risk firm’s whereas ORA is mandated to inspect 75% of the firm’s provided.
- The remaining 25% is determined by ORA
ORA’s Work Planning Criteria

- ORA references Compliance Program Guidance Manual 7382.845 Inspection of Medical Device Manufacturer in determining criteria

  - Pre-market and MDUFA inspections have priority due to strict time frames
  - Manufacturer of Class II and III devices never been inspected
  - Compliance Follow-Up/For Cause Inspections
  - Recall follow-up
  - High Risk devices
ORA’s Work Planning Criteria: High Risk Devices

- High Risk devices
  - Special/Directed Assignment from CDRH
  - Devices with higher frequency of recalls and MDR’s
  - Devices driven by software and those with rapidly evolving technological changes
  - New devices that have not been manufactured or distributed very long
ORA’s Work Planning Other Criteria

- Other criteria:
  - Signals received (complaints, news articles, internet, informants, etc.)
  - Electronic Product Radiation Control (EPRC)
  - DoD contracts-Source Inspections
  - Regulatory history of the firm
  - Industry type (manufacturer, specification developer, repacker/relabeler, sterilizer, etc.)
MDSAP Exceptions

• Routine surveillance inspections of firm’s participating in MDSAP program is removed from work plan with the following exceptions:

  ➢ For Cause Inspections
  - Recalls; Complaints; Adverse Reaction Reports; Result of sample analysis; Suspicion of Fraud; and Observations made during prior inspection.
  - CDRH or Division directed assignments

  ➢ Compliance Follow-up Inspections

  ➢ Pre-Market Approvals

  ➢ Electronic Product Radiation Control (EPRC)

  ➢ Combination products (may be subject to inspection under CFR 211 or CFR 606)
Pre-Inspection

• Preannouncement of routine surveillance inspections continues (the type of inspection to be conducted, expected duration, processes covered, etc.)

• Exceptions to the preannouncement include: For Cause Inspections, Compliance Follow-ups, complaint investigations

• In the event your firm is participating in MDSAP inform the Investigator at the time of the preannouncement.

• Inspections may include representatives from CDRH. Credentials appearance may differ from Investigator and CDRH representatives.
During an Inspection

- During the inspection Investigator updates Supervisor routinely.
- Throughout the inspection Investigator discusses any observations with the firm (at time observation is noted, end of each inspectional day, FDA 483 closeout).
- In the event Investigator observations appear significant discussion may involve the Supervisor, Director of Investigations, Director of Compliance/assigned Compliance Officer, or CDRH SME.
- Labeling and 510(k) issues usually do not appear on FDA 483 however upon consultation with Compliance and CDRH SME’s if a final determination is made (new 510(k), off label use, etc.) prior to conclusion of inspection these items may be included in final FDA 483.
Post-Inspection

• Once inspection is completed generally the Investigator has 30 business days to complete the Establishment Inspection Report (EIR).

• For Inspections that are determined to be Official Action Indicated (OAI) the Investigator has 10 business days to complete the EIR.

• Timeframes for writing up an EIR may vary due to the complexity of the inspections, products and processes covered, documentation and evidence collected.

• Every EIR is reviewed and endorsed by the Investigator’s immediate Supervisor.

• Inspections recommended as OAI are referred to Compliance Branch for final review and decision.
FMD 145’s

- FMD 145 letters and associated EIR’s for inspections where no significant observations were observed (NAI) and inspections where voluntary actions were observed (VAI) are handled by Investigations Branch
- Compliance Branch handles FMD 145’s for inspections referred to their branch.
Compliance’s Role After the Inspection Has Concluded
VAI Inspections

• Perform a substantive review of Firm’s VAI FDA-483 response

• Send an FDA Acknowledge Letter
Advisory Actions
Divisions Have Direct Reference Authority

• Warning Letters, Recidivist Warning Letters (QS violations only), Regulatory Meeting, Untitled Letters for Quality System regulation violations (21 CFR Part 820); certain MDR violations (21 CFR 803); and Correction and Removal violations (21 CFR 806) after Classification determined (Class I or II)
Advisory Actions
Divisions Have Direct Reference Authority

• Would request CDRH review if a Subject Matter Expert review is required (Technical Review)
Advisory Actions that Require CDRH Review

• All 21 U.S.C. 352(j) “dangerous to health” violations;
• Medical device reporting violations which cite failure to report malfunctions as defined in 21 CFR 803.3(n). Center medical and technical expertise is necessary for these evaluations;
• Restricted device violations;
• Radiation Control for Health and Safety Act violations - except for sunlamp products and x-ray assemblers;
• Violation of requirements for post market surveillance studies;
• Any violation of device tracking regulations other than failure of the firm to implement any form of a tracking system;
Advisory Actions that Require CDRH Review

- Failure to submit a premarket notification (510(k)) or premarket approval application (PMA);
- Failure to submit a 510(k) or a PMA supplement for a significant modification(s) and/or the addition of a new intended use(s) to a previously cleared or approved device;
- All violations arising from pre-approval PMA inspections including supplements to a previously approved PMA application;
- All labeling violations and advertising violations; and
- Computer application and software violations
- All violation of Unique Device Identification (UDI) requirements
Administrative and Judicial Actions

Reviewed By CDRH and Office of Chief Counsel
Warning Letter Issued

• Letter is issued

• Firm has 15 working days to submit a written response
  ▪ Response should describe systemic corrective actions for each warning letter item; include timeframes for completion; include evidence of the corrective action.

• Typically – a written update is provided monthly

• FDA provides written response
Regulatory Meeting

- Letter sent to firm requesting Regulatory Meeting
- Meeting Held – Usually at the District Office closest to the firm (CDRH participation, if they reviewed the recommendation)
- Firm submits written response after the meeting describing systemic corrective actions; include timeframes for completion; include evidence of the corrective action
- Typically – a written update is provided monthly
- FDA provides written response
Untitled Letter Issued

• Letter is issued
• Firm is requested to submit a written response within 30 working days
  • Response describes systemic corrective actions for each item; include timeframes for completion; include evidence of the corrective action.
• Typically – a monthly update response
• FDA provides written response
Compliance Follow-up Inspection

- Compliance Officer creates follow-up assignment
- Majority, if not all corrective actions, need to be completed and do not want to inspect until the corrective actions have been implemented. Need at least 2 to 3 months of data to review.
Completion of Follow-up inspection

The endorsed report comes to Compliance Branch for review

- If Investigation Branch recommends VAI/NAI – Send to Compliance Branch for review. After review, the Compliance Officer finalizes the “District Decision” and profiles; and sends the FMD-145 letter

- If Investigation Branch recommends OAI – Send to Compliance Branch for review for further regulatory action
Warning Letter Close-out Letter (WLCO Letter)

Only issued if all Warning Letter observations have been corrected.