FDA Up-Date

Michael D. O'Hara, Ph.D.
Deputy Division Director
Division of Radiological Health
Office of In Vitro Diagnostics and Radiological Health
Michael.ohara@fda.hhs.gov
301-796-0294

Outline

- The Division of Radiological Health
- Total Product Life Cycle
- Some aspects of FDA databases
- Medical device reporting
- Examples of our activities interrogating FDA databases

Reporting Structure of the Division of Radiological Health

Food and Drug Administration

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Center for Devices and Radiological Health

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Office of In Vitro Diagnostics and Radiological Health

Director – Alberto Guterrez, Ph.D.

Deputy Director for Premarket	Deputy Director for Postmarket	Deputy Director for Radiological Health	Director for Personalized Medicine
Donald St. Pierre	James Woods	Mary Pastel, Sc.D.	Elizabeth Mansfield, Ph.D.

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Division of Radiological Health

Division of Radiological Health

- Acting Director – Robert Ochs, Ph.D.
- Deputy Division Directors
- – Michael D. O'Hara, Ph.D.
  - – FDA representative on NRC Advisory Committee on the Medical Use of Isotopes (ACMUI)
- – CAPT. Sean Boyd
  - – Conference of Radiation Control Program Directors (CRCPD)

Division of Radiological Health

- Formed in 2012 from the "old" Radiological Health Group and the Division of Radiological Devices
- Multi-disciplinary team of medical and oncology physicists, physicians, engineers, radiation biologists, Industrial hygienists, laser physicists, technicians and a mathematician
- Composed of four branches
  - NMRT –William Jung, Ph.D.
  - MREP –CAPT Patrick Hintz (Acting)
  - MUIS –Jeffery Ballyns, Ph.D. (Acting)
  - DXRS –Thalia Mills, Ph.D.
- Have two post market team leads
  - Patrick Weixel
  - Charles Myers

Division of Radiological Health

- Total Product Life Cycle based division
  - Means that we approve/clear devices to enter the market, enforce electronic products regulations, investigate device failures once on the market, and regulate manufacturer compliance
  - Before TPLC different organizations handled premarket (Division of Radiological Devices), post market (Office of Statistics and Biometrics), Electronic Products (Radiological Health), Medical Device Compliance (Office of Compliance)
  - Information on medical device recalls and MDRs/AROs can be used to improve the questions asked to device sponsors before new devices are marketed

FDA Database Review

- DRH is now interrogating FDA databases
  - The databases are populated through the post market reporting program
  - MAUDE database (Manufacturer and User Facility Device Experience)
  - Recalls of Medical Devices Database
  - ○
- Want to use the information gleaned from all sources to improve the safety and effectiveness of radiation emitting medical devices

Medical Device Reporting Program

- A medical device is an item either used for diagnosis, treatment or prevention of disease, or intended to affect the body, that does not achieve its primary purpose through chemical action or metabolism within the body (Code 301 Section 201(h) of the FD&C Act.)
- Called MedWatch
- Required reports
  - Medical device industry and certain healthcare facilities
- Voluntary reports
  - Submitted by the public
- Both types of reports contain information that allows the FDA to monitor the safety of medical devices

Medical Device Post Market Reporting Program

- **MedWatch**
  Required reports (form 3500A)
  - Submitted by manufacturers, distributors, importers, and user facility personnel
  - Medical device industry and certain healthcare facilities
  - Reporting of Death, Serious injury and malfunctions

  Voluntary reports (form 3500)
  - Submitted by healthcare professionals, consumers and patients

- **MedSun**: Medical Product Safety Network
  Collaboration with the clinical community
  (over 350 healthcare facilities)
  Goal: identify, understand, and solve problems with the use of medical devices

How does the FDA Use Medical Device Reports

- Event reports are analyzed by FDA staff including health care clinicians, engineers and scientists
- Follow-up actions that the FDA may take
  - Request for additional information
  - Conduct an investigation at the manufacturer, importer or user facility
  - Contact the manufacturer about a recall
  - Issue a public health advisory/safety alert

Diagnostic X-ray Systems Branch (DXRS)

- Devices –conventional x-ray systems, CT, dental devices, fluoroscopy devices
- Members of this branch used accidental radiation reporting to realize that fluoroscopy foot switches were sticking
- DXRS and all of the branches have embraced TPLC and address postmarket device failures in subsequent premarket submissions

Mammography, Ultrasound and Imaging Software (MUIS)

- Devices – mammography, digital breast tomosynthesis, ultrasound, imaging software devices
- Developing methods to interrogate the MAUDE database for issues involving picture archiving and communication systems (PACS devices)
  - PACS devices are grouped in the LLZ product code
  - Very large database
  - Specifically looking for patient problems and medical device problems

MUIS MAUDE Database Interrogation Conclusions

- MDR reports received for product code LLZ < 50 per month
- 95% of the LLZ (PACS) reports are device malfunction reports
- 0.3% of the LLZ (PACS) events resulted in patient deaths or injuries that were attributed to the devices
- A software issue could affect or potentially affect a large number of devices/studies
- Typical LLZ (PACS) problem reported:
  - Incorrect display, delay in image transfer, issues in image storage/backup, data loss, wrong image measurement
  - User error

Distribution on all event types (PACS reports received by July 2014)

Event Type	# of events[1]	# of events attributable to the device[2]	# of events attributable to the device and resulted in adverse outcome in the patient[3]
Death	20	1	1
Injury	30	9	6
Malfunction	2513	2480	2
Other	80	46	1
No answer provided	15	5	0
Blank	7	6	0

1. https://api.fda.gov/device/event.json?search=date_received:[19950101+TO+20141231]+AND+device.device_report_product_code:LLZ&count=event_type.exact
2. https://api.fda.gov/device/event.json?search=date_received:[19950101+TO+20141231]+AND+device.device_report_product_code:LLZ+AND+product_problem_flag:Y&count=event_type.exact
3. https://api.fda.gov/device/event.json?search=date_received:[19950101+TO+20141231]+AND+device.device_report_product_code:LLZ+AND+product_problem_flag:Y+AND+adverse_event_flag:Y&count=event_type.exact

Summary of the deaths not attributable to the device

- Patient died prior to radiologist reading the study
- Patient died subsequent to the images/reports not available in PACS
- Patient died subsequent to the delay of study transmission due to downtime issue
- Radiologist did not realize that the image being viewed was a prior image
- Incorrect images were used for treatment due to study list being in US date/time format
- Hospital did not enter allergy info in the administrative messages in PACS and the patient was discharged and passed away
- Physician did not notice the exam had an exam note, which contained positive findings. Patient went untreated and later died.
- Patient died subsequent to the blacked out video image during the procedure (due to operator error)
- Technologist inadvertently marked a study as "reported" and the radiologist did not receive the study correctly marked for requiring a review until 3 days later. Patient died during this time period.
- Technician mistakenly labelled the wrong patient name on the cassette at the bedside and subsequently uploaded the same incorrect info to the PACS. The patient (whom the imaging study was not intended for) received an incorrect diagnosis. This resulted in a tube being placed down the patient's throat, which reportedly contributed to the patient's death.

Summary of the injuries attributable to the device

- Patients re-imaged (x-rayed) due to images not available on the server
- Loss of images due to drive failure on the server
- Images not accessible on the Medical Device Data System (MDDS) linked to the device
- Information parameters of radiation therapy replaced due to computer file corruption
- Failure in rendering relevant data series without a warning
- Nurse received a burn when plugging in the computer on wheels into the electrical socket
- Patient hospitalized due to wrong dictation reflected in the report (conflicting with 3rd party software)
- Surgery prolonged due to a forced log out from the imaging viewing software

Nuclear Medicine and Radiation Therapy (NMRT)

- Regulate devices like linear accelerators, proton accelerators, brachytherapy, treatment planning, Pet/SPEC devices, radioactive microspheres
- Regulate blood irradiators and security scanners
- Analyzing the device recall database
- Reviewing how we have cleared proton therapy devices in preparation for carbon ion therapy devices

NMRT Device Recall Database Analysis

- NMRT is starting to review the recalls data base and the MAUDE data base to use the information to focus regulatory attention on problematic devices
- Software failures makes up 76% of all radiation therapy device recalls.
- Radiation therapy software recall reports contain varying degrees of failure information

NMRT Device Recall Database Analysis - Methods

- Applying three levels of analysis of software recalls
  - Level 1 using only symptoms (indicators of defect or risk to safety) and triggers (stimuli associated with the defect or risk to safety) to identify and categorize general and specific recall reasons.
  - Level 2 analyzing defects using traditional root cause analysis
  - Level 3 focusing on the software development process

NMRT Device Recall Database Analysis -Results

- Results
  - 246 software-related recalls reviewed
    - 59% resulted in an incorrect dose
    - 25% resulted in an incorrect site
  - Typical radiation therapy workflows triggered 59% of the software-related recalls.
  - While 76% of recalls were software-related, root cause analysis rarely (11%) cited specific defects in the software development process as a contributing factor.
  - Most frequent specific reasons for software-related recalls
    - Errors in data input/output/display/storage (36%)
    - Errors in calculations (28%)
    - Data compatibility issues (17%)

NMRT Device Recall Database Analysis - Conclusion

- Specific defects in the software development process are rarely cited as a contributing factor to radiation therapy device recalls
- The relatively high frequency of calculation and data input/output errors suggest that defects in the software development process is a likely important contributing factor
- This type of data analysis may improve radiation therapy devices by improving software development and FDA oversight of device recalls

Magnetic Resonance and Electronic Products

- Regulate magnetic resonance devices, coils and accessories
- Regulate radiation emitting electronic products like laser pointers, laser light shows, microwave ovens, tanning booths, old style televisions

Analysis of Adverse Events for MRI Systems in the Past 15 years

- The goal is a better understanding of adverse events reported for MRI
- Interrogation of the MAUDE database from Jan 1999 to Jan 2014
- Product Codes LNH (Nuclear Magnetic Resonance systems, 892.1000) and MOS (coil Magnetic Resonance, 892.1000).

MRI Top 10 device problem codes

Rank	Device Problem Code	Count (% of returned events)
1	Unknown/no information available	286 (14.3%)
2	No Information	272 (13.6%)
3	Use of Device Issue	185 (9.2%)
4	Improper or incorrect procedure	165 (8.2%)
5	Device operates differently than expected	91 (4.5%)
6	Other	50 (2.5%)
7	Magnetic interference	46 (2.44%)
8	No known device problem	44 (2.2%)
9	Fire	30 (1.5%)
10	Heat	30 (1.5%)

17.4%

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MRI Top 10 patient problem codes

Rank	Device Problem Code	Count (% of returned events)
1	Second degree burn	265 (9.1%)
2	Blister	264 (8.5%)
3	Burn	243 (8.3%)
4	Burn, thermal	202 (6.9%)
5	Erythema	140 (4.8%)
6	Burning Sensation	138 (4.7%)
7	Additional non-surgical treatment	113 (3.9%)
8	Pain	102 (3.5%)
9	No consequence or impact to patient	98 (3.4%)
10	No known impact or consequence to patient	85 (2.9%)

42.3% are burn events

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MRI Manual review of Thermal Events

- Event text and mfr. narrative of 886 reports reviewed
- 8 burns were cryogen related
  - Injuries to both patients and field service engineers were involved
- 89 reports involved sedated or anesthetized patients
- 7 reports involved field service engineers
  - electrical burns and cryogen related

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MRI MAUDE Interrogation Summary

- This effort will be published in book chapter
- Overview of adverse events for MRI for the past 15 years
  - Thermal events most commonly reported
  - Expected events being reported
- Detailed analysis of thermal events
  - Breakdown by known causes
  - Review of mfrs. instruction on prevention

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Conclusions

- The structure of the Division of Radiological Health is now in a better position to understand the Total Product Life Cycle of Radiological Devices
- Interrogation of available databases will generate results that can be used to follow radiation emitting device failures in premarket
- DRH can use the results to influence device training
- Publication of these methods and results will further discussion with academia and the regulated industry

Thank You

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