



Postmarket Safety Surveillance: A Medical Device Perspective

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U.S. Department of Health and Human Services

Food and Drug Administration



■ ■ ■ Devices Differ from Drugs

■ Drugs

- Pure molecules
- Short half-life
- Systemic effects
- Drug quality problems
- Drug interactions
- Wrong drug/dose
- Patient interface
- Non-compliance

■ Devices

- Complex components
- Durable equipment
- Localized effects
- Malfunctions
- Device interactions
- Use error
- User interface
- Non-compliance

■ ■ ■ Devices Differ from Drugs

■ Drugs

- Long market life
- Clinically studied
- Biologic equivalence
- Toxicology
- Good Manufacturing Practices (cGMP)
- Phase IV studies
- NDC Codes

■ Devices

- Rapid product cycles
- Bench studied
- Engineering equivalence
- Biocompatibility
- Quality Systems (ISO 9000)
- Post-approval studies
- UDI Codes



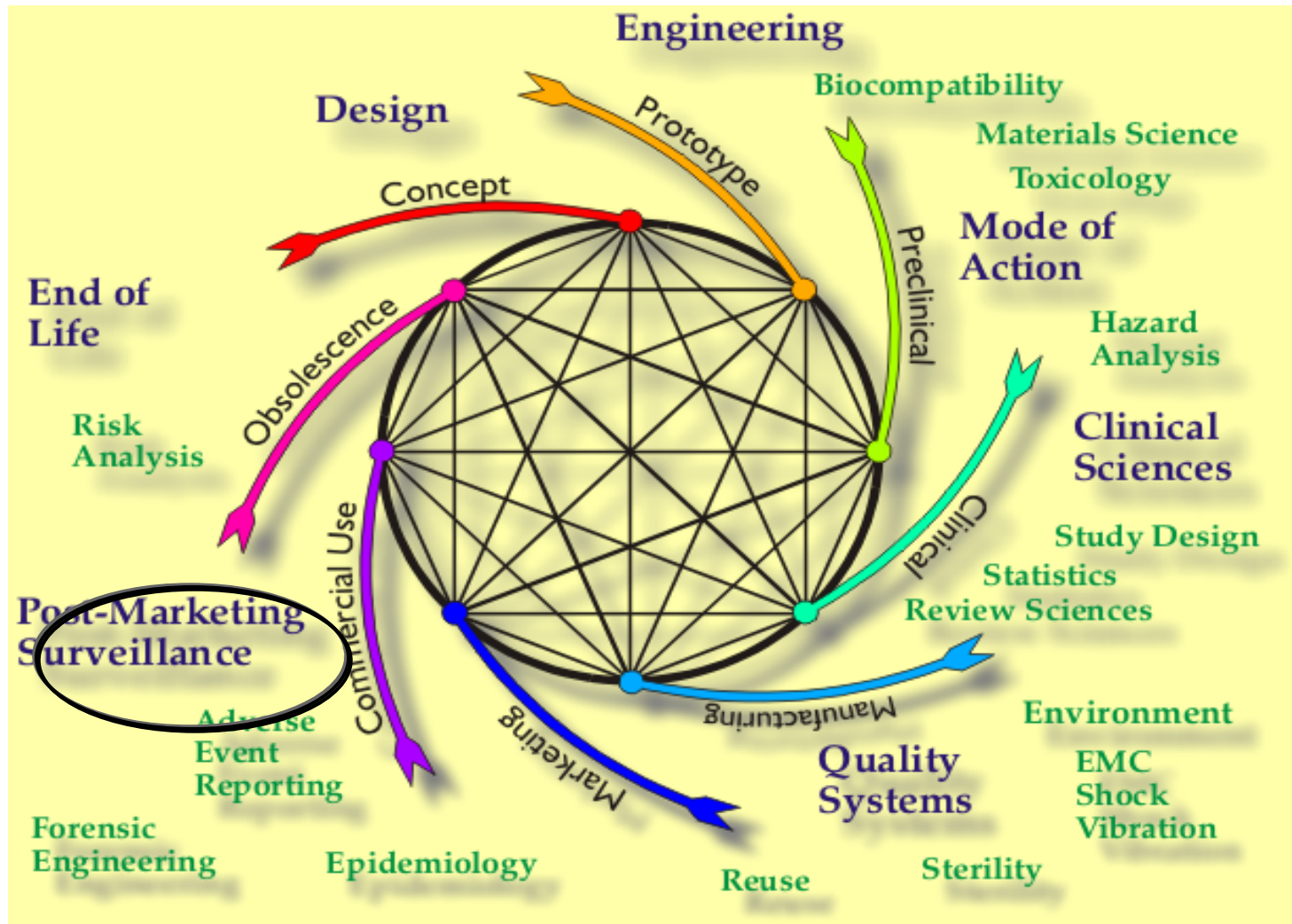
FDA's Balancing Act as a Public Health Agency

Getting safe and effective devices to market as quickly as possible...

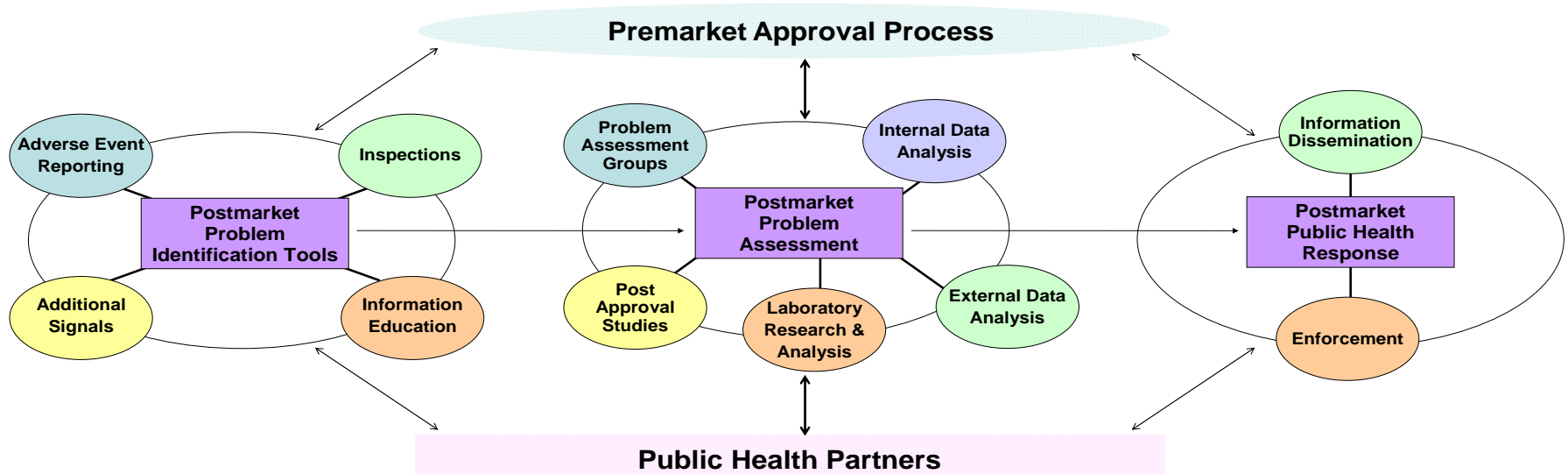


... while ensuring that devices currently on the market remain safe and effective.

Total Product Life Cycle



Components of CDRH's Postmarket Program



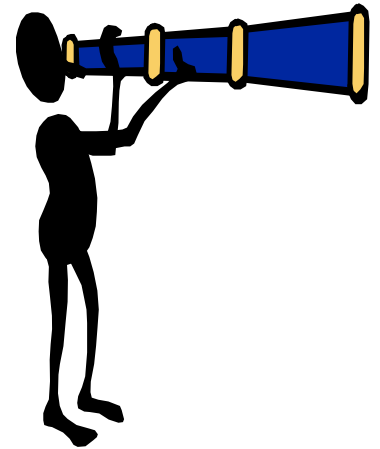
Postmarket Problem Identification

Postmarket Problem Assessment

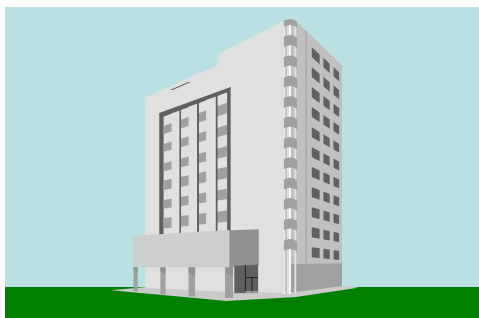
Postmarket Public Health Response

Surveillance Systems

- Medical Device Reporting (MDR)
 - Mandatory reports
- MedWatch
 - Voluntary reports
- Medical Product Safety Network
 - Hospital-based reports
- International vigilance
 - Regulatory authority reports



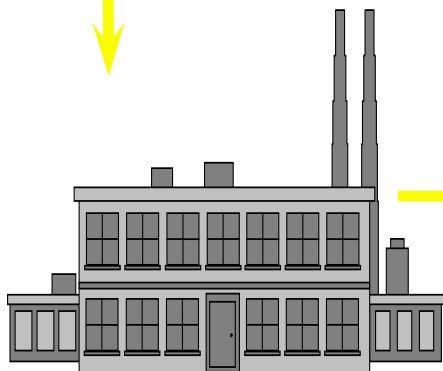
Mandatory Reporting



User Facility

Death
Serious Injury
(only if manufacturer unknown)
10 work days

Death and Serious Injury - **10 work days**

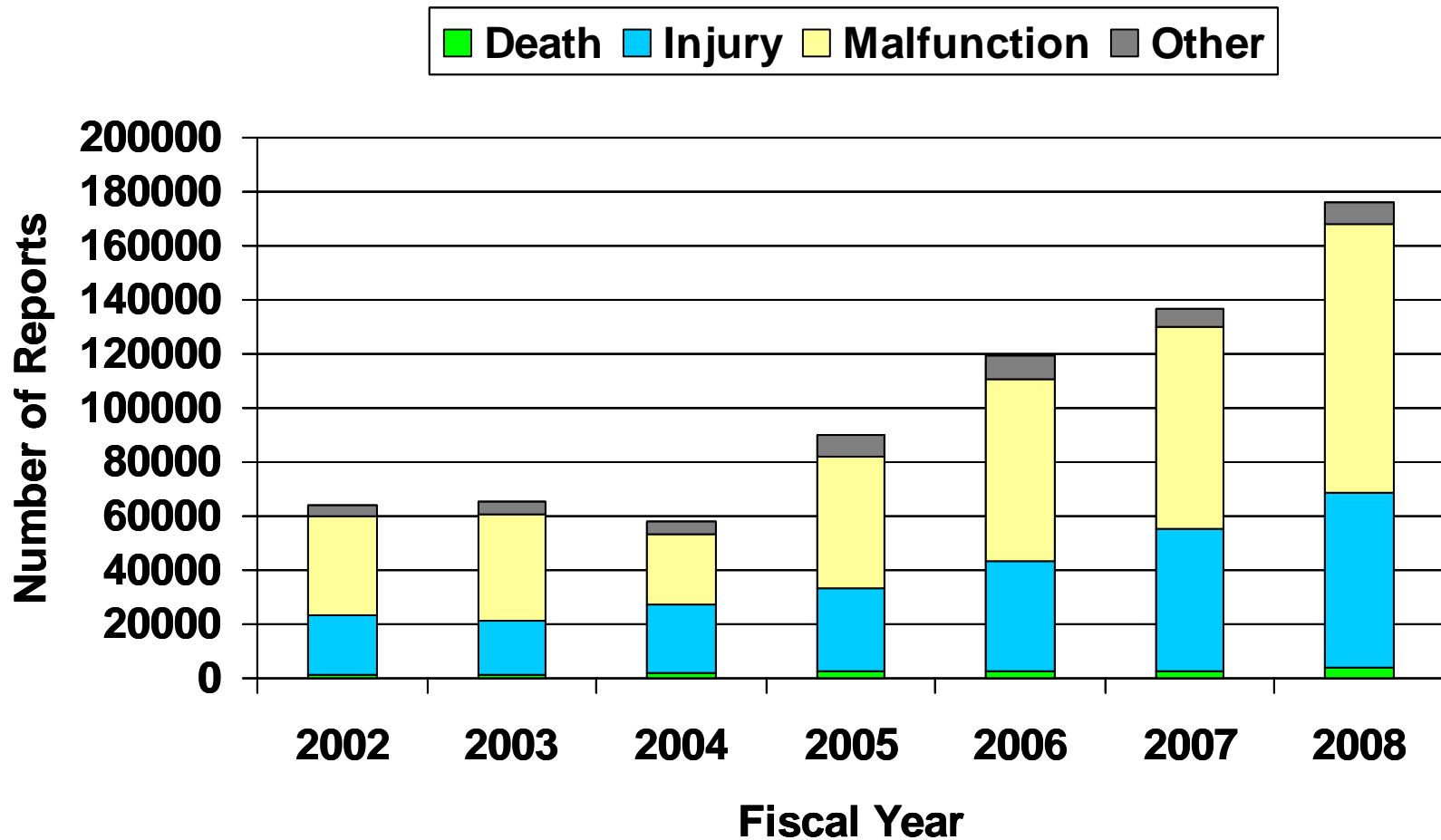


**Manufacturer
(and Importer)**

Death
Serious Injury
Malfunction
30 work days

FDA

Individual Reports of Adverse Events & Product Problems



MEDWATCH

FORM FDA 3500A (10/05)

Page ____ of ____

Mfr Report #
UF/Importer Report #
FDA Use Only

A. PATIENT INFORMATION			
1. Patient Identifier In confidence	2. Age at Time of Event: or _____ Date of Birth: _____	3. Sex <input type="checkbox"/> Female <input type="checkbox"/> Male	4. Weight ____ lbs or ____ kgs

B. ADVERSE EVENT OR PRODUCT PROBLEM	
1. <input type="checkbox"/> Adverse Event and/or <input type="checkbox"/> Product Problem (e.g., defects/malfunctions)	
2. Outcomes Attributed to Adverse Event (Check all that apply)	
<input type="checkbox"/> Death: _____ (mm/dd/yyyy)	<input type="checkbox"/> Disability or Permanent Damage
<input type="checkbox"/> Life-threatening	<input type="checkbox"/> Congenital Anomaly/Birth Defect
<input type="checkbox"/> Hospitalization - Initial or prolonged	<input type="checkbox"/> Other Serious (Important Medical Events)
<input type="checkbox"/> Required Intervention to Prevent Permanent Impairment/Damage (Devices)	
3. Date of Event (mm/dd/yyyy)	4. Date of This Report (mm/dd/yyyy)

5. Describe Event or Problem
6. Relevant Tests/Laboratory Data, Including Dates
7. Other Relevant History, Including Preexisting Medical Conditions (e.g., allergies, renal pregnancy, smoking and alcohol use, hepato/renal dysfunction, etc.)

C. SUSPECT PRODUCT(S)		
1. Name (Give labeled strength & multilabel)		
#1 _____		
#2 _____		
2. Dose, Frequency & Route Used		3. Therapy Dates (If unknown, give duration) from:to (or best estimate)
#1 _____		#1 _____
#2 _____		#2 _____
4. Diagnosis for Use (Indication)		5. Event Abated After Use Stopped or Dose Reduced?
#1 _____		
#2 _____		#1 <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
6. Lot #		#2 <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
#1 _____		8. Event Reappeared After Reintroduction?
#2 _____		
7. Exp. Date		#1 <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
#1 _____		#2 <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
#2 _____		
9. NDC# or Unique ID		
#1 _____		
#2 _____		
10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)		

D. SUSPECT MEDICAL DEVICE		
1. Brand Name		
2. Common Device Name		
3. Manufacturer Name, City and State		
4. Model #	Lot #	5. Operator of Device <input type="checkbox"/> Health Professional <input type="checkbox"/> Lay User/Patient <input type="checkbox"/> Other: _____
Catalog #	Expiration Date (mm/dd/yyyy)	
Serial #	Other #	
6. If Implanted, Give Date (mm/dd/yyyy)		7. If Explanted, Give Date (mm/dd/yyyy)
#1 _____		#1 _____
#2 _____		#2 _____
8. Is this a Single-use Device that was Reprocessed and Reused on a Patient? <input type="checkbox"/> Yes <input type="checkbox"/> No		
9. If Yes to Item No. 8, Enter Name and Address of Reprocessor		
10. Device Available for Evaluation? (Do not send to FDA) <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Returned to Manufacturer on: _____ (mm/dd/yyyy)		
11. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)		

E. INITIAL REPORTER			
1. Name and Address		Phone #	
2. Health Professional? <input type="checkbox"/> Yes <input type="checkbox"/> No		3. Occupation	
4. Initial Reporter Also Sent Report to FDA <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk.			

PLEASE TYPE OR USE BLACK INK

Submission of a report does not constitute an admission that medical personnel, user facility, importer, distributor, manufacturer or product caused or contributed to the event.

MEDWATCH

FORM FDA 3500A (10/05) (continued)

Page _____ of _____

FDA USE ONLY

F. FOR USE BY USER FACILITY/IMPORTER (Devices Only)		
1. Check One <input type="checkbox"/> User Facility <input type="checkbox"/> Importer		2. UF/Importer Report Number
3. User Facility or Importer Name/Address		
4. Contact Person		5. Phone Number
6. Date User Facility or Importer Became Aware of Event (mm/dd/yyyy)	7. Type of Report <input type="checkbox"/> Initial <input type="checkbox"/> Follow-up # _____	8. Date of This Report (mm/dd/yyyy)
9. Approximate Age of Device	10. Event Problem Codes (Refer to coding manual) Patient Code: [] - [] - [] Device Code: [] - [] - []	
11. Report Sent to FDA? <input type="checkbox"/> Yes (mm/dd/yyyy) <input type="checkbox"/> No	12. Location Where Event Occurred <input type="checkbox"/> Hospital <input type="checkbox"/> Outpatient Diagnostic Facility <input type="checkbox"/> Home <input type="checkbox"/> Ambulatory Surgical Facility <input type="checkbox"/> Nursing Home <input type="checkbox"/> Outpatient Treatment Facility <input type="checkbox"/> Other: _____ (Specify)	
13. Report Sent to Manufacturer? <input type="checkbox"/> Yes (mm/dd/yyyy) <input type="checkbox"/> No	14. Manufacturer Name/Address	

G. ALL MANUFACTURERS		
1. Contact Office - Name/Address (and Manufacturing Site for Devices)		2. Phone Number
4. Date Received by Manufacturer (mm/dd/yyyy)		3. Report Source (Check all that apply) <input type="checkbox"/> Foreign <input type="checkbox"/> Study <input type="checkbox"/> Literature <input type="checkbox"/> Consumer <input type="checkbox"/> Health Professional <input type="checkbox"/> User Facility <input type="checkbox"/> Company Representative <input type="checkbox"/> Distributor <input type="checkbox"/> Other: _____
5. If IND, Give Protocol #	5. (A)NDA # _____ IND # _____ STN # _____ PMA/510(k) # _____	
7. Type of Report (Check all that apply) <input type="checkbox"/> 5-day <input type="checkbox"/> 30-day <input type="checkbox"/> 7-day <input type="checkbox"/> Periodic <input type="checkbox"/> 10-day <input type="checkbox"/> Initial <input type="checkbox"/> 15-day <input type="checkbox"/> Follow-up # _____	Combination Product <input type="checkbox"/> Yes Pre-1938 <input type="checkbox"/> Yes OTC Product <input type="checkbox"/> Yes	
9. Manufacturer Report Number	8. Adverse Event Term(s)	

H. DEVICE MANUFACTURERS ONLY		
1. Type of Reportable Event <input type="checkbox"/> Death <input type="checkbox"/> Serious Injury <input type="checkbox"/> Malfunction <input type="checkbox"/> Other: _____		2. If Follow-up, What Type? <input type="checkbox"/> Correction <input type="checkbox"/> Additional Information <input type="checkbox"/> Response to FDA Request <input type="checkbox"/> Device Evaluation
3. Device Evaluated by Manufacturer? <input type="checkbox"/> Not Returned to Manufacturer <input type="checkbox"/> Yes <input type="checkbox"/> Evaluation Summary Attached <input type="checkbox"/> No (Attach page to explain why not) or provide code.		4. Device Manufacture Date (mm/dd/yyyy)
		5. Labeled for Single Use? <input type="checkbox"/> Yes <input type="checkbox"/> No
6. Evaluation Codes (Refer to coding manual) Method: [] - [] - [] - [] Results: [] - [] - [] - [] Conclusions: [] - [] - [] - []		
7. If Remedial Action Initiated, Check Type <input type="checkbox"/> Recall <input type="checkbox"/> Notification <input type="checkbox"/> Repair <input type="checkbox"/> Inspection <input type="checkbox"/> Replace <input type="checkbox"/> Patient Monitoring <input type="checkbox"/> Relabeling <input type="checkbox"/> Modification/Adjustment <input type="checkbox"/> Other: _____		8. Usage of Device <input type="checkbox"/> Initial Use of Device <input type="checkbox"/> Reuse <input type="checkbox"/> Unknown
9. If action reported to FDA under 21 USC 360(k), list correction/removal reporting number.		
10. <input type="checkbox"/> Additional Manufacturer Narrative		and / or 11. <input type="checkbox"/> Corrected Data

The public reporting burden for this collection of information has been estimated to average 66 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration - MedWatch
10203 New Hampshire Avenue
Building 22, Mail Stop 4447
Silver Spring, MD 20993-0002
Please DO NOT RETURN this form to this address.

OMB Statement:
"An agency may not conduct or sponsor and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."



Electromagnetic Compatibility Codes

Electromagnetic Compatibility Issue C63215; FDA 2927

Issue associated with the ability of a system to function in its electromagnetic environment without introducing intolerable disturbances to anything in its environment.

- **Electromagnetic Interference (EMI) C63214; FDA 1194**
Issue associated with a measure of electromagnetic radiation from equipment.
- **Electro-Static Discharge C63213; FDA 2149**
Issue associated with the discharge of electricity between two bodies previously electrically charged.
- **Radiofrequency Interference (RFI) C62855; FDA 2314**
Issue associated with the degradation of the reception of a wanted signal caused by RF disturbance.



Device Hazards

- Device failure
 - Sudden failure of ceramic femoral heads related to change in manufacturing process
- Device malfunction
 - Inappropriate shocks and death from ICD lead fractures
- Use error
 - Retained tissue in arthroscopic shaver handpieces secondary to human factors/design issues
- Interactions
 - CT scans and changes in pacemaker output pulse rate
 - MRIs and medicated patches resulting in skin burns



Device Hazards

- Environmental effects
 - Improper analysis of heart rhythms in AEDs secondary to high humidity
- Allergic reactions
 - Chlorhexidine-impregnated medical devices
- Toxic events
 - Corneal damage from heavy metals post sterilization of ophthalmic instruments
- Packaging defects
- Poor maintenance

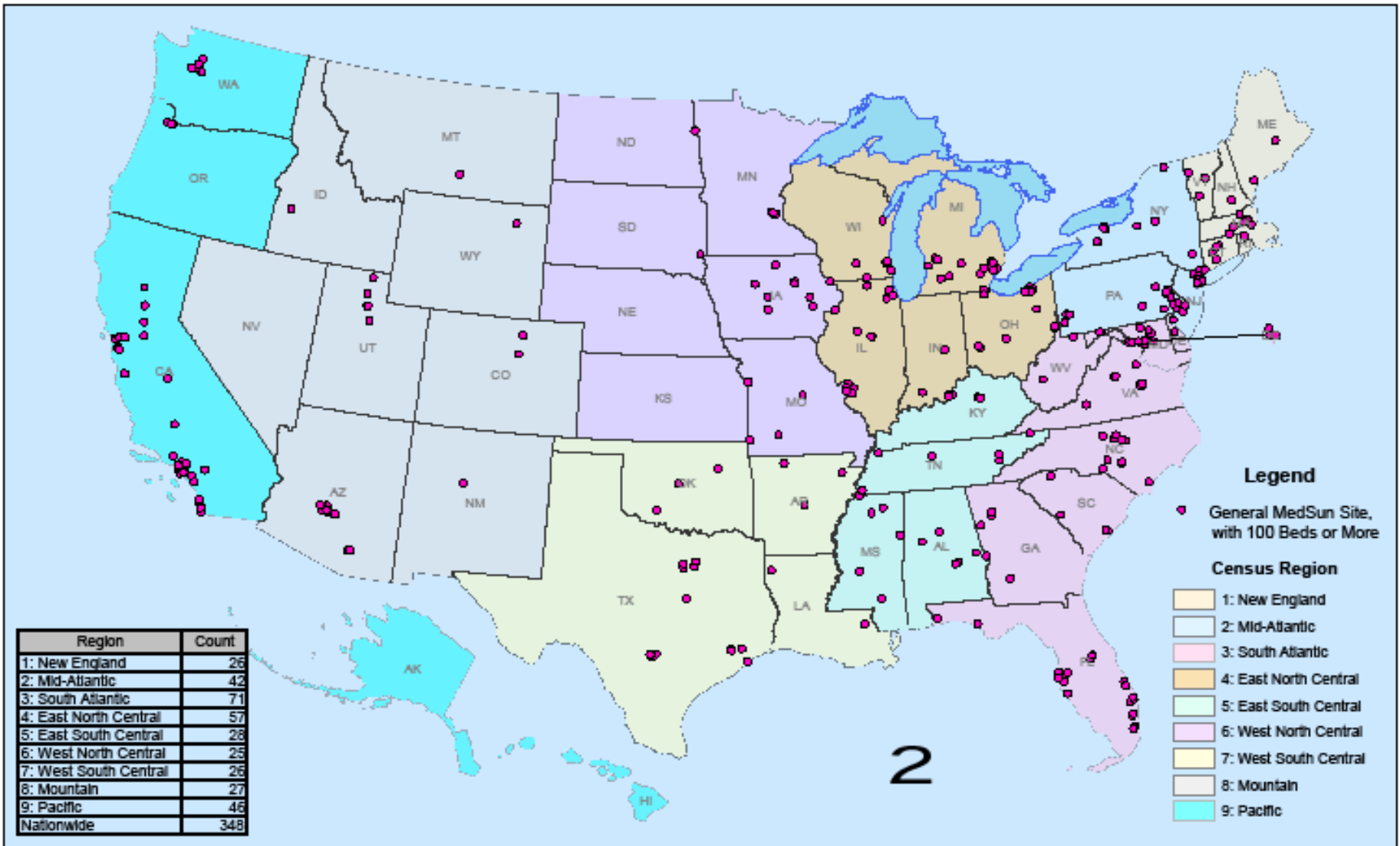
■■■ Electromagnetic Interference

A family brought their 87-year-old grandmother to live with them. She was on a ventilator and needed continuous monitoring. When her grandson used his cell phone in the room, the ventilator monitor screen went blank. He left the room to inform others. His mother entered the room and found the monitor to be working. The grandson later made another cell phone call and the monitor went blank again.

■ ■ ■ Medical Product Safety Network (MedSun)

- A national network of 350 user facilities
- Each facility has program liaisons; specifically trained to recognize and report
- Electronic reporting to reduce burden
- Robust program of feedback
- Connection to clinical community
- Emphasis on use issues, near misses

Sites in General MedSun with 100 Beds or More, September 29, 2009



2



Initiatives in 2-way Surveillance

- MedSun Tools
 - Targeted surveillance via surveys
 - Limited to 9 sites unless OMB-cleared
 - Networks: “real-time” data
 - *LabNet* - from hospital laboratories
 - *KidNet* - from pediatric/neonatal ICUs



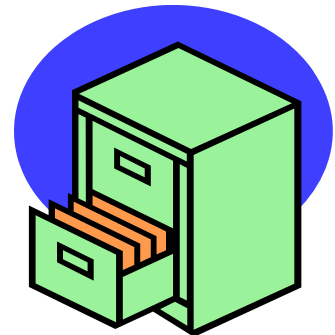


Electronic Failure in Neonatal ICU

- Several reports over span of a few months of GE DASH portable monitors going blank
- Follow-up with GE revealed an “inverter circuit board” was failing at higher than expected rate
- Inverter board provides high voltage to the display screen
- 3rd party vendor supplies component part
- GE worked with firm to determine that capacitor in inverter board was failing prematurely
- GE worked with supplier to improve design and extend life
- GE contacted consignees for replacement

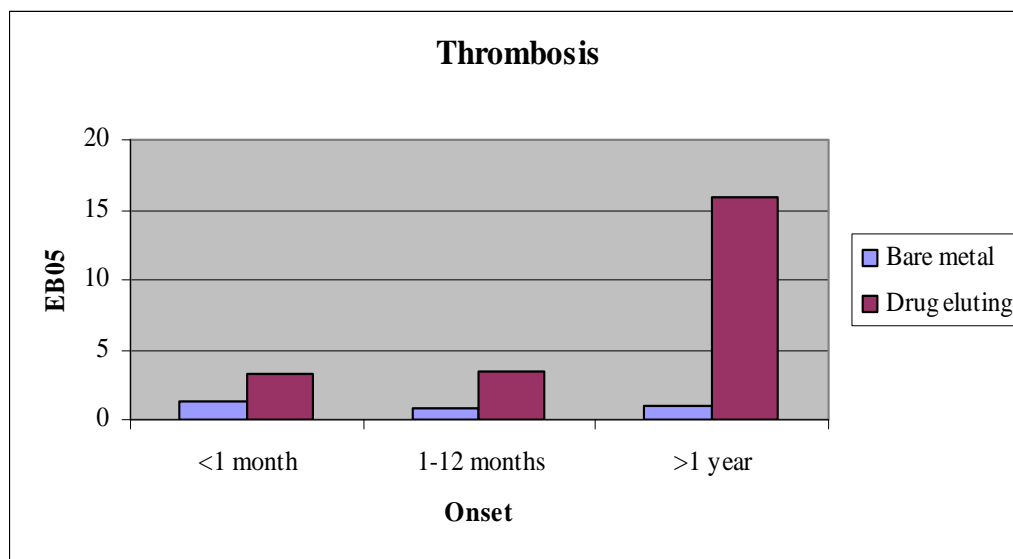
Enhanced Surveillance: Electronic Infrastructure

- Electronic Medical Device Reporting (eMDR)
 - Via agency-wide portal
 - Individual and pilot batch reporting
 - ~1/3 of reports come in electronically
 - Regulation under consideration



Enhanced Surveillance: Datamining

- Aid to finding device-event associations
- Web-based system using Bayesian algorithms
- System allows for tabular and graphical methods and drilldown to case details
- Data cleaning and application phase





Enhanced Surveillance: Device Nomenclature

- Develop unique device identification (UDI)
 - **Device Identifier:** [static] manufacturer, make, model
 - **Production Identifier:** [dynamic] if currently serialized – serial number; if currently identified at the lot, the lot number, and expiration date
- Three distinct steps
 - Develop standardized system for UDIs
 - Place UDI in human readable and/or autoID on a device, its label, or both
 - Create and maintain UDI database
- Regulation under consideration



Observational Study:

Post-approval Studies

- “Conditional” studies as a post-approval requirement for highest risk devices
- Studies used to address important, but not essential, questions of device safety and/or effectiveness
 - Performance: long-term, “real-world,” subgroup
 - Effectiveness of training programs
 - Outcomes of concern
 - Balance premarket burdens



Post-approval Studies (PAS)

- “Phase IV” studies: ~ 15 orders per year
- About 170 ongoing studies
- Various methods used
 - Active surveillance to de novo cohorts
 - Use of concurrent or historical controls
- Leverage existing infrastructure
 - Use of registries
 - Use of trials



Post-approval Studies (PAS)

- Medtronic Revo MRI Sure-Scan Pacing System
- Proposed patient enrollment when they are indicated for a MRI scan
- A design which tests whether the MRI-related complication rate will be less than 2% (one-sided confidence interval upper bound)
- Also will characterize the cumulative change in pacing capture thresholds for subjects with multiple (2 or more) MRI scans.

■■■ Postmarket “Surveillance”:

(Section 522 of F, D & C Act)

- Studies ordered on class II/III devices
- FDA may require Section 522 for...
 - failure...reasonably likely to have serious adverse health consequences OR
 - expected to have significant use in pediatric populations OR
 - implanted > 1 year OR
 - life-supporting/life-sustaining used outside device user facility



“Surveillance” Approaches

- Detailed review of complaint history
- Review of the literature
- Non-clinical testing of device
- Use of secondary data sources
- Telephone or mail follow-up of patients
- Use of product registries
- Observational studies
- Randomized trials



Sentinel Initiative



- An effort to develop a national, integrated infrastructure of electronic healthcare data systems for medical product safety surveillance
 - Will augment, not replace, existing functionality
- Putting observational data to use, from active surveillance to more formal comparative safety studies
- The proposed model is based on distributed data systems (i.e., the data sources remain at remote locations and are maintained by owners)
 - Convey query results according to strict privacy and security safeguards
 - System will enable FDA to partner with existing data owners

Sentinel Initiative



U.S. Department of Health & Human Services

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FDA U.S. Food and Drug Administration

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Safety

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Sentinel Initiative - Transforming How We Monitor Product Safety

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FDA's Sentinel Initiative

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A national electronic system that will transform FDA's ability to track the safety of drugs, biologics, medical devices--and ultimately all FDA-regulated products once they reach the market--is now on the horizon. Launched in May 2008 by FDA, the Sentinel Initiative aims to develop and implement a proactive system that will complement existing systems that the Agency has in place to track reports of adverse events linked to the use of its regulated products.

Monitoring the safety of its regulated products is a major part of FDA's mission to protect public health. The Sentinel System would enable FDA to actively query diverse automated healthcare data holders, like electronic health record

Join the Discussion

- [FDA's Sentinel Initiative - Discussion Room](#)

Contact Us

- 301-827-1512
- 301-443-9718 Fax
- [SentinelInitiative](#)
FDA's Sentinel Initiative



www.fda.gov/Safety/FDAsSentinelInitiative/default.htm



It's Not Only FDA



The NEW ENGLAND JOURNAL of MEDICINE

Perspective
AUGUST 13, 2009

The New Sentinel Network — Improving the Evidence of Medical-Product Safety

Richard Platt, M.D., M.Sc., Marcus Wilson, Pharm.D., K. Arnold Chan, M.D., Sc.D.,
Joshua S. Benner, Pharm.D., Sc.D., Janet Marchibroda, M.B.A., and Mark McClellan, M.D., Ph.D.

In 2007, Congress directed the Food and Drug Administration (FDA) to create a new post-marketing surveillance system that will, by 2012

insurers. Medicare and Medicaid databases of prescriptions and other information on the use of

■ ■ ■ Automated Active Surveillance*

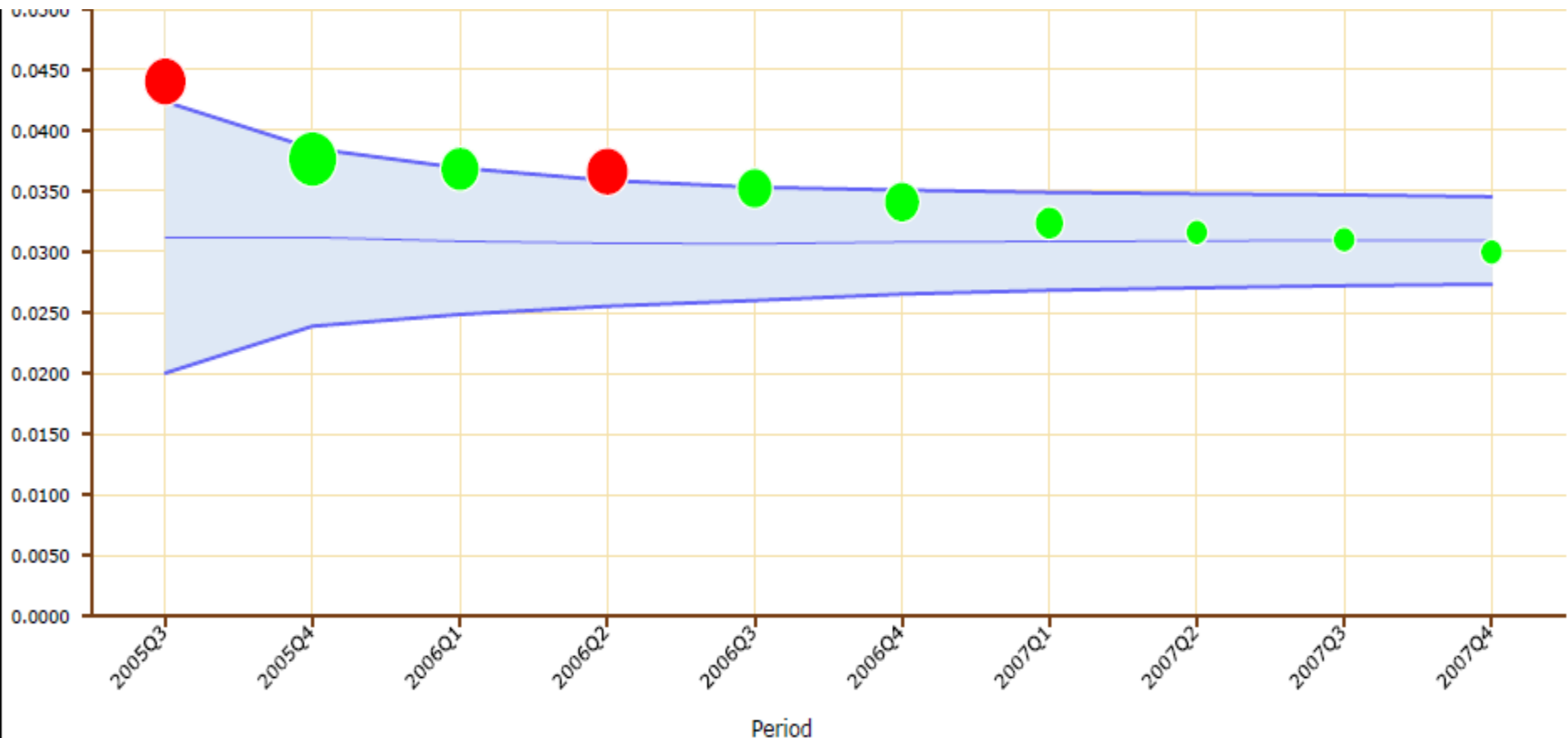
- Active surveillance in a network of hospitals
- Based on mandated percutaneous coronary intervention (PCI) data
 - Coronary stents, embolic protection, hemostasis devices
- Common data model with centralized analytics
- Potential to link to other data (e.g., vital statistics, hospital discharge data)

*Resnic FS. DELTA © Copyright Brigham and Women's Hospital 2005

■■■ Medical Device Surveillance*

Risk-adjusted vascular complication rates following the introduction of new vascular closure device. May indicate increased complications early in experience with newly introduced device (may represent the learning curve effect).

*Copyright Brigham and Women's Hospital 2005©



■ ■ ■ Thanks for Your Attention!



For further information: thomas.gross@fda.hhs.gov