

Postmarket Regulatory Tools Supporting Use of Patient- Generated Health Data

Thomas Gross, MD, MPH

Director

Office of Surveillance and Biometrics

Center for Devices and Radiological Health

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Various Tools for Various Purposes

- **Passive and Enhanced Surveillance**
 - Ongoing systems of reporting of device-related adverse events and product problems (so called Medical Device Reports or MDRs)
- **Mandated Postmarket Studies**
 - Formal protocol-driven assessments of remaining questions about a device's safety and/or effectiveness
- **Compliance Oversight**
 - Various means to assure compliance with FDA laws and regulatory requirements
- **Signal Management**
 - Processes to further evaluate and communicate potential safety signals

Sources of MDR Reporting to FDA



Patients Are a Key Component to Initiating Process

Manufacturer

(and importer)

- Mandatory, Passive Surveillance
- Deaths, Serious Injuries, Malfunctions
- 98% of reports

User Facility

- Mandatory, Passive Surveillance
- Deaths, Serious Injuries
- <1%

Voluntary

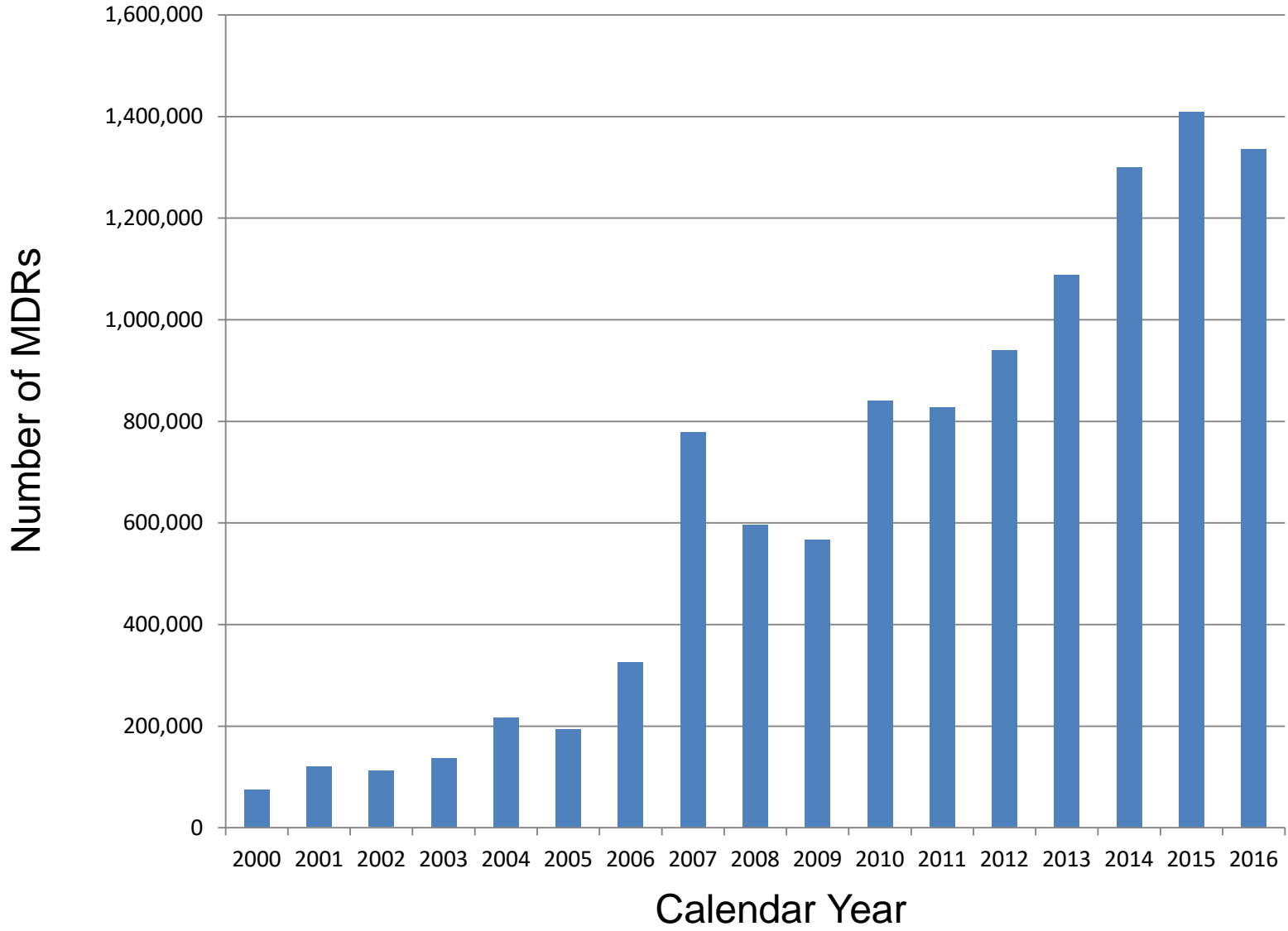
- Patients/Consumers, Healthcare Providers
- All types, Passive Surveillance
- <1%

MedSun

(Medical Product Safety Network)

- Mandatory and Voluntary (near-misses)
- Enhanced Surveillance; Patient Interactions
- <1%

Increases in Medical Device Reports



Value of MDRs



- **Qualitative profile of adverse events and product problems**
 - Reflects device use in real world; insight into subgroups
- **Monitor device performance**
 - Short- to long-term use, failure modes
- **Signal detection**
 - Rare or unexpected events
 - Change in severity of expected events
 - Use error/human factors issues

Limitations

- **Underreporting**
 - Cannot establish rates
- **Insufficient, inadequate information**
 - Not obtainable; device not available
- **Difficult to establish causality**



Mandated Postmarket Studies

Post-approval Studies (PAS)

- Class III devices
- As condition of approval
- Non-clinical or clinical
 - Longer-term follow-up
 - Remaining benefit/risk issues

Section 522 Studies

- Class II or III
- For cause, time of clearance or approval
- Non-clinical or clinical
 - Failure and serious health consequences
 - Significant use in pediatric population
 - Implanted for more than one year
 - Life-sustaining/life-supporting used outside of user facility
- Protocol-driven with analysis plan
- Newly created study (hospital/clinic, registry-based), existing cohort follow-up, active surveillance
 - IRB approval and FDA oversight
- Numbers: ~300 active PAS and ~35 active Section 522 studies (Examples: remote monitoring and patient reported outcomes)

Public Transparency



U.S. Department of Health & Human Services

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Post-Approval Studies (PAS)

FDA Home | Medical Devices | Databases

The FDA has the authority to require sponsors to perform a post-approval study (or studies) at the time of approval of a premarket approval (PMA), humanitarian device exemption (HDE), or product development protocol (PDP) application. Post-approval studies can provide patients, health care professionals, the device industry, and other stakeholders information on the continued safety and effectiveness (or continued probable benefit, in the case of an HDE) of approved medical devices. This database allows you to search Post-Approval Study information by applicant or device information.

[Learn more...](#)

Search

To sort by data column: 256 orders

Active Orders

Application Number	Application	Device Name	Medical Specialty	Date PMA Approved	Study Name	Date Original Protocol Accepted	Study Status
↑ Application ↓	↑ Application ↓	↑ ↓	↑ ↓	↑ ↓			

Suggest Enhancement / Report Issue |

General	
Study Status	Progress Adequate
Application Number	P030006 / PAS001
Data Current Protocol Accepted	03/11/2005
Study Name	OSB Lead Prolieve PAS
General Study Protocol Parameters	
Study Design	Prospective Cohort Study
Data Source	New Data Collection
Comparison Group	No Control
Analysis Type	Descriptive
Study Population	Adult: >21
Detailed Study Protocol Parameters	
Study Design Description	This is an open label non-randomized prospective study. The primary objective of the study is to provide descriptive data on the long-term safety and effectiveness of Prolieve for Benign Prostatic Hyperplasia. A secondary objective is to assess safety and effectiveness of re-treatment and to assess the proportion of patients electing re-treatment with Prolieve compared to alternative therapy (other localized therapy, surgery or drug therapy).
Study Population Description	Study population is as per device indication. Adult men men with prostate volume of 20 to 80 grams and in whom drug therapy (Proscar) is typically indicated.
Sample Size	The protocol proposes to enroll 250 new subjects in up to 30 study sites in the United States. The protocol states this will ensure at least 100 subjects will be followed for 5 years. In addition to newly enrolled subjects, the sponsor planned to encourage Pivotal Study participants and Continued Access Study participants to transfer to the postmarket study for the completion of 5 years of follow-up.
Data Collection	Efficacy is evaluated using the following: Time to re-treatment, American Urological Association (AUA) Symptom Index, (Classifies the severity of subject symptoms related to urinary difficulties based on seven questions that form a total score. The score can range from 0-35). Pain/Discomfort, Sexual Function, Impact of Lower Urinary Tract Symptoms (LUTS) on quality of life (QOL), (Six questions related to urinary problems and how they interfere with daily living. The score ranges from 5-24). Quality of Life Questionnaire, (Six questions related to the subjects feelings about his urinary condition, perception of urinary difficulties, sexual function, activities of daily living, general well-being and social activities. The seven-point scale ranges from delighted to terrible and scores can range from 6-42). Bival Symptom Inventory (BSI), (Seven questions related to the interference of the subject's urinary problems with common activities, scores range from 7-35). BPH Impact Index (BII), (Four questions related to concern about urinary problems and the amount of physical discomfort experienced. Scores can range from 4-17. Safety is measured by: Use of pain medication pre-treatment and during treatment, Pain associated with treatment, Local and systemic symptoms during Prolieve treatment.
Follow-up Visits and Length of Follow-up	Catheterizations associated Hospitalizations, and MDR Study participants are to be

OSB Lead-Prolieve PAS Schedule

Report Schedule	Report Date Due	FDA Receipt Date	Applicant's Reporting Status
2 year report	02/18/2006	03/20/2006	Overdue/Received
3 year report	02/18/2007	07/02/2007	Overdue/Received
4 year report	02/18/2008	02/19/2008	On Time
5 year report	02/17/2009	02/18/2009	Overdue/Received
6 year report	02/19/2010	02/19/2010	On Time
7 year report	02/22/2011	02/22/2011	On Time
72 month report	02/18/2013	12/21/2012	On Time
7 year report (83 month)	04/18/2014	04/21/2014	Overdue/Received
8 year report	05/18/2015	05/14/2015	On Time
9 year report	06/18/2016	06/21/2016	Overdue/Received
10 year report/final report	06/02/2017	06/15/2017	Overdue/Received

- Detailed Information Available to the Public on the Webpage
 - Protocol Basics and Study Status
 - Reporting Schedule and Report Status
- Similar for both PAS and Section 522 Studies

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm



Value of Mandated Studies

- Addresses important benefit/risk issues when data are not available elsewhere
- Leads to regulatory actions: support for breakthrough devices, labeling changes, safety communications
- Increasingly aligned with national initiatives [e.g., NEST, registry development]

Limitations

- Resource-intensive to develop and approve study protocols
- Study results may take time
 - Enrollment may be challenging
 - Assuring follow-up may be challenging
- Device modifications may occur while studies are conducted

Compliance Oversight

- Complaints and allegations (~1250/year)
 - Notifications of potential violations or risks (from variety of sources including patients, caregivers)
 - Many different types: misleading advertising, quality system problems, illegal marketing, health fraud, MDRs
- Recalls (~1150/year)
 - Removal or correction of violative product that may involve repair, modification, relabeling, destruction, patient monitoring
 - Involve FDA assessment of violation, risk, recall strategy and notification, classification

Signal Management: What is it?

- A set of activities to determine whether a safety signal identified for a marketed device or group of devices represents a risk which may warrant further Center:
 - assessment, communication, and/or
 - other risk mitigation actions and the actions which are undertaken accordingly.
- Potential signals may come from or involve: MDRs, complaints, peer-reviewed literature (including patient case series), mandated studies, premarket
- An avenue for sharing knowledge and information about the performance of the products we regulate
 - Feedback to improve premarket review
 - Identification of science research needs

Emerging Signals Notifications

Contains Nonbinding Recommendations

Public Notification of Emerging Postmarket Medical Device Signals ("Emerging Signals")

Guidance for Industry and Food and Drug Administration Staff

Document issued on December 14, 2016.

The draft of this document was issued on December 31, 2015.

For questions about this document, contact the Office of Communication and Education, 301-796-5660 or the Office of Surveillance and Biometrics, 301-796-6006.

Potential Outcomes*



- **Public Communications/Outreach**
- **Labeling Changes**
- Compliance Actions (recalls, letters, inspections)
- (Premarket) Guidance Documents
- Product Redesign and/or Premarket Submissions
- Standards Work
- Research Projects
- Section 522 Studies
- Increase Risk Classification
- Advisory Committee Meetings
- No Action Required

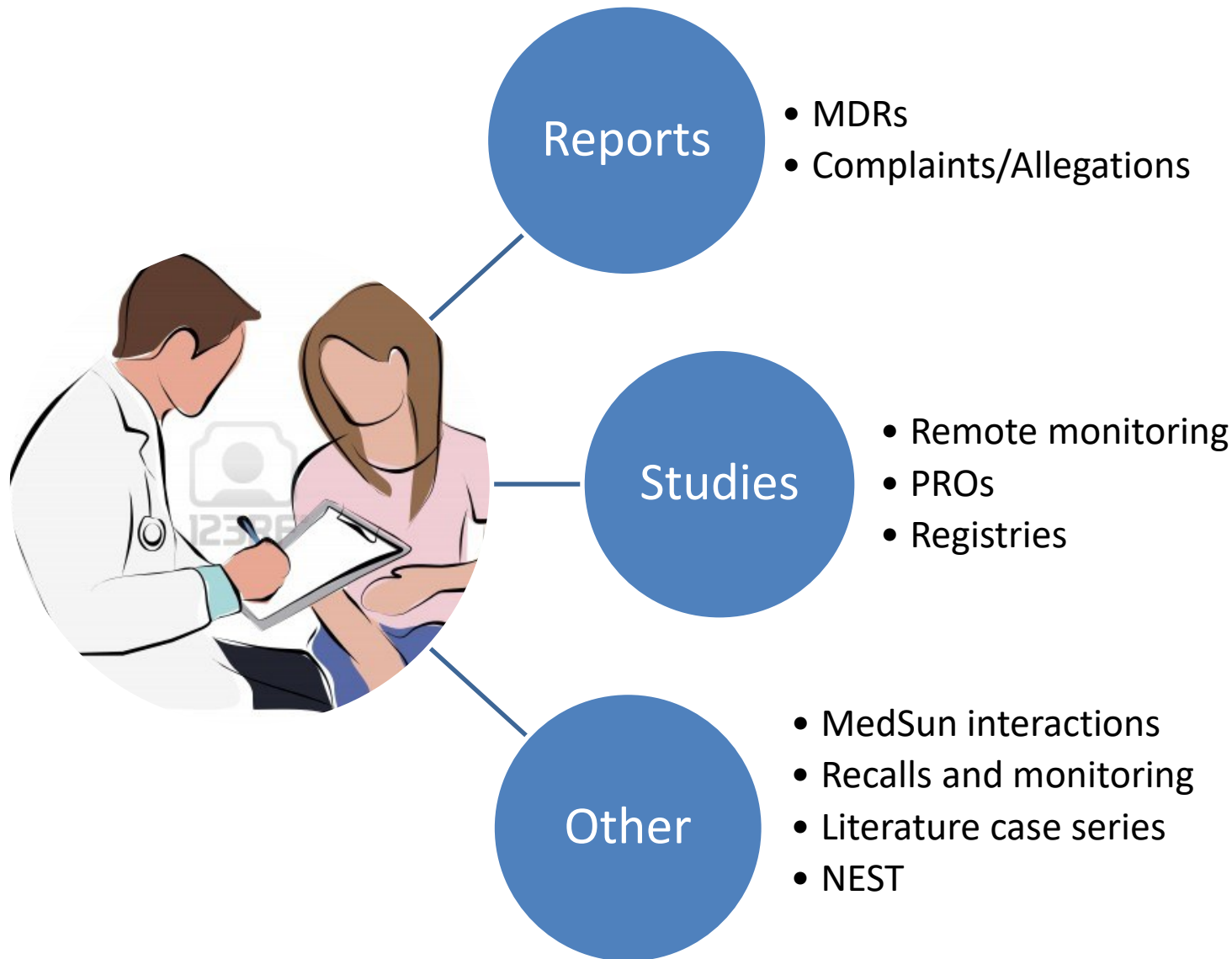
* Out of ~170 signals since 2012

National Evaluation System for health Technology (NEST)



- FDA is member of Governing Committee and works closely with the Coordinating Center
- Figures prominently in FDA's Medical Device Safety Action Plan
- Will help establish a robust medical device patient safety net in the U.S.
 - To create capabilities to perform active surveillance
 - To perform timely, efficient postmarket safety studies

Patients are a Key Component





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