Exploration of Real World Data for Drug Safety Monitoring

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FDA CDER OSE

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Outline

- Postapproval drug safety surveillance
- Current sources and applications of real world data for drug safety surveillance
- Exploration of novel real world data sources

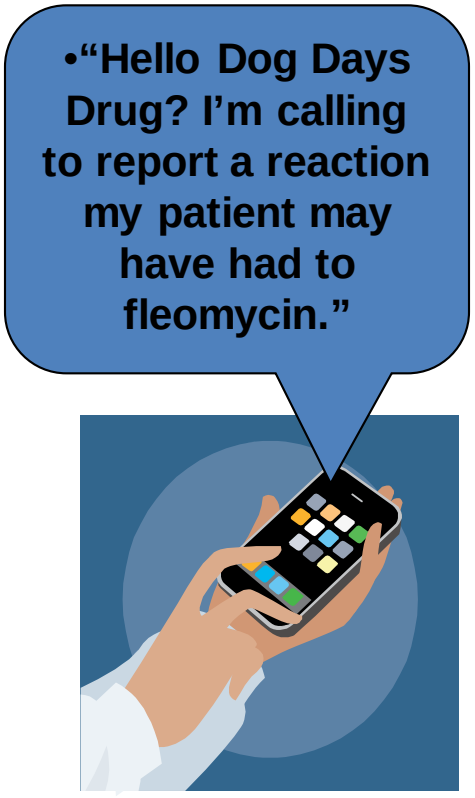
Postapproval Drug Safety Surveillance

- Preapproval clinical trials are conducted to provide substantial evidence that a drug product will be effective and safe.
- Postapproval phase is part of drug product life cycle continuum.
- Longer or chronic use, medically heterogeneous patients, and larger numbers of patients.
  - Rare adverse events not seen in clinical trials
  - Drug-drug or drug-food interactions
  - Increased severity of adverse events seen in clinical trials
  - Patient intolerance of less serious adverse events
  - Errors occurring with use of the product

Existing Real World Data Used for Drug Safety Monitoring

- Adverse Event Reporting Systems
  - FDA Adverse Event Reporting System (FAERS) Database
  - MedWatch reporting system
- Drug utilization data
  - Wholesale sales to retail, hospital, clinic pharmacies
  - Dispensed prescriptions and drug products
- Healthcare insurance claims and billing data
  - FDA Sentinel System
- Paper and electronic health records
- Registries for products and diseases

The Life Cycle of a FAERS Report
From Patient to Safety Signal



•Image: National Institutes of Health

U.S. Department of Health and Human Services

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

For VOLUNTARY reporting of adverse events, product problems and product use errors

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Form Approved: OMB No. 0910-0291, Expires: 12/31/2011
See OMB statement on reverse.

FDA USE ONLY
Triage unit sequence #

PLEASE TYPE OR USE BLACK INK

A. PATIENT INFORMATION

1. Patient Identifier	2. Age at Time of Event or Date of Birth:	3. Sex	4. Weight
SAM In confidence	12/11/46	☑ Female ☐ Male	145 lb or 65.9 kg

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR

Check all that apply:

1. ☑ **Adverse Event** ☐ **Product Problem** *(e.g., defects/malfunctions)*
☐ **Product Use Error** ☐ **Problem with Different Manufacturer of Same Medicine**

2. **Outcomes Attributed to Adverse Event** *(Check all that apply)*
☐ Death: _____ *(mm/dd/yyyy)*
☐ Disability or Permanent Damage
☐ Life-threatening
☐ Congenital Anomaly/Birth Defect
☑ Hospitalization - initial or prolonged
☐ Other Serious (Important Medical Events)
☐ Required Intervention to Prevent Permanent Impairment/Damage (Devices)

3. Date of Event *(mm/dd/yyyy)*	4. Date of this Report *(mm/dd/yyyy)*
10/10/2009	10/11/2009

5. **Describe Event, Problem or Product Use Error**
Patient developed toxic epidermal necrolysis after taking fleomycin for sinus infection. Required hospitalization. Hospital discharge summary and relevant laboratory data attached. Patient recovered.

6. **Relevant Tests/Laboratory Data, Including Dates**
See attached records

7. **Other Relevant History, Including Preexisting Medical Conditions** *(e.g., allergies, race, pregnancy, smoking and alcohol use, liver/kidney problems, etc.)*
Nonsmoker.
History of atopic dermatitis at age 25.
No other medical conditions.

C. PRODUCT AVAILABILITY

Product Available for Evaluation? *(Do not send product to FDA)*
☐ Yes ☐ No ☐ Returned to Manufacturer on: _____ *(mm/dd/yyyy)*

D. SUSPECT PRODUCT(S)

1. **Name, Strength, Manufacturer** *(from product label)*
#1 Name: Fleomycin
Strength: 200mg
Manufacturer: Dog Days Pharmaceuticals

#2 Name:
Strength:
Manufacturer:

2. Dose or Amount	Frequency	Route
#1 200mg	twice a day	oral
#2		

3. **Dates of Use** *(If unknown, give duration) from/to (or best estimate)*
#1 10/03/2009 – 10/09/2009
#2

4. **Diagnosis or Reason for Use** *(Indication)*
#1 Sinus infection
#2

6. Lot #	7. Expiration Date
#1	#1
#2	#2

5. **Event Abated After Use Stopped or Dose Reduced?**
#1 ☑ Yes ☐ No ☐ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Does Apply

8. **Event Reappeared After Reintroduction?**
#1 ☐ Yes ☐ No ☑ D
#2 ☐ Yes ☐ No ☐

9. **NDC # or Unique ID**

E. SUSPECT MEDICAL DEVICE

1. **Brand Name**
2. **Common Device Name**
3. **Manufacturer Name, City and State**

4. Model #	Lot #	5. Operator of Device
Catalog #	Expiration Date *(mm/dd/yyyy)*	☐ Health Professional ☐ Lay User/Patient
Serial #	Other #	☐ Other:

6. **If Implanted, Give Date** *(mm/dd/yyyy)* 7. **If Explanted, Give Date** *(mm/dd/yyyy)*

8. **Is this a Single-use Device that was Reprocessed and Reused on a Patient?**
☐ Yes ☐ No

9. **If Yes to Item No. 8, Enter Name and Address of Reprocessor**

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

Product names and therapy dates *(exclude treatment of event)*
No other medical products

G. REPORTER *(See confidentiality section on back)*

1. **Name and Address**
Name: Dr. Smith
Address: 5454 Skyline Drive
City: Phoenix State: AZ ZIP: 00023

Phone #	E-mail
301-555-1212	smith@gmail.com

2. Health Professional?	3. Occupation	4. Also Reported to:
☑ Yes ☐ No	Physician	☑ Manufacturer ☐ User Facility ☐ Distributor/Importer

5. **If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box:** ☐

FORM FDA 3500 (1/09) Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

- **FAERS**
- **Database**
- **@FDA**

•This is a pretty clear case of an adverse reaction to this new drug fleomycin..This looks like a potential safety signal.

FDA U.S. Food and Drug Administration

FDA MedWatch Reporting Website

Source: https://www.fda.gov/Safety/MedWatch/default.htm

What to Report to FDA MedWatch

Use the MedWatch form to report adverse events that you observe or suspect for human medical products, including serious drug side effects, medication errors/product use errors, product quality problems, and therapeutic failures for:

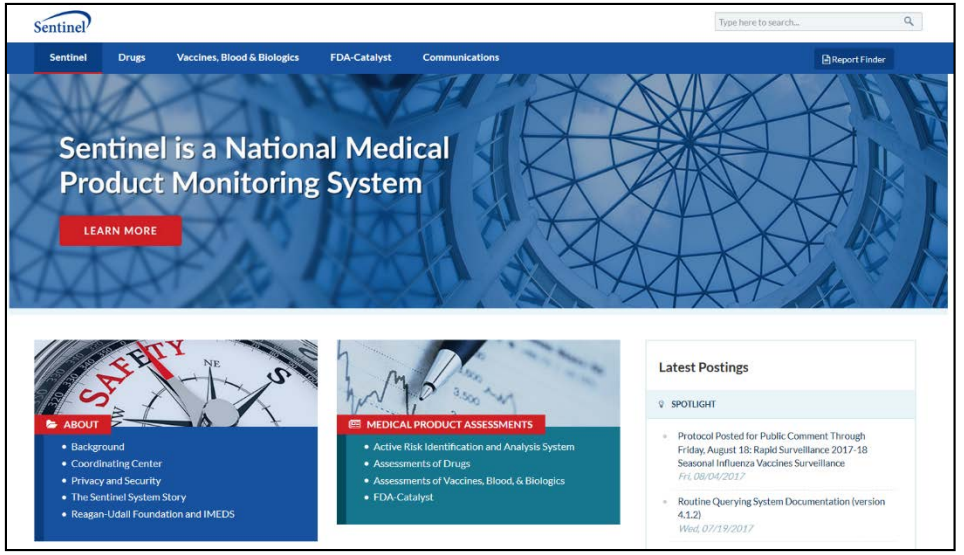
- Prescription or over-the-counter medicines, as well as medicines administered to hospital patients or at outpatient infusion centers
- Biologics (including blood components, blood and plasma derivatives, allergenic, human cells, tissues, and cellular and tissue-based products (HCT/Ps))
- Medical devices (including in vitro diagnostic products)
- Combination products
- Special nutritional products (infant formulas, and medical foods)
- Cosmetics
- Foods/beverages (including reports of serious allergic reactions)

Source: https://www.fda.gov/Safety/MedWatch/default.htm

FDA Sentinel System

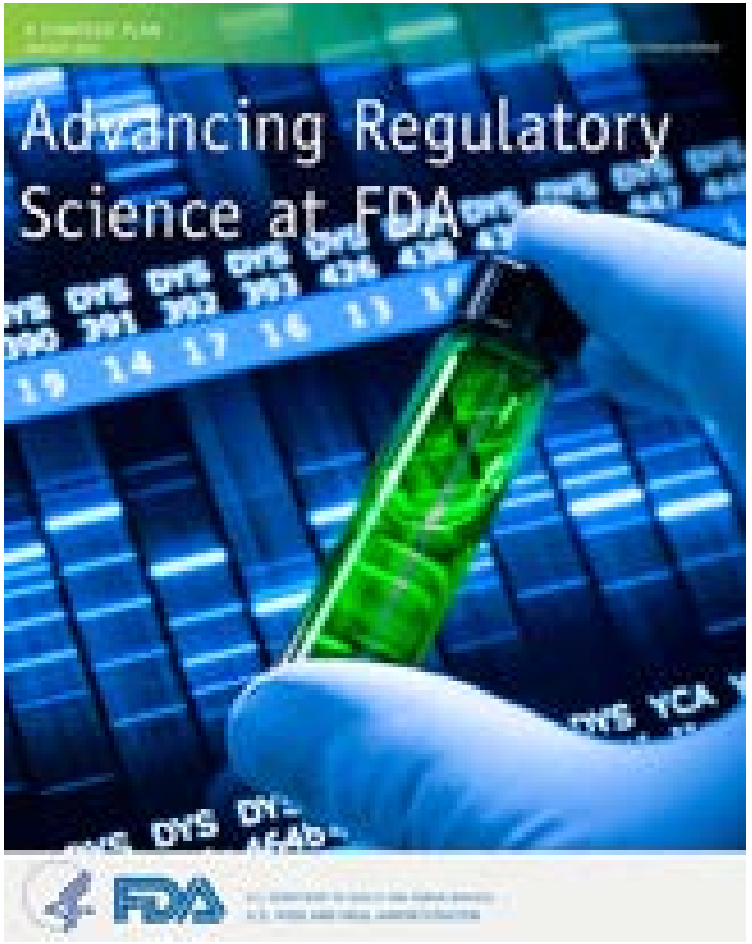
- National medical product monitoring system
- 17 data partners with 178 million members with pharmacy and medical coverage
- Distributed system where data partners retain physical control of data to protect privacy and security

•https://www.sentinelinitiative.org/



FDA Exploration of Real World Data Sources

- Social media data
  - Facebook
  - Twitter
- Patient-generated Health Data
  - FDA-PatientsLikeMe Research Collaboration



Evaluation of Facebook and Twitter Monitoring to Detect Safety Signals for Medical Products An Analysis of Recent FDA Safety Alerts

Pierce CE, Bouri K, Pamer C, Proestel S, Rodriguez HW, Le HV, Freifeld C, Brownstein J, Walderhaug M, Edwards R, Dasgupta N

Drug Saf. 2017 Apr;40(4):317-331.

- **Objective:** To examine whether specific product–adverse event pairs were reported via social media before being reported to the US FDA Adverse Event Reporting System (FAERS).
- **Methods:** A retrospective analysis of public Facebook and Twitter data was conducted for 10 recent FDA postmarketing safety signals at the drug–event pair level with six negative controls. Drug safety physicians conducted a manual review to determine causality using World Health Organization-Uppsala Monitoring Centre assessment criteria. Cases were also compared with those reported in FAERS.
- **Findings:** A total of 935,246 posts were harvested from Facebook and Twitter. The automated classifier identified 98,252 Proto- AEs. Of these, 13 posts were selected for causality assessment of product–event pairs. Clinical assessment revealed that posts had sufficient information to warrant further investigation for two possible product–event associations: dronedarone–vasculitis and Banana Boat Sunscreen– skin burns. In one of the positive cases, the first report occurred in social media prior to signal detection from FAERS, whereas the other case occurred first in FAERS.
- **Conclusions:** An efficient semi-automated approach to social media monitoring may provide earlier insights into certain adverse events. More work is needed to elaborate additional uses for social media data in pharmacovigilance and to determine how they can be applied by regulatory agencies.

What are Patient-Generated Health Data?

- Patient-generated health data (PGHD) are health-related data created, recorded, or gathered by or from patients (or family members or other caregivers) to help address a health concern.

- PGHD include, but are not limited to:
  - health history
  - treatment history
  - biometric data
  - symptoms
  - lifestyle choices

Source: HHS Office of the National Coordinator for Health Information Technology

What makes Patient-Generated Health Data distinct from other health data?

- PGHD are distinct from data generated in clinical settings and through encounters with providers in two important ways:
  - Patients, not providers, are primarily responsible for capturing or recording these data.
  - Patients decide how to share or distribute these data to health care providers and others

Source: HHS Office of the National Coordinator for Health Information Technology

Why are Patient-Generated Health Data Important?

- The use of PGHD supplements existing clinical data, filling in gaps in information and providing a more comprehensive picture of ongoing patient health.

- PGHD can:
  - Provide important information about how patients are doing between medical visits.
  - Gather information on an ongoing basis, rather than only at one point in time.
  - Provide information relevant to preventive and chronic care management.

- The use of PGHD offers an opportunity to capture needed information for use during care, with potential cost savings and improvements in quality, care coordination, and patient safety.

Source: HHS Office of the National Coordinator for Health Information Technology

FDA/PatientsLikeMe Research Collaboration

- FDA and PatientsLikeMe entered a Research Collaboration Agreement (RCA) in April 2015

- Systematically explore the potential of patient-generated health data
  - To assess drug risks
  - To assess risk management interventions

- Explore similarities and differences in each type of data
  - How to preserve and utilize the patient voice

PatientsLikeMe

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Join now! (It's free)
Already a member? Sign in

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Testimonials
Careers
Patient Programs
"Value of Openness" blog
PatientsLikeMeInMotion™ events
Policies & Resources
Privacy policy
User agreement
FAQs and screencasts

About us

We've partnered with 500,000+ people living with 2700+ conditions on 1 mission: to put patients first

Imagine this: a world where people with chronic health conditions get together and share their experiences living with disease
can improve their outcomes by connecting with and learning from others who've gone before them. Where researchers learn
not, and where the gaps are, so that they can develop new and better treatments.

It's already happening at PatientsLikeMe. We're a free website where people can share their health data to track their progress
for good.

*"We started with the assumption that patients had knowledge we needed, rather than we had knowl
the answers, but patients had the insights that could help us collectively find them."*

Jamie Heywood, Co-founder and Chairman

FDA/PatientsLikeMe RCA

- Some questions of interest:
  - Can we characterize safety issues faster using patient-generated data?
  - Can we evaluate and improve effectiveness of risk management activities (such as REMS) using patient-generated data?
  - Can we improve communications with patient communities?
  - Can we improve patient outcomes using patient-generated data?

FDA/PatientsLikeMe RCA Accomplishments

- Eight (8) research projects have been initiated or completed
  - MedDRA Coding Validation Study
  - PatientsLikeMe Individual Case Safety Report Quality Study
  - Drug Treatment Coding Validation Study
  - PatientsLikeMe Patient Population Characterization Study
  - Data Density and Site Engagement of the PatientsLikeMe Population
  - PatientsLikeMe Community and FDA Drug Safety Communications
  - Detection of Medication Errors in the PatientsLikeMe Platform
  - Patient Counts for PatientsLikeMe Communities

- Study reports will be published to share findings.

Conclusions

- Use of certain Real World Data for postapproval drug safety monitoring is well-established.

- Initial exploratory research of novel data sources such as social media and PGHD is promising
  - Structured PGHD may have the potential to be a source for patient insights, experiences and preferences.
  - Additional exploration is needed to fully develop analytic methods.
  - Need to understand potential application to regulatory decision-making process.

Questions?