FDA Drug Topics: Reporting and Public Viewing of Individual Case Safety Reports (ICSRs)

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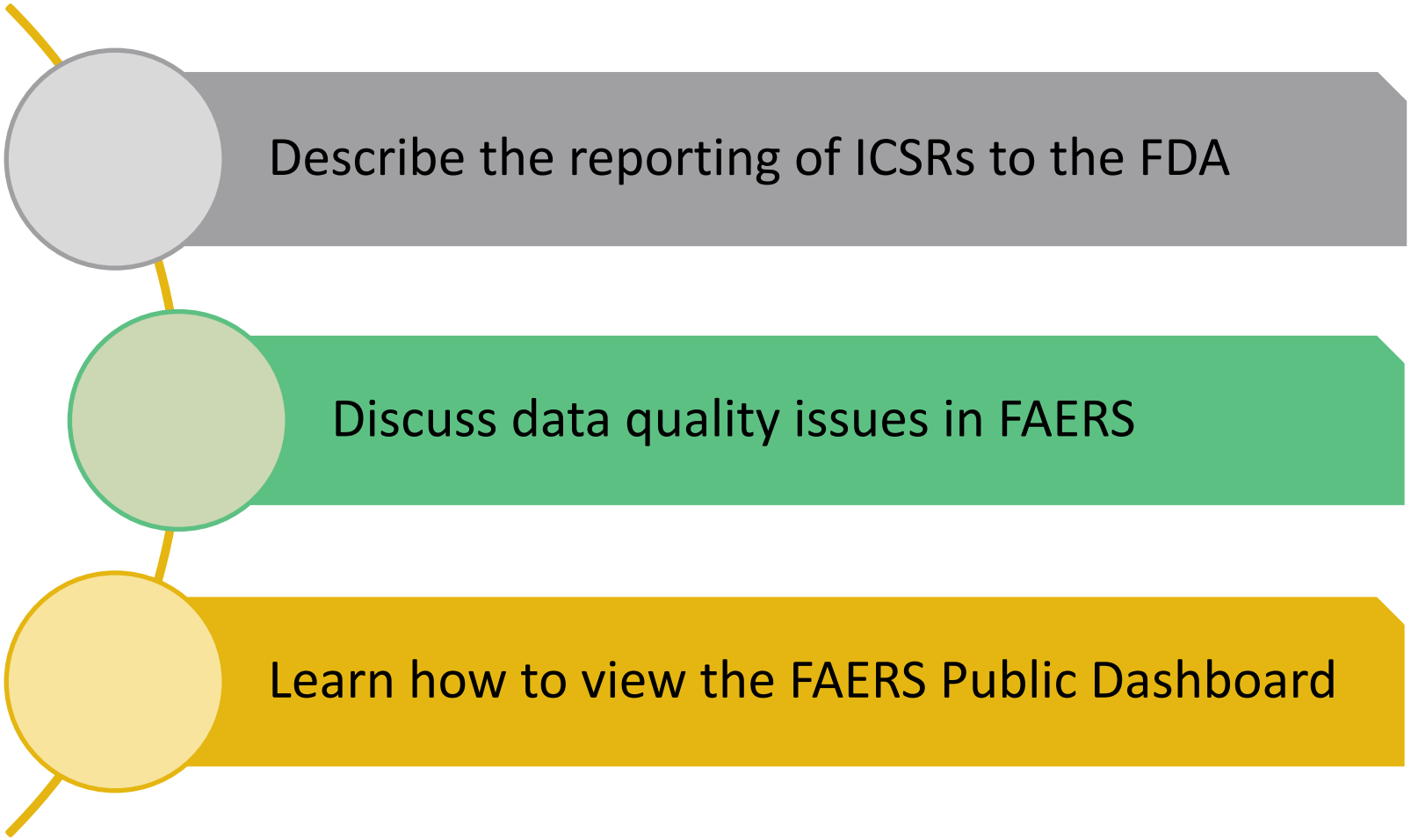
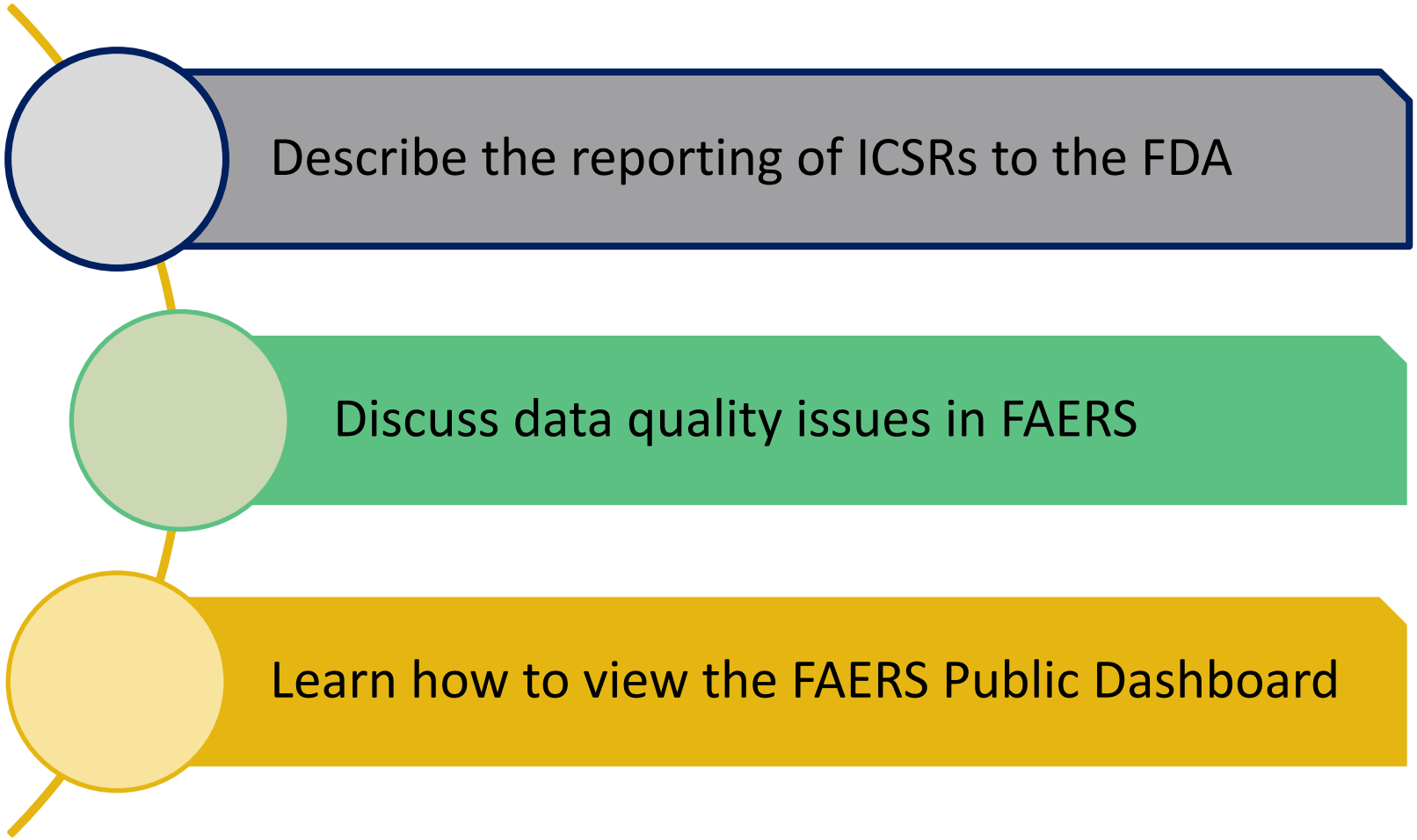
Learning Objectives



Learning Objectives



FDA Adverse Event Reporting System (FAERS)

The FDA Adverse Events Reporting System (FAERS) is a database that contains **spontaneous adverse event reports** that are **submitted to FDA** by the **product manufacturer or directly from the consumer, healthcare professional, or other reporter**. The database supports the FDA's post marketing safety surveillance program for **drug and therapeutic biological products**.

The database consists of more than **twenty-four (24) million reports** since 1969 to March 2022. Each year, FDA receives **over two (2) million** adverse events and medication error reports associated with the use of drug or biologic products.

FDA modernized the FAERS system in Nov 2021

FDA Adverse Event Reporting System

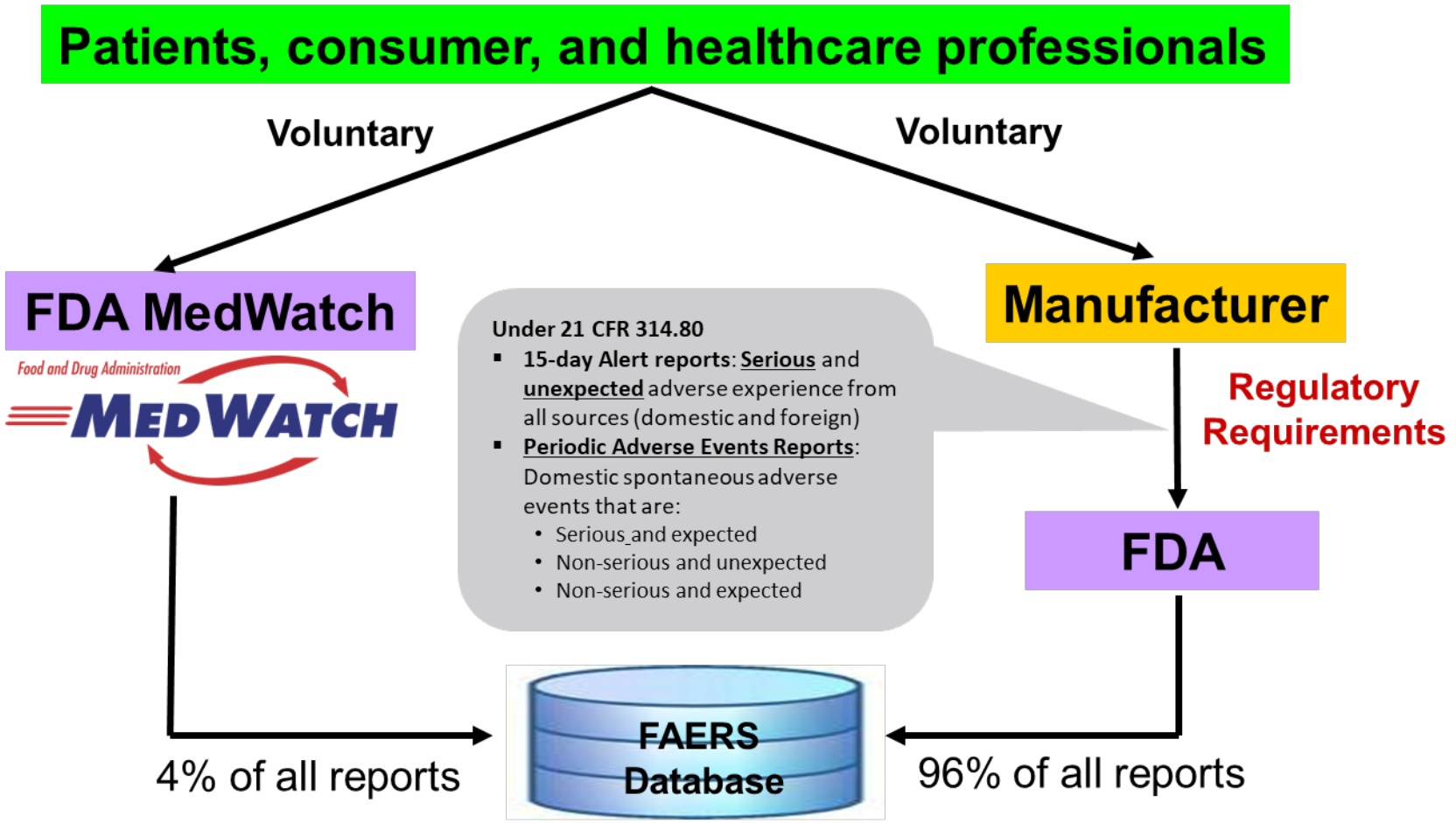
FDA's postmarketing safety surveillance database for **drugs and therapeutic biologics**

FDA uses FAERS data to **monitor, identify and analyze adverse event and medication errors**

FDA staff in CDER and CBER **regularly examine** the FAERS database as part of **routine safety monitoring**

When a **safety signal is identified** from FAERS data, it is further evaluated

How post-marketing adverse event reports get to FDA



What Reports are in the FAERS Database?

For

Drugs and therapeutic biologics (Rx + OTC) - CDER

Tissue products, therapeutic blood products - CBER

Source of Reports in FAERS

- Adverse event reporting is a **voluntary process** for healthcare professionals in the U.S.
- Healthcare professionals and consumers may send reports to **manufacturers and/or the FDA** (spontaneous reporting)
- Manufacturers are **required to forward reports** to FDA as per regulation
- Manufacturers have **additional reporting requirements**, such as post-marketing study reports

Direct Reports

- Reports submitted directly to FDA through MedWatch by:
  -  Internet – on-line reporting form
  -  Mail - MedWatch form (FDA 3500/3500B)
  -  Fax - MedWatch form (FDA 3500/3500B)
  -  Telephone 1-800-FDA-1088

www.fda.gov/safety/medwatch

Food and Drug Administration
MedWatch

- How to Report:
  - Online (www.fda.gov/medwatch)
  - Download the form
    - Mail
    - Fax 1–800–332–0178
- For questions about the form:
  - 1–800–332–1088

U.S. Food and Drug Administration. MedWatch: The FDA Safety Information and Adverse Event Reporting Program. Available at: https://www.fda.gov/Safety/MedWatch/default.htm

Food and Drug Administration

MEDWATCH

MedWatch Voluntary Report

SHARE | TWEET | LINKEDIN | PIN IT | EMAIL | PRINT

PATIENT — PROBLEM — PRODUCT — DEVICE — CONCOMITANT — REPORTER — REVIEW & SUBMIT

About Patient

* Required Information

For all other data fields please provide information, if available. ONLY fields with * are mandatory.

Patient Identifier:

Please do NOT enter the Patient's Name or Social Security Number

Age or Date of Birth:

Age *(specify unit of time for age)* | Unit | OR | Date of Birth (mm/dd/yyyy)

mm/dd/yyyy

Gender:

- ○ Female
- ○ Male
- ○ Intersex
- ○ Transgender
- ○ Prefer not to disclose

Weight and Unit:

Weight | Unit

Food and Drug Administration

MEDWATCH

FDA

U.S. Department of Health and Human Services
Food and Drug Administration

MEDWATCH

FORM FDA 3500 (2/20)

The FDA Safety Information and Adverse Event Reporting Program

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

Form Approved: OMB No. 0910-0291, Expires: 11-30-2021
See PRA statement on reverse.

FDA USE ONLY	
Triage unit sequence #	
FDA Rec. Date	

Note: For date prompts of "dd-mmm-yyyy" please use 2-digit day, 3-letter month abbreviation, and 4-digit year; for example, 01-Jul-2018.

A. PATIENT INFORMATION

1. **Patient Identifier**

In Confidence

2. **Age**

☐ Year(s) ☐ Month(s)
☐ Week(s) ☐ Day(s)

or Date of Birth *(e.g., 08 Feb 1925)*

3. **Gender** *(check one)*

☐ Female
☐ Male
☐ Intersex
☐ Transgender
☐ Prefer not to disclose

4. **Weight**

☐ lb
☐ kg

5. **Ethnicity** *(check one)*

☐ Hispanic/Latino
☐ Not Hispanic/Latino

6. **Race** *(check all that apply)*

☐ Asian ☐ American Indian or Alaskan Native
☐ Black or African American ☐ White
☐ Native Hawaiian or Other Pacific Islander

B. ADVERSE EVENT, PRODUCT PROBLEM

1. **Type of Report** *(check all that apply)*

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

2. **Dose or Amount** | **Frequency** | **Route**

#1			
#2			

3. **Treatment Dates/Therapy Dates** *(give best estimate of length of treatment (start/stop) or duration.)*

#1 Start
#1 Stop
Is therapy still on-going? ☐ Yes ☐ No

#2 Start
#2 Stop
Is therapy still on-going? ☐ Yes ☐ No

4. **Diagnosis for Use** *(Indication)*

#1

#2

5. **Product Type** *(check all that apply)*

#1	#2
☐ OTC	☐ OTC
☐ Compounded	☐ Compounded
☐ Generic	☐ Generic
☐ Biosimilar	☐ Biosimilar

6. **Expiration Date** *(dd-mmm-yyyy)*

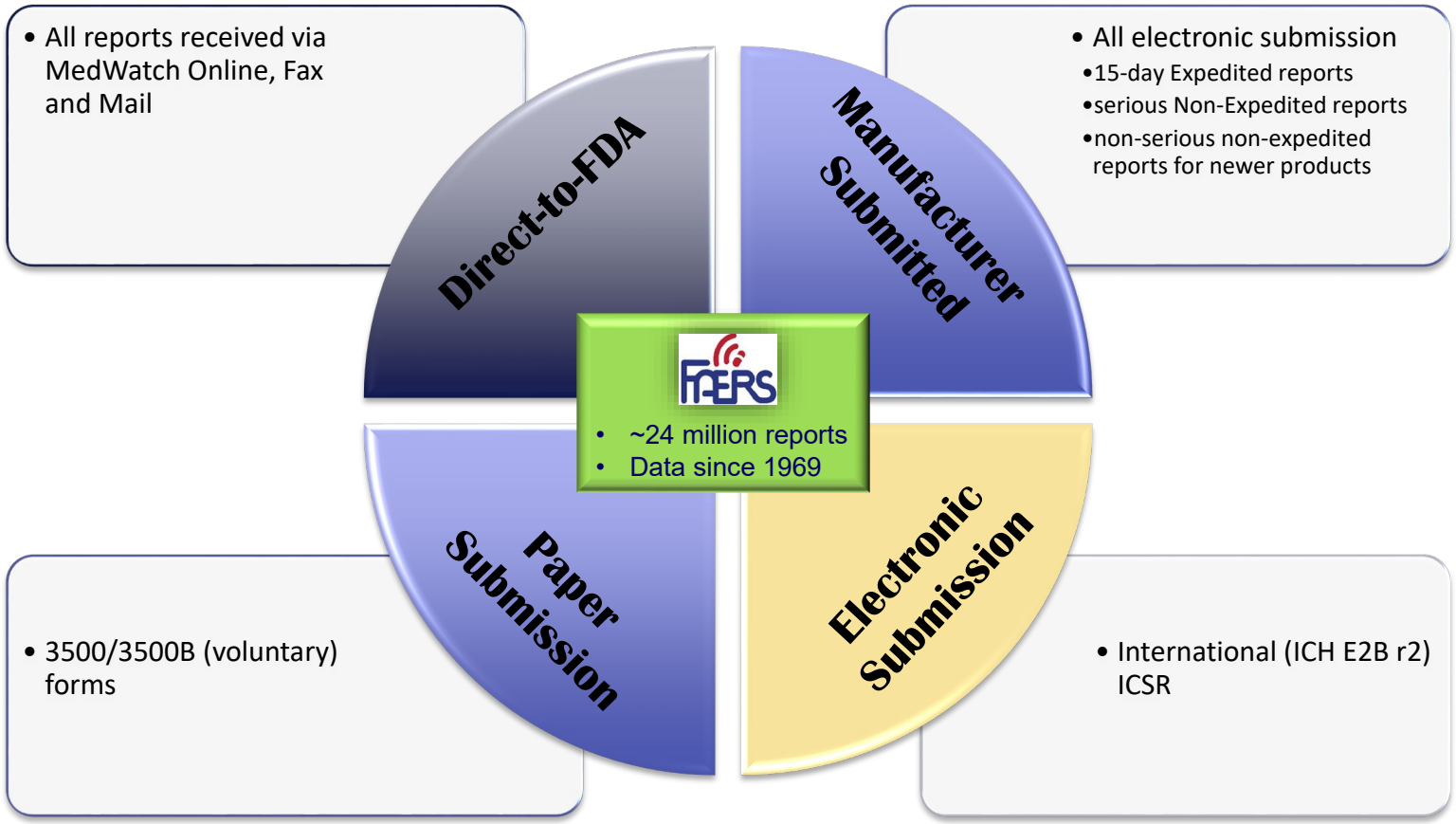
#1

#2

7. **Event Abated After Use Stopped or Dose Reduced?**

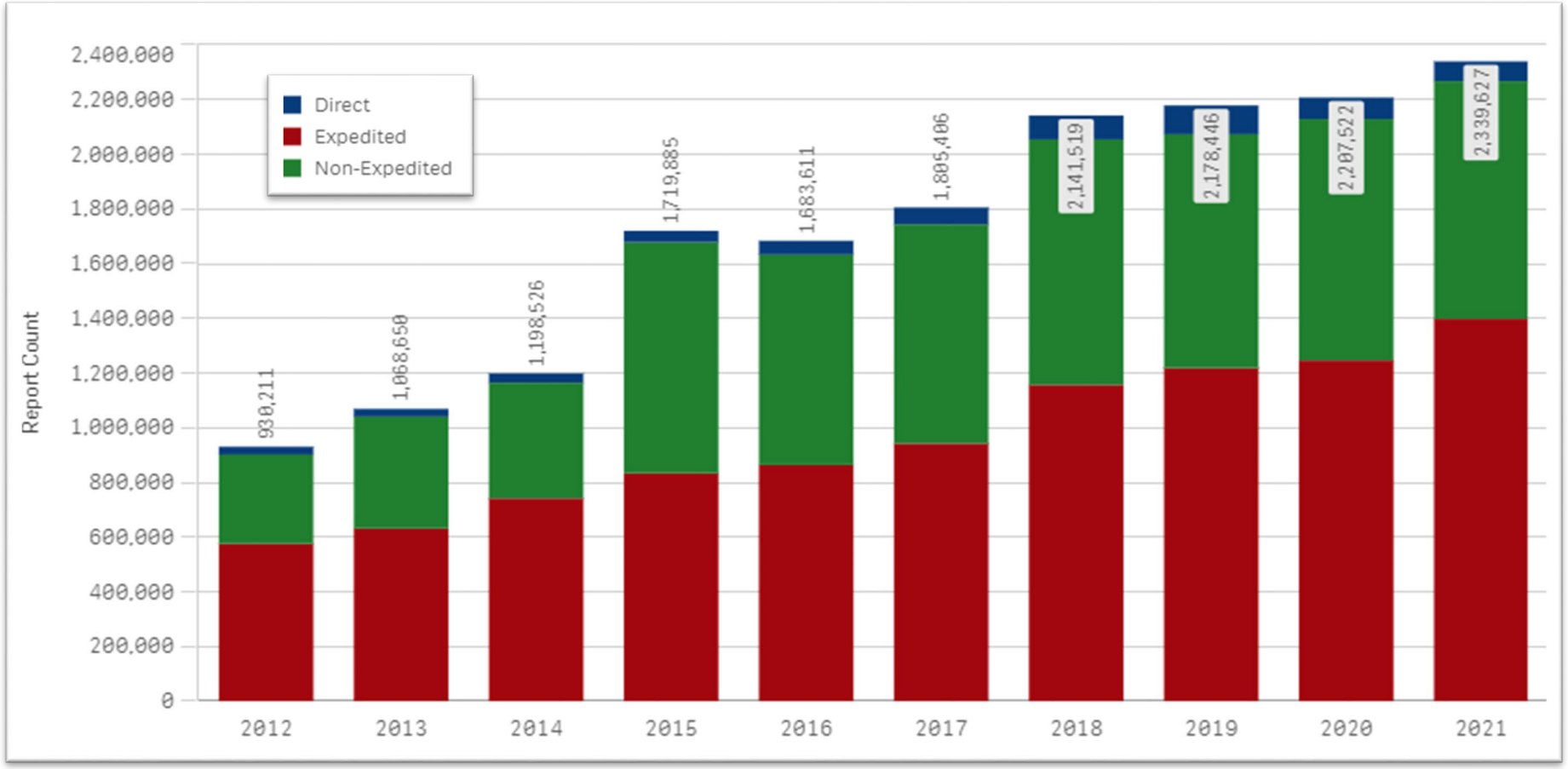
8. **Event Reappeared After Reintroduction?**

What gets entered into FAERS?



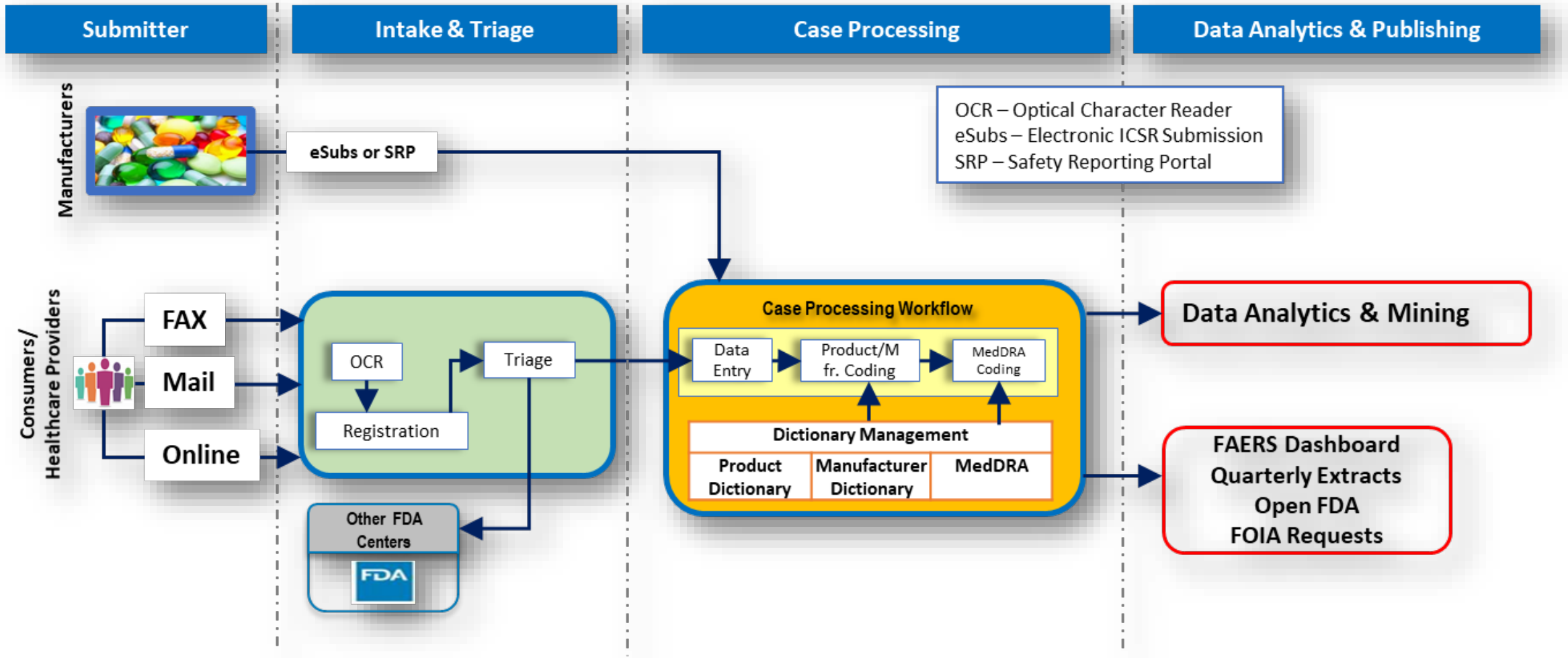
FAERS Report Volume

Last 10 years



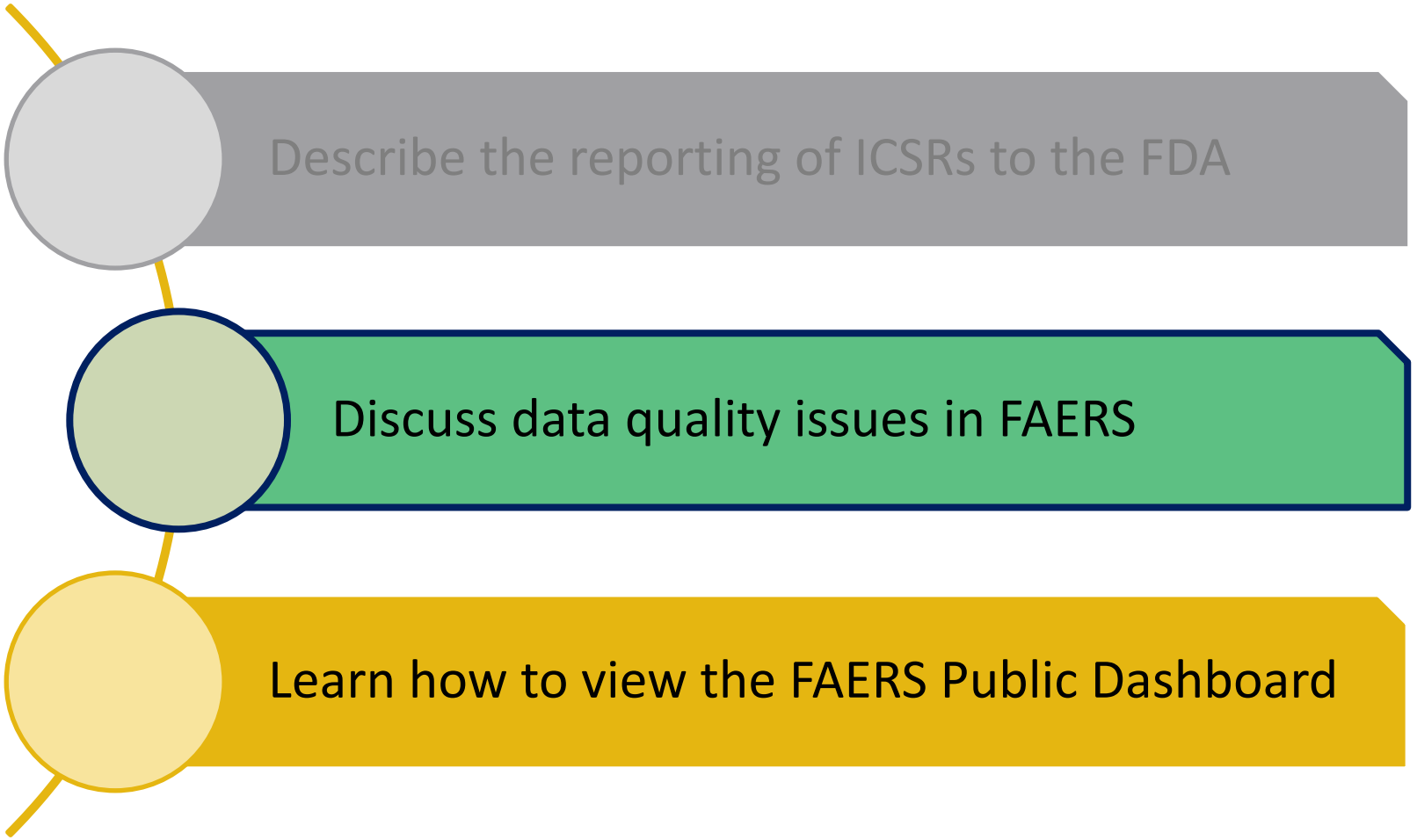
Source: [FAERS Public Dashboard]

Processing of Adverse Event Reports




Factors Affecting Reporting
Media attention
Litigation (class action lawsuits)
Nature of the adverse event
Type of drug product and indication
Length of time on market
Extent and quality of surveillance system
Prescription or OTC product status
Reporting regulations

Learning Objectives



Topics Covered

- Issues with reported suspect products and recommendations
- Other data issues

Main Data Sources for Product Validation in FAERS

- **Substance Registration System (SRS) for all products**
  - ‘Preferred name’ for active ingredient, active moiety
  - SRS public database (NLM): https://fdasis.nlm.nih.gov/srs/
- **Structured Product Labeling (SPL) for US marketed products**
  - Product name with active ingredient and moiety from SRS
- **Non-US marketed products**
  - Product information: WHODrug Global
  - Active ingredient: SRS Preferred name
- **Other validated sources**

Issues with Reported Suspect Products

Two products reported as one multi-ingredient product (which does not exist as a single formulation):

- *"IPILIMUMAB/NIVOLUMAB"*
- *"SULFAMETHOXAZOLE\TRIMIPRAMINE"*
- *"EPIRUBICIN/VINORELBINE"*

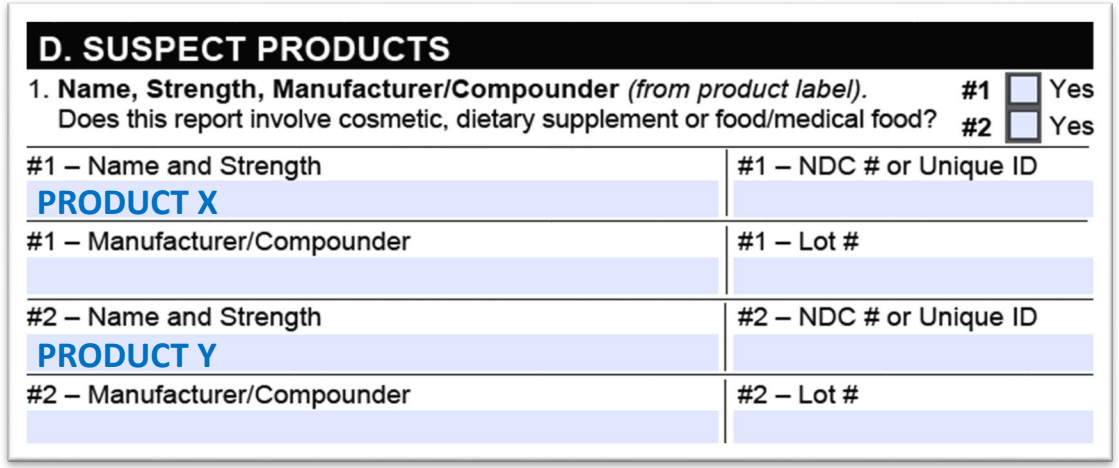
❖ Recommend to separate suspect products that do not exist as a single multi-ingredient formulation.

Issues with Reported Suspect Product

Two product names reported for the first suspect product in the MedWatch Form

- Example:
  - PRODUCT X and PRODUCT Y

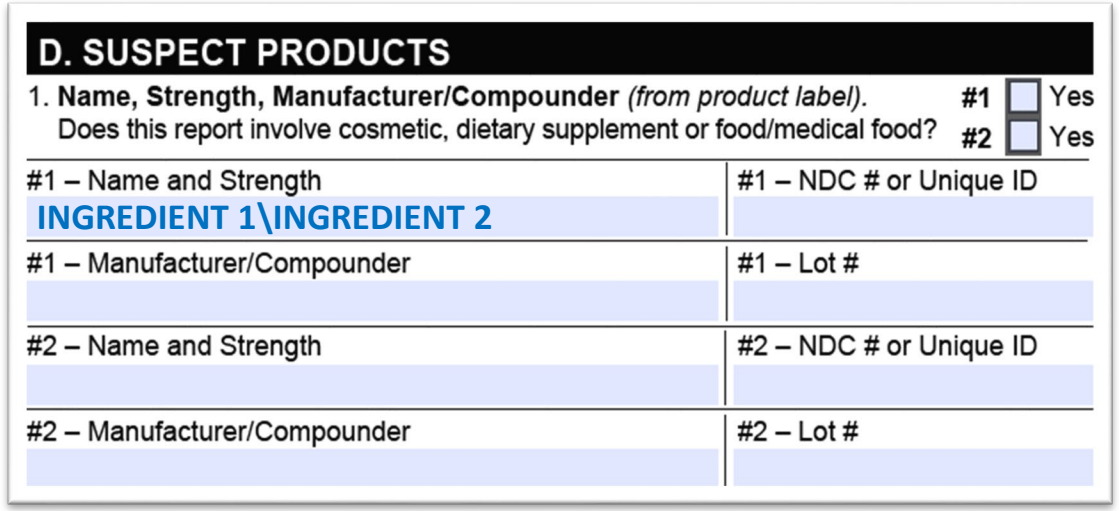
❖ Recommend to report one product name per each line in the MedWatch Form. If brand name is unknow and reporting a product with multi active ingredients, then report as



D. SUSPECT PRODUCTS

1. **Name, Strength, Manufacturer/Compounder** *(from product label).* **#1** ☐ Yes
   Does this report involve cosmetic, dietary supplement or food/medical food? **#2** ☐ Yes

#1 – Name and Strength	#1 – NDC # or Unique ID
PRODUCT X	
#1 – Manufacturer/Compounder	#1 – Lot #
#2 – Name and Strength	#2 – NDC # or Unique ID
PRODUCT Y	
#2 – Manufacturer/Compounder	#2 – Lot #



D. SUSPECT PRODUCTS

1. **Name, Strength, Manufacturer/Compounder** *(from product label).* **#1** ☐ Yes
   Does this report involve cosmetic, dietary supplement or food/medical food? **#2** ☐ Yes

#1 – Name and Strength	#1 – NDC # or Unique ID
INGREDIENT 1\INGREDIENT 2	
#1 – Manufacturer/Compounder	#1 – Lot #
#2 – Name and Strength	#2 – NDC # or Unique ID
#2 – Manufacturer/Compounder	#2 – Lot #

Issues with Reported Suspect Product

Narrative and structured field(s) do not match

- Ingredient salt stated in narrative, structured field populated with a different salt form
  - Narrative: "…received Pseudoephedrine hydrochloride"
  - Structured field: "Pseudoephedrine hydrobromide"

- Inconsistency
  - Narrative: "…given treatment of INETETAMAB"
  - Substance name in structured field: "INOTUZUMAB"

- Report the product name as mentioned in the label

Issues with Reported Suspect Product

Non-unique product name with different active ingredients

ACIDEX

ICY HOT

- Recommend to append the active ingredient to the reported drug name. For example,

ACIDEX [OMEPRAZOLE]

ACIDEX [RANITIDINE HYDROCHLORIDE]

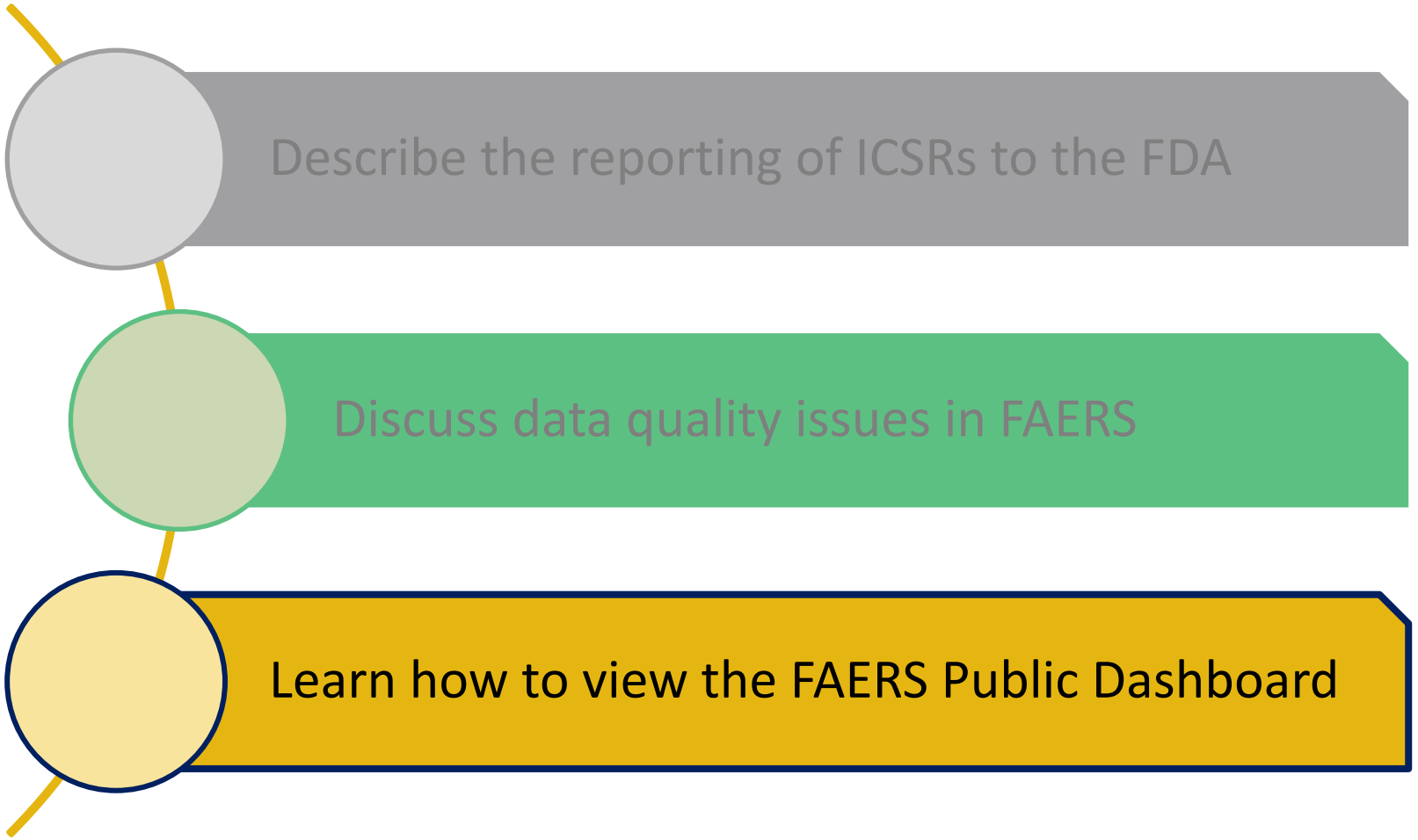
CLAMISIN [CLARITHROMYCIN]

CLAMISIN [TERBINAFINE]

Other Data Issues

- Demographic information in narrative but not in structured data elements
- Demographic information incomplete or off limits
- Reports submitted having information with low value
- Information not presented correctly via structured data elements (e.g., abated and reappeared)
- Outcome inappropriately documented
- Date mismatch (e.g., event date prior to therapy date)

Learning Objectives



Topics Covered

- Describe the FAERS public database
- Demonstrate how view adverse event reporting metrics
- Illustrate viewing of adverse event information for COVID-19 EUA products

FAERS Public Dashboard

FDA provides information to the public in an accessible and transparent manner. FAERS dashboard gives the public and industry a more **user friendly platform** for accessing FAERS reports and making adverse event data more **accessible and transparent**.

FAERS data outlets for public:

JSON File(s)

openFDA

Open FDA

FAERS Quarterly Data Extracts (QDE)

FAERS Public Dashboard

The FAERS Public Dashboard is an **interactive application**, which enables the user to search for information related to adverse events reported to the FDA by the pharmaceutical industry, healthcare providers and consumers.

Key Points to Consider

❑ Data Quality

- There are many instances of duplicative reports and some reports do not contain all the necessary information.

❑ Existence of a report does not establish causation

- There is no certainty that a suspected drug caused the adverse events.
- Adverse events may have been related to the underlying disease being treated, or caused by some other drug being taken concurrently, or occurred for other reasons.
- The information in these reports reflects only the reporter's observations and opinions.

❑ Information in reports has not been verified

- Submission of a report does not mean that the information included in it has been medically confirmed.

Key Points to Consider

- **Rates of occurrence cannot be established with reports**
  - The number of adverse events should not be used to determine the likelihood of a side effect occurring.
  - Factors such as the time a product has been marketed and publicity can influence reporting.

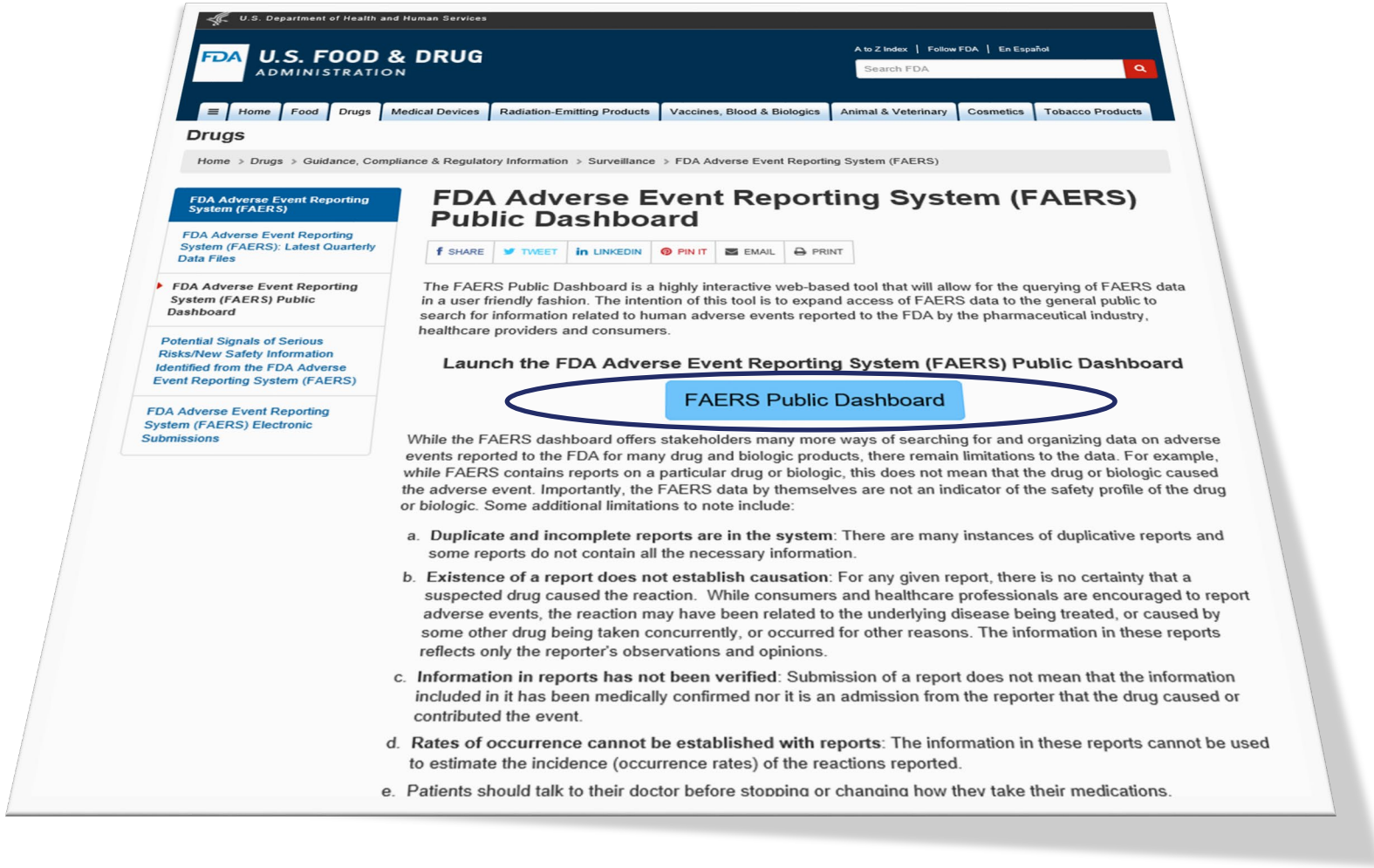
- **Patients should talk to their doctor** before stopping or changing how they take their medications

- **Patient Outcomes received in FAERS**
  - A reported serious outcomes does not necessarily mean that the suspect product(s) named in the report was the cause of these outcomes.

FAERS data by themselves are not an indicator that the drug is causing the reported adverse events.

Launch FAERS Public Dashboard

https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm070093.htm



Conclusion

- FAERS dashboard gives the consumer, healthcare professionals and industry a more user-friendly platform for accessing FAERS reports
- FAERS dashboard makes adverse event data more accessible and transparent
- Existence of a report does not establish causation
- Rates of occurrence cannot be established with FAERS reports

Question 1

For reporting adverse events, HCP should use the MedWatch Form 3500, whereas consumers should use the MedWatch Form 3500B

a. True

b. False

Question 2

What are the submission methods?

a. MedWatch Online
b. Faxes
c. USPS Mail
d. All of the above

Question 3

While reporting an adverse event, clearly identify the suspect product using the trade name, if not available then report the active substance name

a. True

b. False

Question 4

Typical data issues encountered in a voluntary safety report submission

a. Demographic information in narrative but not in structured data elements
b. Demographic information incomplete or off limits
c. Reports submitted having low value
d. Date mismatch
e. All of the above

Question 5

Select all the key points to consider while viewing the contents of the dashboard

a. Quality of adverse event data
b. Existence of a report does not establish causation
c. Information has not been verified and rates of occurrence cannot be established
d. Patients should talk to their doctor before stopping or changing their medication
e. All of the above

Question 6

A private physician views adverse event data on a product. Looking at the volume of the data set for that product he concludes that the product is risky to prescribe. Did the physician make an informed decision?

a. Yes

b. No

Questions 7

An HCP is searching for reports on a product. Select the applicable options to perform this search?

a. By NDA number

b. By Brand Name

c. By Generic Name

d. By Brand Name or Generic Name

e. None of the above


Thank You