U.S. FOOD & DRUG ADMINISTRATION

"FDA Adverse Event Reporting System (FAERS) Overview"

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Outline

- Introduction to FAERS
- Understanding an ICSR
- Electronic Reporting of ICSRs
- FAERS Public Dashboard

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- **Introduction to FAERS**
- Understanding an ICSR
- Electronic Reporting of ICSRs
- FAERS Public Dashboard

Introduction to FAERS

- 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

Introduction To FAERS

The FDA Adverse Events Reporting System (FAERS) is a database that contains

- spontaneous adverse event reports that are
- submitted to FDA from
- 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 biologic products.

Introduction to FAERS

How do reports get to FDA?

Patients, consumer, and healthcare professionals

Voluntary

Voluntary

FDA MedWatch

Food and Drug Administration
MEDWATCH

Under 21 CFR 314.80

- **15-day Alert reports**: **Serious** and **unexpected** adverse experience from all sources (domestic and foreign)
- **Periodic Adverse Events Reports**: Domestic spontaneous adverse events that are:
  - Serious and expected
  - Non-serious and unexpected
  - Non-serious and expected

Manufacturer

Regulatory Requirements

FDA

4% of all reports

FAERS Database

96% of all reports

Introduction to FAERS

Reports in FAERS Database

For

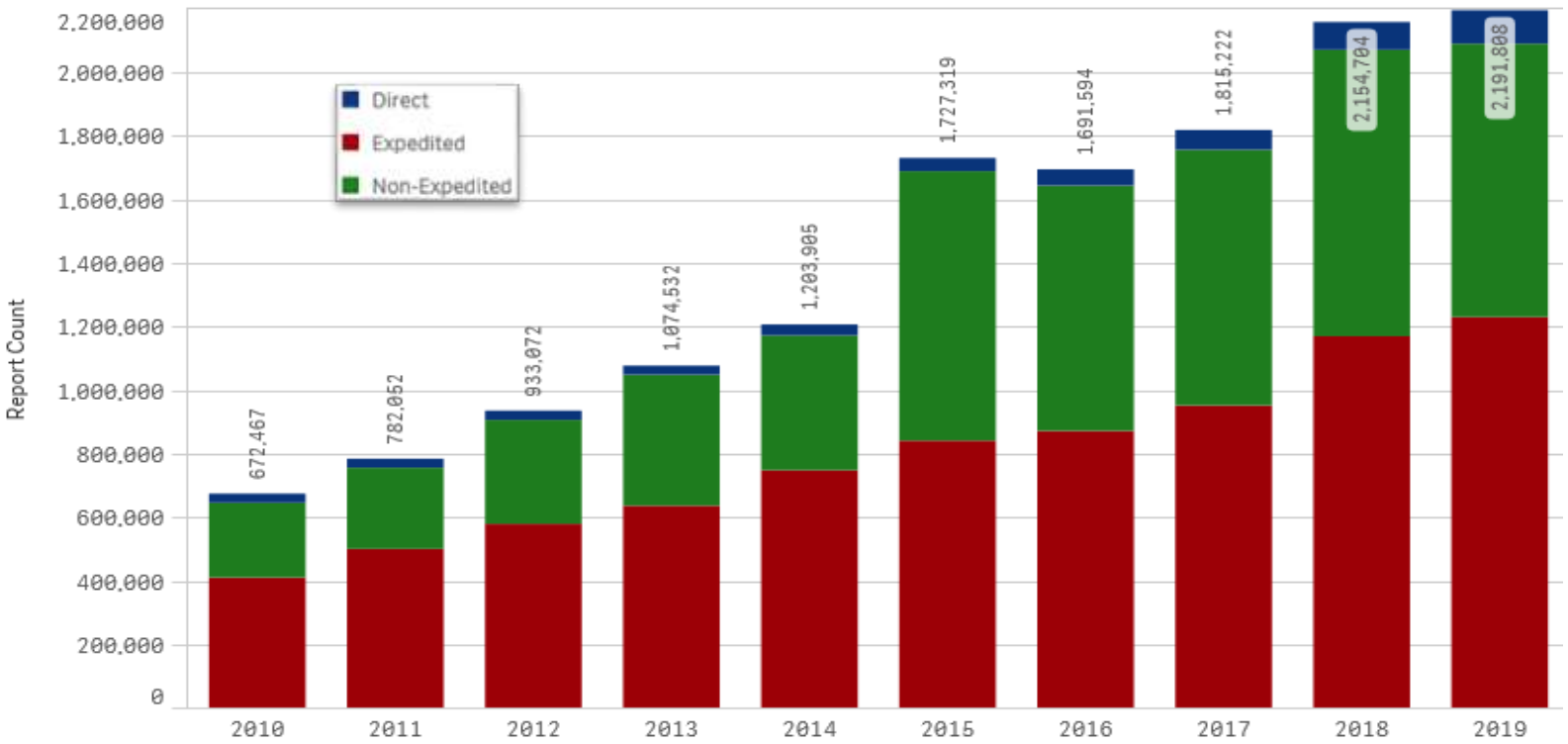
Drugs and therapeutic biologics (Rx + OTC) - CDER

Tissue products, therapeutic blood products - CBER

Introduction to FAERS

Reports Received by Report Type

The database consists of more than nineteen (19) million reports since 1969 to Dec 2019. Each year, FDA receives over two (2) million adverse events and medication error reports associated with the use of drug or biologic products.



Introduction to FAERS

Spontaneous Reports

- A communication from an individual (e.g., health care professional, consumer) to a company or regulatory authority
- Describes a suspected adverse event(s)
- Passive and voluntary reports

Introduction to FAERS

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 manufacturer's surveillance system
- Prescription or over-the-counter (OTC) product status
- Reporting regulations

Introduction to FAERS

FAERS Strengths

- Includes all U.S. marketed products
- Includes all uses
- Includes broad patient populations:
  - elderly, children, pregnant women, co-morbidities
- Especially good for events with a rare background rate
- Useful for events that occur shortly after exposure
- Detection of events not seen in clinical trials ("signal generation")
- Identification of reporting trends, possible risk factors, at risk populations, and other clinically significant emerging safety concerns

Introduction to FAERS

FAERS is Less Useful For

- ❑ Events with high background rates
- ❑ Worsening of pre-existing disease
- ❑ Issue that goes beyond data captured from the MedWatch Form or electronic reporting
- ❑ Comparative incidence rates
- ❑ Comparing drugs in the same class
- ❑ Adverse events that could also be manifestations of the disease for which the drug is indicated

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- **Understanding an ICSR**
- Electronic Reporting of ICSRs
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Understanding an ICSR

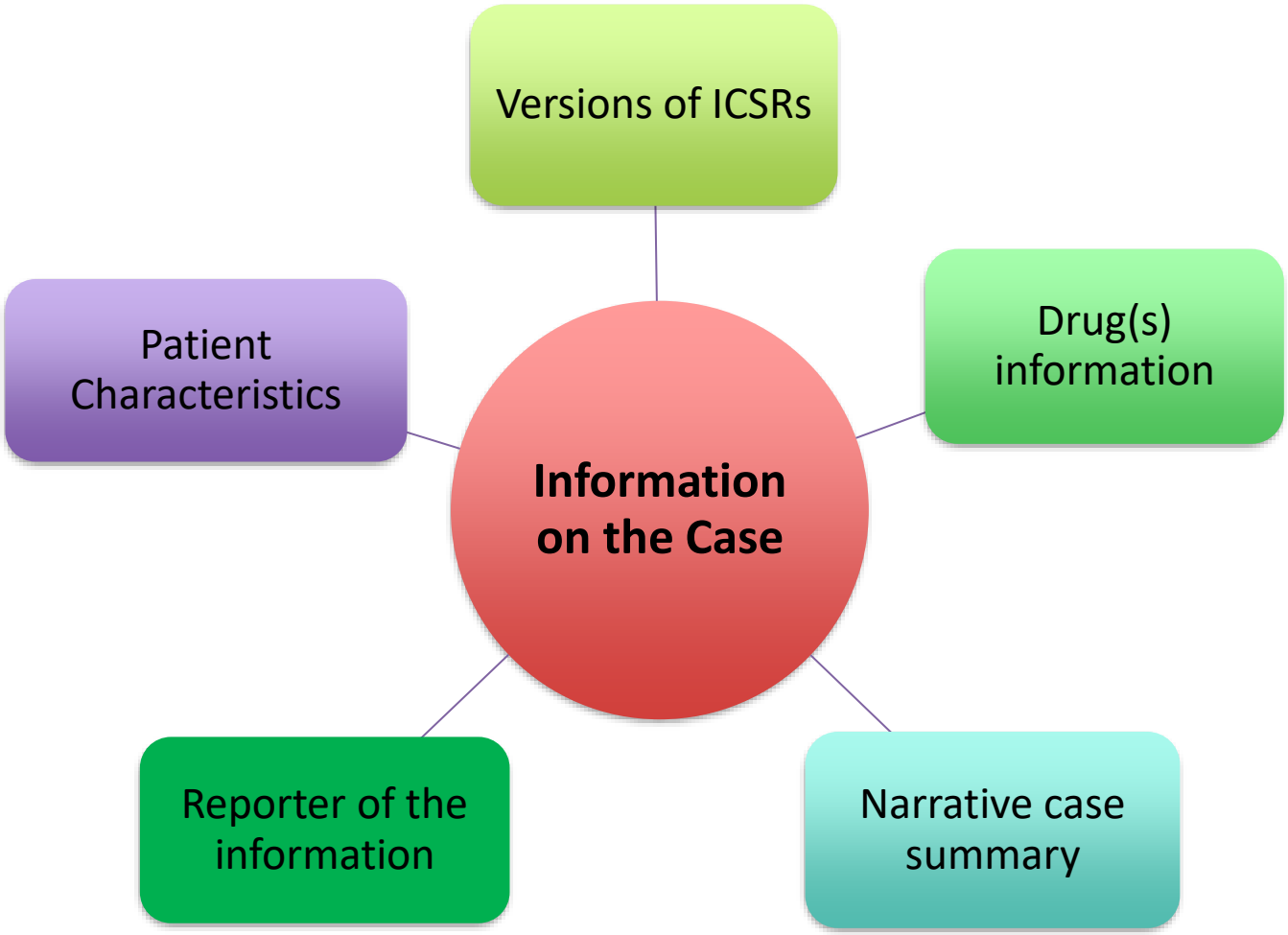
- ❑ During Electronic Submission
- ❑ Case Information
- ❑ Version of ICSRs
- ❑ Patient Characteristics
- ❑ Drug(s) Information
- ❑ Other Required ICSR Administrative Elements
- ❑ Reporter of the Information
- ❑ Narrative Case Summary
- ❑ Conclusion

Understanding an ICSR

During Electronic Transmission

- Standardized data elements for the electronic transmission of Individual Case Safety Reports (ICSRs)
- Scope
  - All types of ICSRs regardless of source or destination
  - ICSRs referring to post-marketing safety reports
  - FAERS is only for CDER and CBER (therapeutic biologics and tissue reports)
    - Tissue reports are excluded from the mandatory electronic reporting rule

Understanding an ICSR



Understanding an ICSR

Versions of ICSRs

- FAERS receiving ICSRs with the same Manufacturer Control Number (MCN) (i.e. safety report id from industry) creates a case with versions
- MCN should be used for the life of the case, to avoid duplications
- All reports should have a Mfr. received date, even for literature reports
- Sender is the manufacturer, never the CROs who are processing and sending the reports to FDA on behalf of the manufacturer

Understanding an ICSR

Patient Characteristics

- Different ways to include the same data. Example: age information can be sent as:
  - Date of birth and date of reaction
  - Age at the time of reaction
  - Patient age group

Note: Age should be provided by the most **precise** available data element.

Understanding an ICSR

Patient Characteristics (continued)

- If the information is provided in the narrative regarding the patient characteristics, it should be included in the patient section.

- Example:

  - Narrative: A 50 year (Age) old female (Sex) weighting 60 Kg (Weight) experienced a rash when exposure to this drug.

Patient ID should NOT contain patient's personal information, only initials or unique identifier

Understanding an ICSR

Drug(s) information

- The first drug listed in the ICSR should be the primary suspect drug with the appropriate application number:

Type of Application	Recommended Format
NDA / ANDA	NDA or ANDA 012345
STN/BLA/PLA	STN or BLA or PLA 123456
Rx No Application	000000
Non-Rx No Application	999999
Compounding (503B)	COMP99

Understanding an ICSR

Drug(s) information (continued)

- No pre-marketing IND reports as primary suspect drug
- If the clinical trial involves a suspect drug which has an approved application, the case has to be submitted to FAERS after the blind is broken, with the application number, if it meets the criteria and regulations of a post-marketing safety report.
- No study reports until the blind is broken

Understanding an ICSR

Other Required ICSR Administrative Elements

Element	DTD Descriptor 2.1	Length	Element Values for DTD 2.1
A.1.9	<fulfillexpeditecriteria>	1N	1=yes (expedited) 2=no (non-expedited) 4=5-Day 5=30-Day
A.1.0.1	<safetyreportid>	100AN	Sender's (Case) Safety Report Unique Identifier
A.1.10.1	<authoritynumb>	100AN	Regulatory authority's case report number
A.1.10.2	<companynumb>	100AN	Other sender's case report number
A.3.1.2	<senderorganization>	60AN	Sender identifier

Understanding an ICSR

Reporter information

Multiple reporters	• First one is the primary reporter
Medically confirmed flag	• One of the reporters is a physician
Literature and Study Reports	• Provide the title of the literature or study • Link the literature document as a PDF to the ICSR
Occupation of each reporter	• Whether the information was provided by consumer or medical personnel?

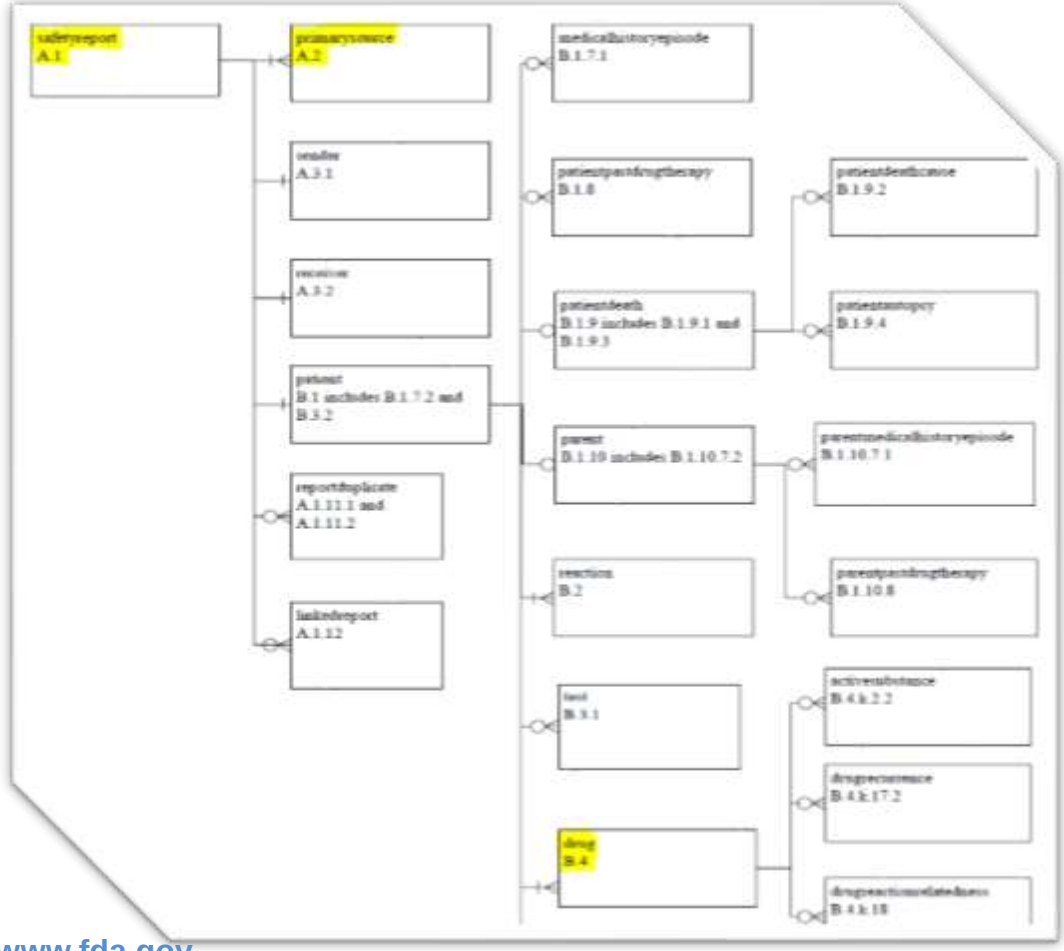
Understanding an ICSR

Narrative case summary

- Narrative is limited to **20,000 characters**
- Should **describe the story** of the adverse event(s) and product(s) associated from onset to the outcome
- Follow-up narrative should contain the **complete narrative with the additional information** in the body
- All ICSRs (expedited and non-expedited) **should have a full narrative**

Understanding an ICSR

Combination Product Data Elements



- Regional Spec based on ICH E2B (R2)
- Updated DTD to version 2.2
- Sections updated
  - Safetyreport (A.1)
  - Primarysource (A.2)
  - Drug (B.4)
- Refer to technical specification for all combination product data elements (https://www.fda.gov/media/132096/download)

Understanding an ICSR

Conclusion

- Format of ICSRs includes:
  - provisions for transmitting all the relevant data elements useful for assessing an individual adverse drug reaction report
- Not every data element is applicable for every transmission
- A substantial number of non-required data elements may not be known for each case
- The most current information on the case available to the sender must be provided

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Electronic Reporting of ICSRs

Postmarketing Safety Reports for Human Drug and Biological Products; Electronic Submission Requirements

- **Submit safety reports in an electronic format** that FDA can process, review, and archive
- **Improve** the Agency's systems for **collecting and analyzing** postmarketing safety reports
- **Enable** Agency to **more rapidly review** postmarketing safety reports, **identify and evaluate** emerging safety problems, and **disseminate** safety information in support of FDA's public health mission
- Electronic submission of ICSRs **enhances** global pharmacovigilance by **facilitating electronic transmission and exchange of appropriate information** from ICSRs among regulatory bodies and regulated entities through use of **common data elements and transmission standards**

Electronic Reporting of ICSRs

Postmarketing Safety Reports for Human Drug and Biological Products; Electronic Submission Requirements

Document Information

Date Posted:
May 27, 2015

RIN:
0910-AF96

CFR:
21 CFR Parts 310, 314, 329, and 600

Federal Register Number:
2015-12753

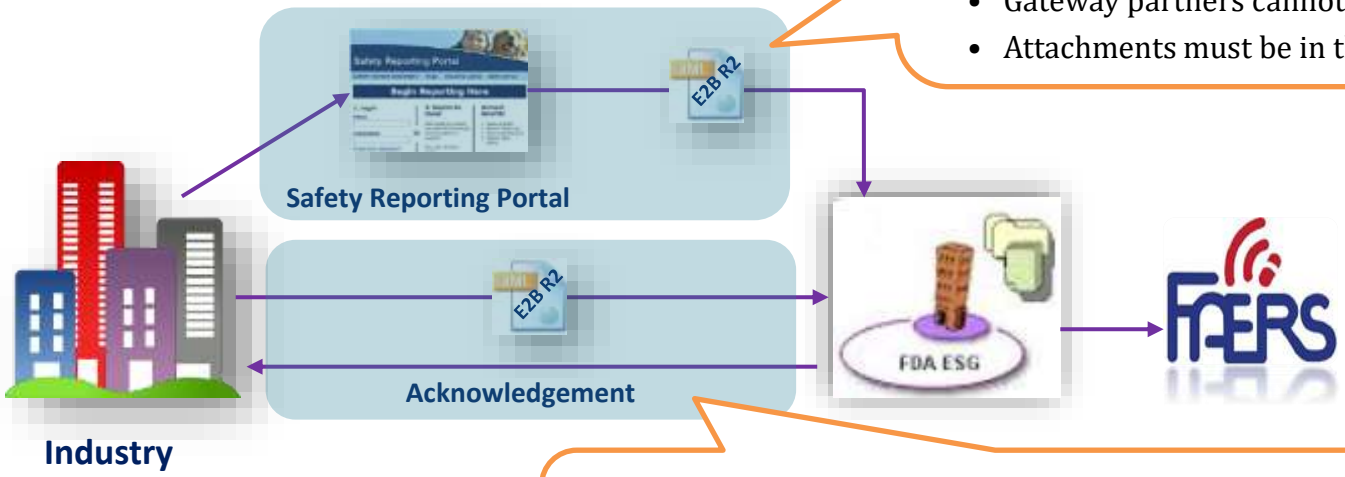
https://www.regulations.gov/#!documentDetail;D=FDA-2008-N-0334-0009

Electronic Reporting of ICSRs

Submission Methods

- There are two options for submitting ICSRs electronically

- **The Safety Reporting Portal (SRP) by manually entering data via web form**
  - Do not have database-to-database capability
  - Must have an account to access the portal site
  - Gateway partners cannot use the SRP
  - Attachments must be in the PDF format



- **Database-to-database transmission ("E2B")**
  - Use standardized ICH E2B(M) data elements
  - ICSRs must be submitted in the XML format
  - Attachments must be in the PDF format

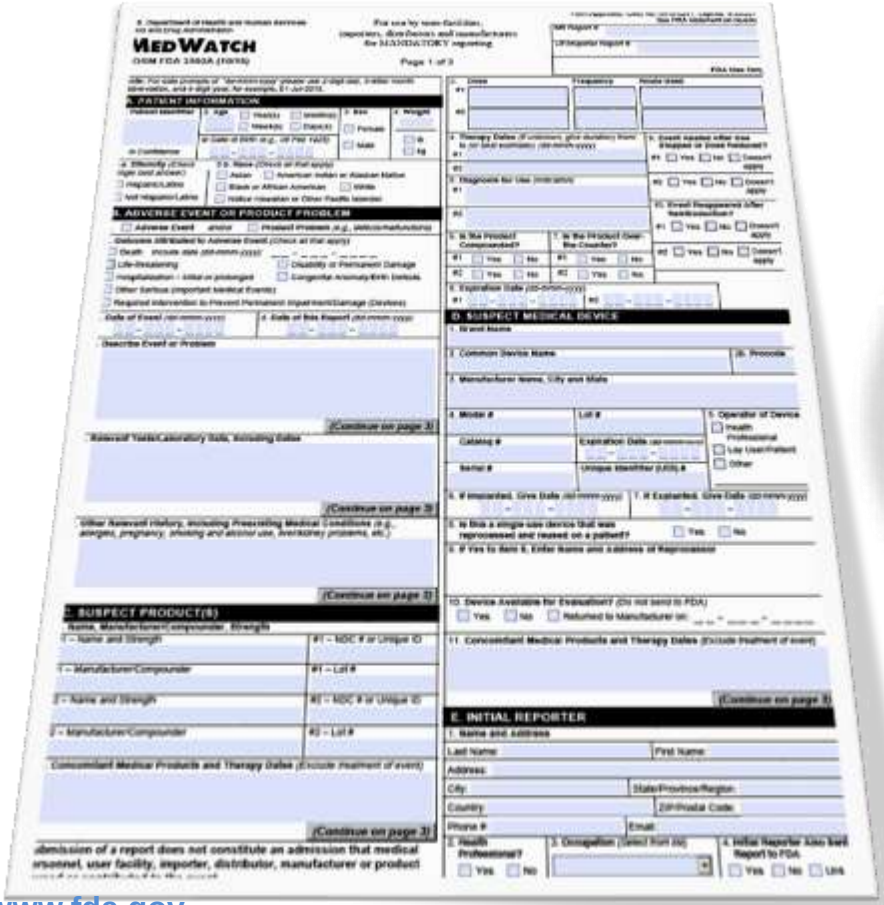
Electronic Reporting of ICSRs

Safety Reporting Portal (SRP)

Electronic Reporting of ICSRs

Safety Reporting Portal (SRP)

- SRP is based on the data elements from the MedWatch 3500A



Electronic Reporting of ICSRs

Submitting Periodic Safety Reports (PSR)

- Periodic safety reports are comprised of a **descriptive portion** and **non-expedited ICSRs** (21 CFR 314.80 and 600.80), regardless of the format.

- **Descriptive Portion:**
  - Use **Electronic Common Technical Document (eCTD)** specifications to submit the descriptive portion electronically.
  - **Indicate** in the descriptive portion that the **ICSRs have been submitted electronically** as XML files to the FDA Electronic Submissions Gateway (ESG) or via the Safety Reporting Portal (SRP).

- **Non-expedited ICSRs:** must be submitted as described in the options **on or before** the periodic safety report due date. Do NOT submit expedited ICSRs previously submitted.

Electronic Reporting of ICSRs

Future state of electronic submission

- Electronic submission of premarket safety reports
- "FDA Regional Implementation Specifications for ICH E2B(R3) Implementation: Postmarket Submission of Individual Case Safety Reports (ICSRs) for Drugs and Biologics, Excluding Vaccines" posted on June 23, 2016
- Follow core ICH E2B R3 with a few regional requirements
- For all regional E2B R3 elements refer to Feb 19, 2020 meeting materials located at https://www.fda.gov/drugs/news-events-human-drugs/electronic-submission-adverse-event-reports-fda-adverse-event-reporting-system-faers-using

Challenge Question #1

Methods to submit ICSR.

a. Database-to-database
b. Safety Reporting Portal
c. Paper MedWatch
d. a and b

Answer: D

Electronic Reporting of ICSRs

References

- FDA Adverse Event Reporting System (FAERS) - Electronic Submission
  http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm

- FDA issues final rule on postmarketing safety report in electronic format
  http://www.regulations.gov/#!documentDetail;D=FDA-2008-N-0334-0009

- Specifications for Preparing and Submitting Electronic ICSRs and ICSR Attachments
  http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM153588.pdf

- Steps to Submitting E2B(R2) ICSRs Electronically in the XML Format
  http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115914.htm

- Electronic Common technical Document (eCTD)
  http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm

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- Introduction to FAERS
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- **FAERS Public Dashboard**

FAERS Public Dashboard

- Describe the FAERS public database
- Demonstrate how to use the FAERS public dashboard to view adverse event reporting metrics
- Illustrate use of FAERS public dashboard to view adverse event information on a specific product

FAERS Public Dashboard

FDA provides information to the public in an accessible and transparent manner. This new 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 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.

FAERS Public Dashboard

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.

FAERS Public Dashboard

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.

Challenge Question #2

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 in reports has not been verified
d. Rates of occurrence cannot be established with reports
e. Patients should talk to their doctor before stopping or changing their medication
f. All of the above

Answer: F

Challenge Question #3

Dr. Doe 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 Dr. Doe make an informed decision?

a. Yes

b. No

Answer: B

- Existence of a report does not establish causation
- Rates of occurrence cannot be established with reports

FAERS Public Dashboard

Launch FAERS Public Dashboard

FDA Adverse Event Reporting System (FAERS) Public Dashboard

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The FAERS Public Dashboard is a highly interactive web-based tool that will allow for the querying of FAERS data in a user friendly fashion. The intention of this tool is to expand access of FAERS data to the general public to search for information related to human adverse events reported to the FDA by the pharmaceutical industry, healthcare providers and consumers.

Launch the FDA Adverse Event Reporting System (FAERS) Public Dashboard

FAERS Public Dashboard

While the FAERS dashboard offers stakeholders many more ways of searching for and organizing data on adverse events reported to the FDA for many drug and biologic products, there remain limitations to the data. For example, while FAERS contains reports on a particular drug or biologic, this does not mean that the drug or biologic caused the adverse event. Importantly, the FAERS data by themselves are not an indicator of the safety profile of the drug or biologic. Some additional limitations to note include:

a. **Duplicate and incomplete reports are in the system**: There are many instances of duplicative reports and some reports do not contain all the necessary information.

b. **Existence of a report does not establish causation**: For any given report, there is no certainty that a suspected drug caused the reaction. While consumers and

https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard

FAERS Public Dashboard

Conclusion

- FAERS dashboard gives the public 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 reports

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