

Digital IND Safety Reporting Program

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Agenda

- Background
- Implementation plans
 - Description of new process, including requirements and implementation
 - Data flow
 - Types of IND safety reports to be sent to FAERS
 - Data elements for IND safety reports using ICH E2B(R2)

Learning Objectives

- Understand that FDA will be requiring the submission of IND safety reports to FAERS using the ICH E2B data standard
- Describe several of the unique E2B(R2) fields required for IND safety reporting to FAERS
- Recognize that there will be two separate submission paths for premarket and postmarket adverse event reports

IND Safety Reports



Sponsors of clinical trials are required to submit IND safety reports
as per 21 CFR 312.32

<u>Current Process:</u> PDFs in eCTD format	<u>New Process:</u> ICH E2B XML files to FAERS
<ul style="list-style-type: none">• Inefficient and labor intensive review• No data standards• Lack of universal tracking system	<ul style="list-style-type: none">• Allows for use of data visualization and analytic tools for review and tracking• Leverages existing processes in use for postmarket safety reporting (ICH E2B data standards & FDA gateway)• Complies with existing federal regulations 21 CFR 312.32(c)(1)(v)

Requirements and Timelines

- **Required change in format under 745A(a) of FD&C Act**
 - Sponsors of commercial INDs will be required to submit certain IND safety reports* to FAERS by one of two methods:
 - Electronic Submissions Gateway (ESG)
 - or
 - Safety Reporting Portal (SRP)
 - Requirement effective **24 months** after publication of final guidance
 - Voluntary submissions from all sponsors will be accepted and encouraged prior to requirement

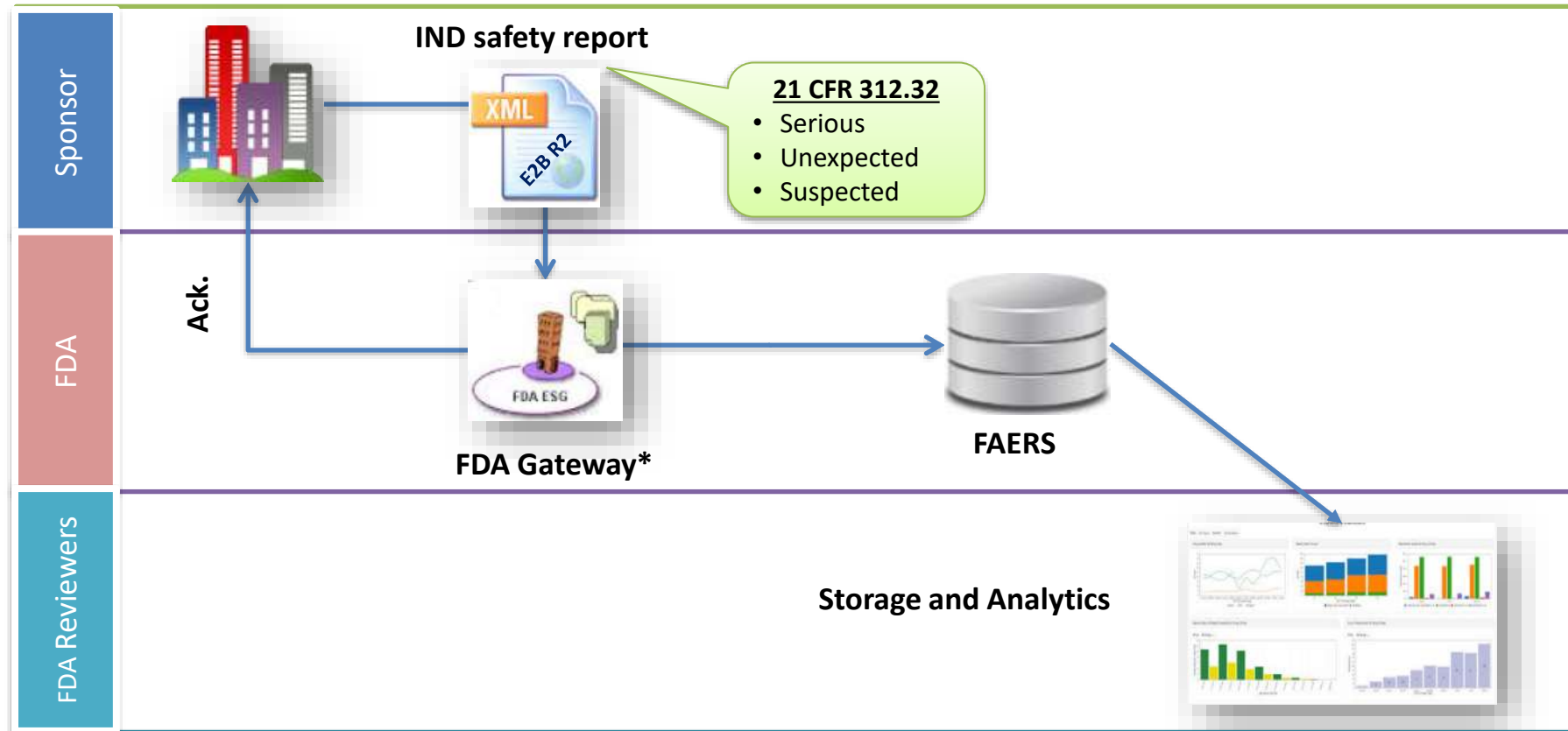
FDA will announce when the voluntary submission process will begin

*Serious and unexpected suspected adverse reactions that contain individual patient data

Communication Plan

- *Providing Regulatory Submissions in Electronic Format: IND Safety Reports - Draft Guidance for Industry (October 2019)*
- *Electronic Submission of IND Safety Reports - Technical Conformance Guide (October 2019)*
- *Revised Specifications for Preparing and Submitting Electronic ICSRs and ICSR Attachments (February 2020)*
- [FAERS website](#) updated with links the Guidance and technical specification documents specific to IND safety reports
- Other FDA communications when voluntary submissions begin

IND Safety Report Data Flow



Ack= Acknowledgement

FAERS= FDA Adverse Event Reporting System

*= separate submission path for IND safety reports

Separate Submission Paths for IND and Postmarket Safety Reports

- FDA has defined new [header attributes](#) and [routing IDs](#) for IND safety reports and attachments
 - AS2 Headers
 - Destination: CDER
 - XML files: AERS_PREMKT
 - PDFs: AERS_ATTACHMENTS_PREMKT
 - Routing IDs
 - XML files: FDA_AERS_PREMKT
 - PDFs: FDA_AERS_ATTACHMENTS_PREMKT
- Two pathways allow separation of premarket from postmarket reports so that premarket reports are NOT posted to the public dashboard

Where to Submit IND Safety Reports

Type of IND safety report	Submit to FAERS	Submit in eCTD format
A single occurrence of an event that is uncommon and known to be strongly associated with drug exposure (21 CFR 312.32(c)(1)(i)(A))	X	
One or more occurrences of an event that is not commonly associated with drug exposure, but is otherwise uncommon in the population exposed to the drug 21 CFR 312.32(c)(1)(i)(B)	X	
An aggregate analysis of specific events observed in a clinical trial (known consequences of the underlying disease or condition) that indicates those events occur more frequently in the drug treatment group than in a concurrent or historical control group. (21 CFR 312.32(c)(1)(i)(C))	X	
Findings from other studies (21 CFR 312.32(c)(1)(ii))		X
Findings from animal or in vitro testing (21 CFR 312.32(c)(1)(iii))		X
Increased rate of occurrence of serious suspected adverse reactions (21 CFR 312.32(c)(1)(iv))		X

Technical specifications

- *Specifications for Preparing and Submitting Electronic ICSRs and ICSR Attachments* has been updated with information for IND reporting
 - IND numbers
 - Cross-reporting
 - Reports from aggregate analysis
 - Other IND safety report specific data elements

Technical specifications

- **IND numbers**

- Data elements for IND number = A.2.3.2

- *Primary* IND number is the IND where the event occurred, or “parent” IND if report is from an aggregate analysis from more than one IND
 - cross-reported INDs listed separately in the report

- ***Required for processing and routing to appropriate FDA review division***

Technical Specifications



- **Cross-reporting**

- As per 2012 guidance, [Safety Reporting Requirements for INDs and BA/BE Studies](#), sponsors should submit IND safety reports to all INDs where they are evaluating the drug
 - To avoid duplicate reports submitted to FAERS, all relevant IND numbers should be listed in a single report
- Submit only ONE IND safety report per event
 - *Primary* IND number (where the event occurred or “parent” IND if report is from an aggregate analysis) listed in the first A.2.3.2
 - IND number(s) for cross-reported IND(s) placed in repeated block A.2 using A.2.3.3=5 “Cross-reported IND safety report” as many times as needed for cross-reported INDs

Technical Specifications

- **Reports from aggregate analysis**
 - Required as per (21 CFR 312.32(c)(1)(i)(C) or (21 CFR 312.32(c)(1)(i)(B) where several events are included
 - A.2.3.3=4 Report from aggregate analysis
 - Submit one report describing event and drug information and link individual cases that made up the aggregate analysis with data element A.1.12

Technical Specifications

- **Other IND safety report specific data elements**
 - 7-day expedited report (A.2.3.3 =6)
 - Causality information (B.4.k.18)
 - B.4.k.18.2 (<drugassessmentsource>) =Sponsor or Investigator
 - B.4.k.18.3 (<drugassessmentmethod>) =FDA
 - B.4.k.18.4 (<drugresult>) 1=Suspected, 2 =Not suspected
 - Drug product information
 - Use INN or USAN name, if available. Use company code if no established name, with multi-ingredient products, or if name exceeds character length
 - If applicable, submit drug naming information to the IND prior to submitting IND safety reports to FAERS

Benefits to Industry

- **Efficiency gains** in processing and submission
 - Direct electronic submission to FDA from PV
 - no 1571 or cover letter
 - Eliminates need to send duplicate reports
- More comprehensive and structured format than Medwatch form
- Consistent with format for NDA/BLA and ex-US submissions

Summary



- FDA will be requiring the submission of IND safety reports to FAERS
- The process has not yet begun; FDA will communicate when the systems are available for testing and submission
- Consult the [FAERS website](#) for guidances including technical documents and additional information

Challenge Question #1



Which of the following IND safety reports should be submitted to FAERS?

- A. Findings from animal or in vitro testing
- B. Increased rate of occurrence of serious suspected adverse reactions
- C. Serious and unexpected suspected adverse reactions
- D. Findings from other studies

Challenge Question #2



Which of the following is a new E2B(R2) data element value for IND safety reports

A. Clinical Trials

B. 7-day

C. Report From Study

D. Spontaneous

QUESTIONS

