U.S. FOOD & DRUG ADMINISTRATION

FDA Drug Topics
Electronic Submission of Safety Reports: Ready for Primetime

Suranjan De
Deputy Director
Regulatory Science Staff
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Overview

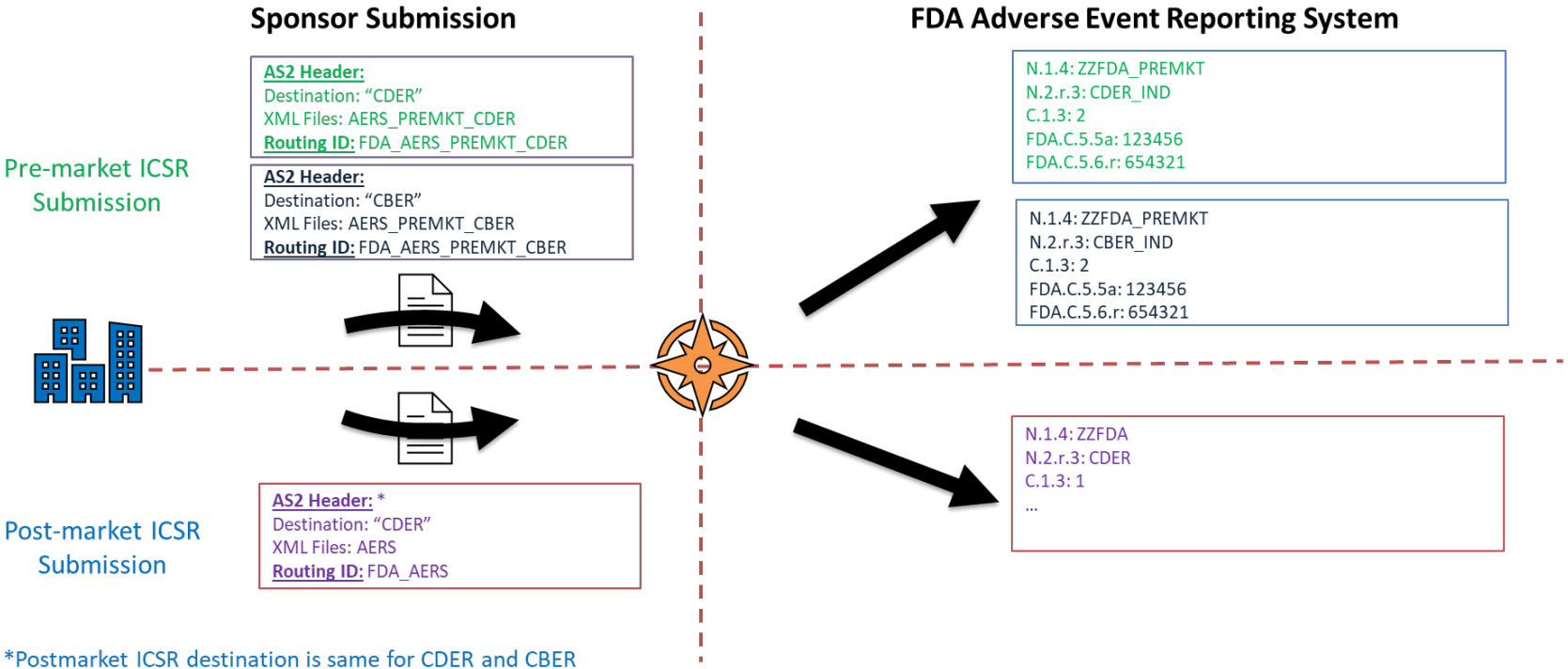
- Recognize that FDA will require reporting of IND and postmarket safety reports to be submitted in the ICH E2B(R3) format to FAERS via the Electronic Submission Gateway or the Safety Reporting Portal.
- Identify the updated requirements since the last publication that are key for postmarket, IND, and IND-exempt BA/BE safety reporting.
- Describe the implementation status and progress of premarket and postmarket safety reports in E2B (R3) format.
- Explain how to prepare for the electronic exchange of safety reports

Reporting in E2B(R3) format

- Implement electronic submission for both premarket and postmarket safety report using ICH E2B(R3) data standard
- Separate Submission Path and Business Rules for permarket and postmarket safety reports
- All Technical Specification documents posted on FAERS Electronic Submission* web page
- All communication via FAERS Electronic Submission* web page on FDA.gov

*https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions

Approach to Triage ICSRs via ESG



*Postmarket ICSR destination is same for CDER and CBER (excluding vaccine)

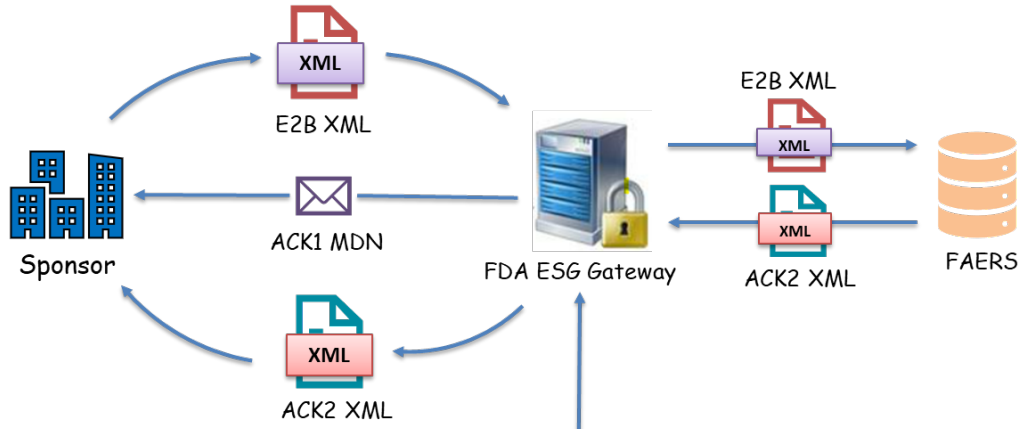
Separate Submission Path

- Section N.1: Transmission Identification
  - Batch Receiver Identifier (N.1.4) and Message Receiver Identifier (N.2.r.3)

		AS2 Header	Routing ID	N.1.4 Value	N.2.r.3 Value
Premarket	CDER IND ICSR	Destination: "CDER" XML Files: AERS_PREMKT_CDER	XML Files: FDA_AERS_PREMKT_CDER	ZZFDA_PREMKT	CDER_IND
	CBER IND ICSR	Destination: "CBER" XML Files: AERS_PREMKT_CBER	XML Files: FDA_AERS_PREMKT_CBER	ZZFDA_PREMKT	CBER_IND
	CDER IND-exempt BA/BE ICSR	Destination: "CDER" XML Files: AERS_PREMKT_CDER	XML Files: FDA_AERS_PREMKT_CDER	ZZFDA_PREMKT	CDER_IND_EXEMPT_BA_BE
Postmarket	Postmarket ICSR	Destination: "CDER" XML Files: AERS	XML Files: FDA_AERS	ZZFDA	CDER

Submission Methods

Option A:
via Database-to-Database Transmission



OR

Option B:
via Safety Reporting Portal (SRP)

SRP requires Sponsors to register and receive login credentials

Safety Reporting Portal (SRP)

- **SRP Intended for**
  - Sponsors and CROs without infrastructure for direct ESG (gateway-to-gateway) submission
  - Individual reports only; no batch reporting via SRP
  - Can be used for both commercial and research INDs safety reporting
  - Not available for vaccine reporting
- **If CRO**
  - Separate account needed for each sponsor/license holder

Safety Reporting Portal (SRP)

- **Post-market and premarket reporting**
  - Maintained separately—select up front, can navigate between them
  - Complete an on-line form
  - Do not upload E2B R3 XML via SRP
  - Emails acknowledgement on submission – keep for records
- **“Free” (no added cost to use)**
- **Availability**
  - Both SRP and E2B R3 for premarket submission available at the same time
  - No additional action required by existing SRP users for postmarket reporting
- Contact FAERSESUB@fda.hhs.gov to request an SRP account

E2B (R3) FDA Implementation Package

Filename:	FDA Regional Implementation Guide for E2B(R3) Electronic Transmission of Individual Case Safety Reports for Drug and Biological Products.pdf (August 2022)
Content:	• Purpose of this technical specifications document is to assist submitters transmitting electronic ICSRs with attachments to the (FAERS) database • Describes FDA's technical approach for submitting ICSRs, for incorporating its regionally controlled terminology, and for implementing regional extensions that are not in ICH ICSR IG

Filename:	FDA E2B(R3) Core and Regional Data Elements and Business Rules – Version 1.6.xlsx (January 2024)
Content:	• Provides a comprehensive list of core ICH and FDA regional data elements, data element attributes, conformance, business rules, XPaths and acknowledgement attributes • Some of the regional data elements in this document are detailed in the FDA Regional Implementation Technical Specification for E2B(R3) • Revision History describes all the updates

E2B (R3) FDA Implementation Package

Filename: FDA E2B(R3) Forward Compatible Rules.xlsx (April 2022)

Content:
- Assist reporters and recipients in implementing systems with special focus on the recommended rules for conversion of data from regional E2B R2 and regional E2B R3
- Applicable to postmarket safety reporting

Filename: FDA ICSR XML Instances.zip (September 2023)

Content:
- This document lists the scenarios provided as FDA ICSR XML Instance and acknowledgement examples based on FDA ICH E2B(R3) Technical Specifications Document
- The zip file has a Read Me.txt file describing the different scenarios

Submission for Different Types of IND Safety Reports

- Not all IND safety reports will go to FAERS

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

Benefits of electronic submission of IND Safety Reports

No need to submit 1571 or cover letter for IND safety reports

No separate submission for cross-reported IND

Immediate acknowledgement of your ICSR submission

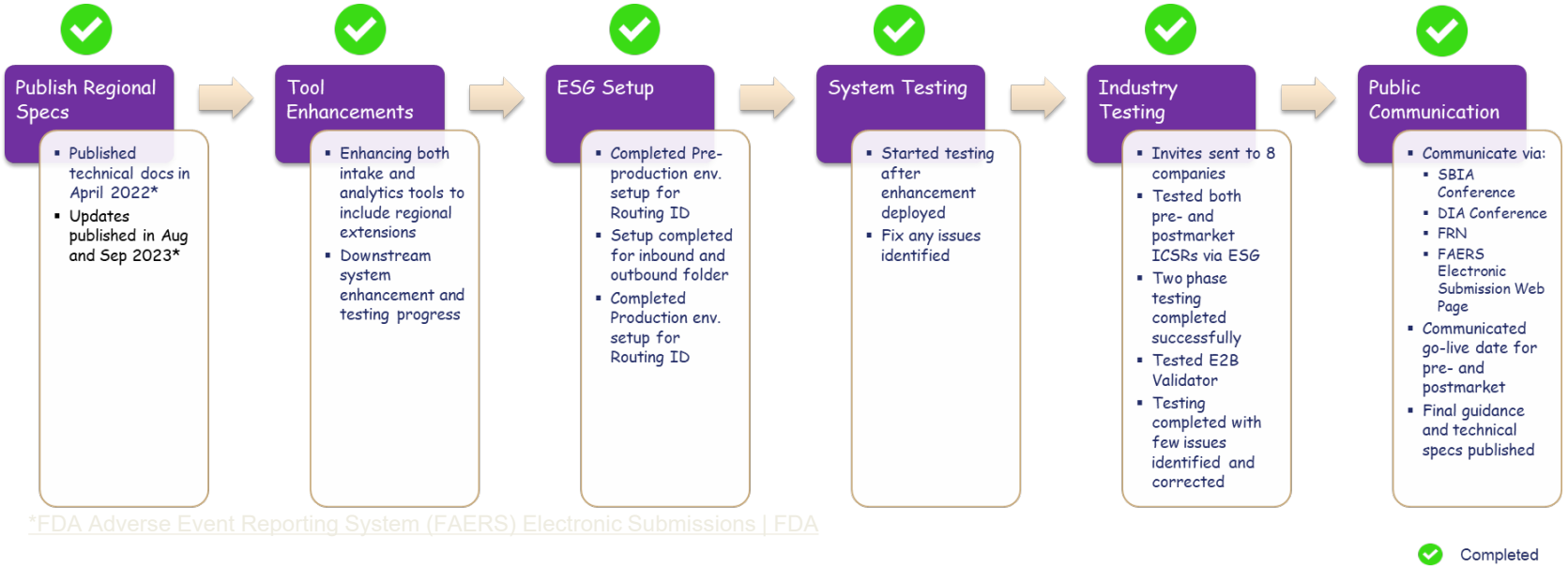
Additional Benefits

- Submit ICSR directly from your safety database
- Eliminates need to send ICSRs to your Regulatory Affairs

Updated Requirements

- Corrected XPath for FDA.G.k.12.r.11.r
- Corrected Xpath for FDA.G.k.12.r.2.r
- Corrected Xpath for FDA.C.2.r.2.8
- Removed rule for rejection "R0102"
- Updated rejection "R0008" to include C.5.4 = (1, 2 or 3) in the rule
- Updated values allowed for FDA.G.k.12.r.6 to use FDA Device Component Code

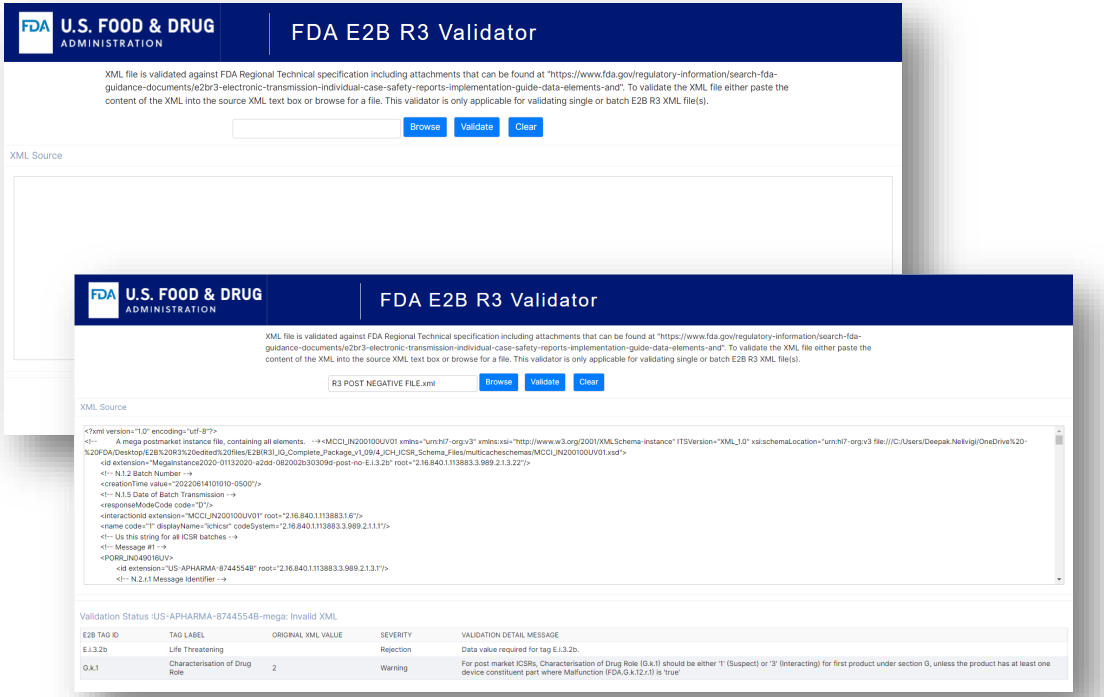
Implementation Plan and Progress



Sponsors can now submit premarket and postmarket ICSRs in **electronic format** using **E2B(R3) standard** or use the **Safety Reporting Portal (SRP)**.

Mechanism to validate E2B(R3) XML files

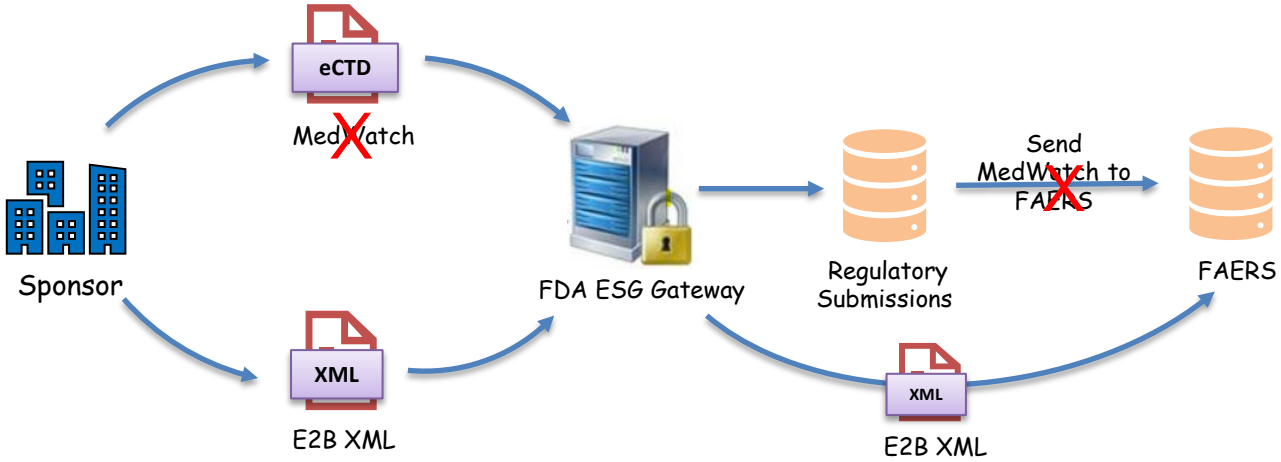
- FDA has provided the FDA E2B(R3) Validator* tool to facilitate validation of the E2B(R3) XML files generated from your safety database
- This validator has a web-based interface that enables submitter to select a E2B(R3) XML file and validate
- The validation status and results are displayed to the user



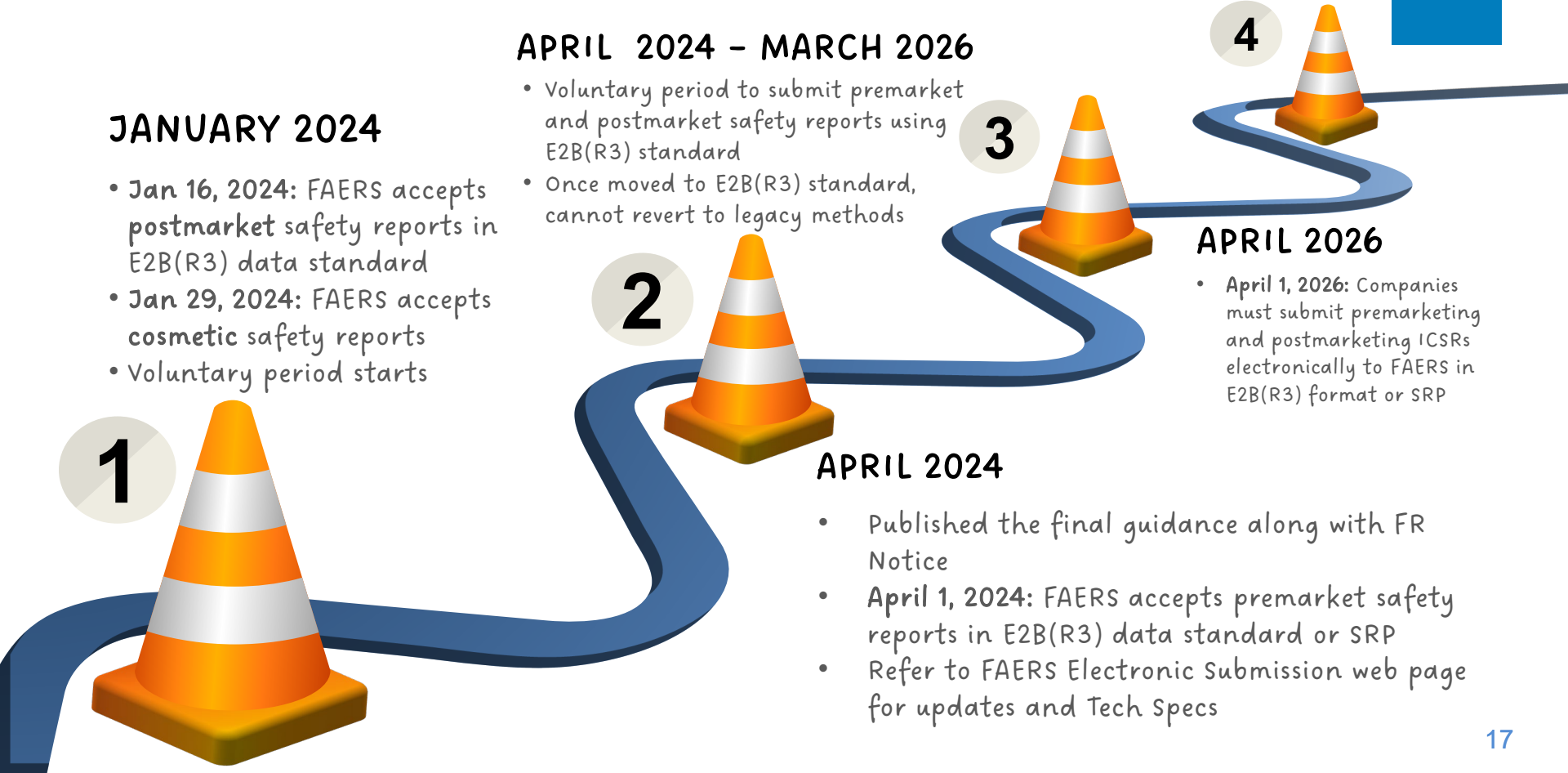
*https://faers2-validator.preprod.fda.gov/LSMV/Validator

E2B R3 Implementation Plan

- Data Submission Changes for IND safety reports



Proposed Implementation Timelines



JANUARY 2024

- **Jan 16, 2024:** FAERS accepts **postmarket** safety reports in E2B(R3) data standard
- **Jan 29, 2024:** FAERS accepts **cosmetic** safety reports
- Voluntary period starts

APRIL 2024 – MARCH 2026

- Voluntary period to submit premarket and postmarket safety reports using E2B(R3) standard
- Once moved to E2B(R3) standard, cannot revert to legacy methods

APRIL 2024

- Published the final guidance along with FR Notice
- **April 1, 2024:** FAERS accepts premarket safety reports in E2B(R3) data standard or SRP
- Refer to FAERS Electronic Submission web page for updates and Tech Specs

APRIL 2026

- **April 1, 2026:** Companies must submit premarketing and postmarketing ICSRs electronically to FAERS in E2B(R3) format or SRP

Electronic Submission Methods

Methods	Setup	Benefits
Direct to FDA Electronic Submission Gateway (ESG) using E2B(R3) standard	❑ WebTrader or AS2 (System-to-System) https://www.fda.gov/industry/electronic-submissions-gateway ❑ Generate E2B (R3) XML using the ICH Implementation Guide and FDA Regional Requirements	✓ No need to submit 1571 or cover letter for IND safety reports ✓ No separate submission for cross-reported IND ✓ Immediate acknowledgement of your submission ✓ Submit reports directly from your safety database (ESG) ✓ Eliminates need to send ICSRs to your Regulatory Affairs
Safety Reporting Portal (SRP)	❑ Contact faersesub@fda.hhs.gov to request for SRP account ❑ SRP account activation ▪ Account activated in about 7 to 10 business days from the date of request. ▪ Notified via email the Web link and account information to start reporting.	

Electronic Submission Methods

- Encourage to use the Safety Reporting Portal during the E2B (R3) implementation period
- Once ready with E2B (R3) switch over to ESG submission
- Please contact faersesub@fda.hhs.gov for questions on the specification to support your implementation

Submitter Preparedness

Download the Guidance and Technical specification documents posted on FAERS Electronic Submission web page

Review the regional extensions carefully

Prepare your safety database accounting for the regional extensions

Account for the regional forward compatibility R2 -> R3

Generate the XML files and test them using the FDA E2B Validator

Correct any issues identified by the validator

Perform Gateway setup for AS2 Header / Routing ID in pre-production as defined in the FDA technical specification

Test sample XML files that has cleared FDA E2B Validator via the pre-production Gateway

Perform Gateway setup for AS2 Header / Routing ID in production as defined in the FDA technical specification

Submitting Reports via SRP

Submitting Reports via SRP

Submitting Voluntary Safety Reports Electronically

- **MedWatch Online**
  - Health professionals can voluntarily report observed or suspected adverse events for human medical products to FDA
  - Individual reports only; no batch reporting
  - Submit via mobile device or a computer
  - MedWatch Online allows reporters to start a report and complete it within 3 days.
  - Reporters can save an incomplete report and provide an email address to receive instructions on how to complete & submit a report with Report ID and Report Date.
  - After submitting, you cannot retrieve the report and edit it

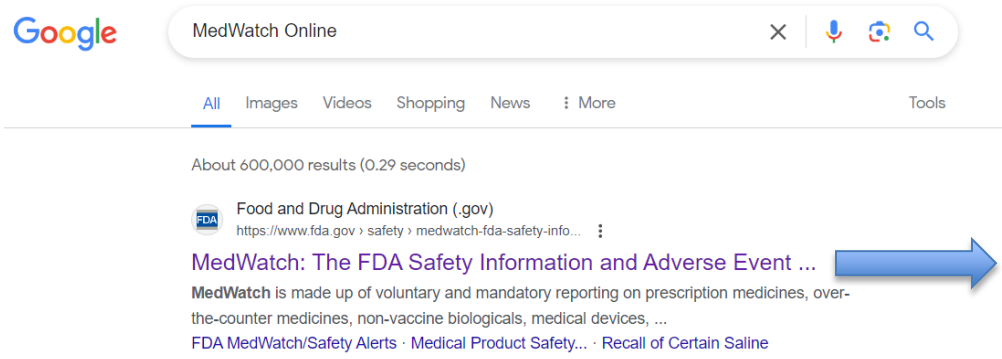
Information You Should Report to MedWatch

- **Unexpected side effects or adverse events** can include everything from skin rashes to more serious complications.
- **Product quality problems** such as information if a product isn't working properly or if it has a defect.
- **Product Use/Medication Errors that can be prevented**. These can be caused by various issues, including choosing the wrong product because of labels or packaging that look alike or have similar brand or generic names. Mistakes also can be caused by difficulty with a device due to hard-to-read controls or displays, which may cause you to record a test result that is not correct.
- **Therapeutic failures**. These problems can include when a medical product does not seem to work as well when you switch from one generic to another.

Voluntary Reporting Recommendations

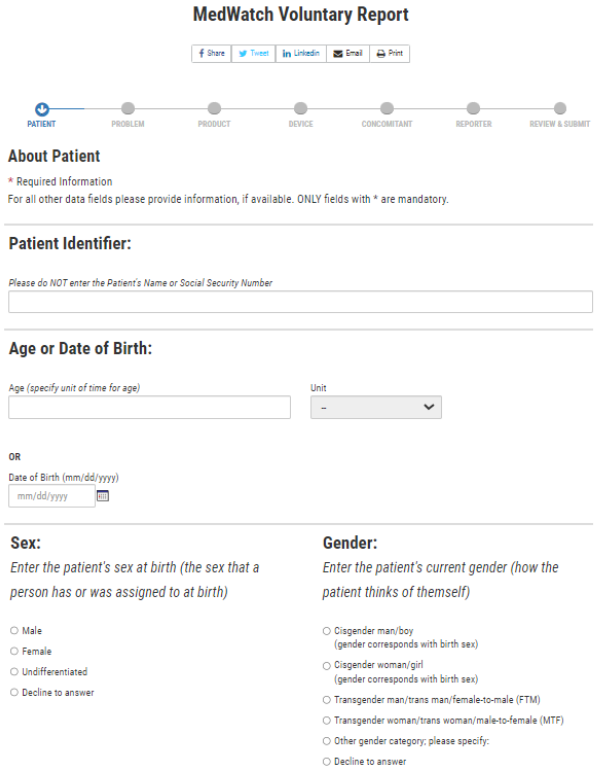
- Fill in all the information possible to support detailed analysis
- Provide detailed narrative of the incident/event
- Complete the structured data fields as much as possible
- Encourage reporters to provide their contact information in case FDA needs more information

Submitting Voluntary Safety Reports via MedWatch Online



https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program

Submitting Voluntary Safety Reports via MedWatch Online



Closing Thought

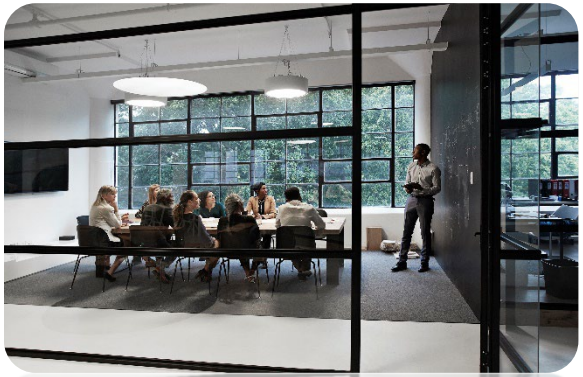
Use Safety Reporting Portal for mandatory submission of IND safety report by Investigators

Use MedWatch Online for submitting voluntary safety reports by HCPs

BA/BE Study Safety Reporting for Generic Drugs

Jung Lee, RPh, MPH
Division of Clinical Safety and Surveillance
Office of Safety and Clinical Evaluation
Office of Generic Drugs
Center for Drug Evaluation and Research

Generic Drug Pharmacovigilance: a Collaborative Process



Across FDA Centers:

- Center for Drug Evaluation and Research (CDER)
- Center for Devices and Radiological Health (CDRH)

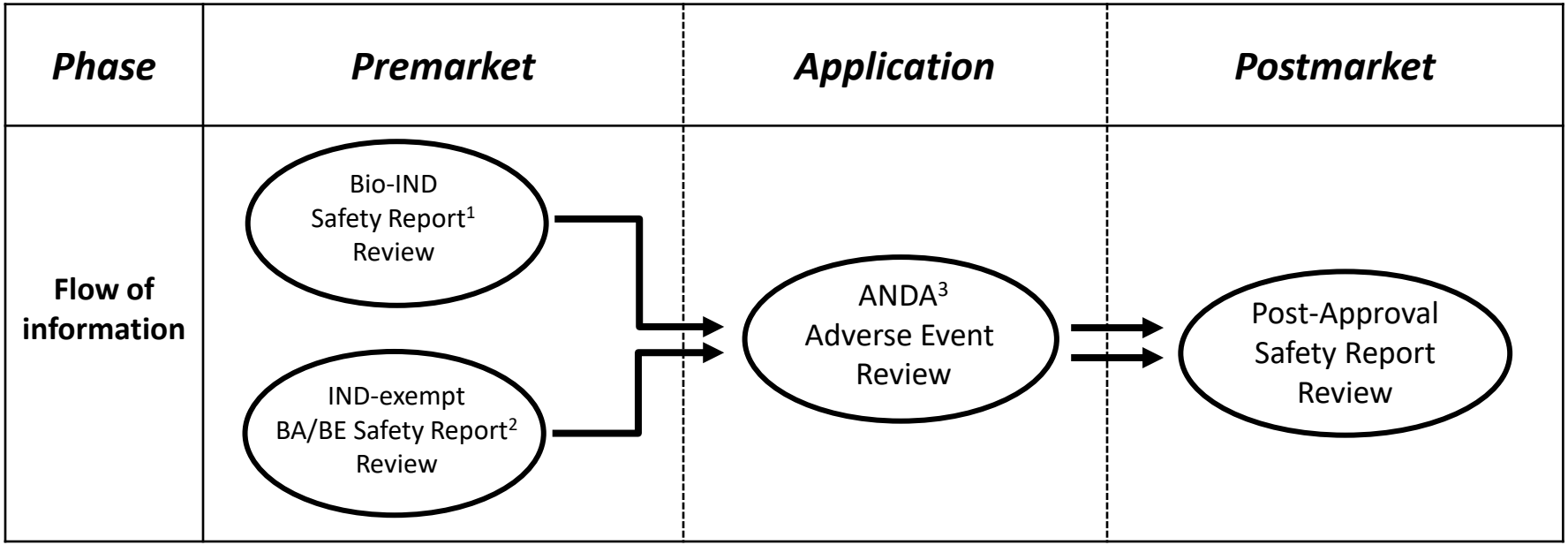
Across CDER Offices:

- Office of Generic Drugs (OGD)
- Office of Surveillance and Epidemiology (OSE)
- Office of New Drugs (OND)
- Office of Pharmaceutical Quality (OPQ)
- Office of Compliance (OC)

Across OGD Offices:

- Office of Safety and Clinical Evaluation (OSCE)
- Office of Bioequivalence (OB)
- Office of Research and Standards (ORS)
- Office of Generic Drug Policy (OGDP)
- Office of Regulatory Operations (ORO)

Generic Drug Pharmacovigilance



[1]**Bio-IND Safety Report** = A safety report submitted from a **BA/BE study conducted under an Investigational New Drug application (IND)**. Refer to MAPP 5210.5 rev. 3. (https://www.fda.gov/media/72562/download).

[2]**IND-exempt BA/BE Safety Report** = A safety report submitted from a **BA/BE study NOT conducted under an IND**.

[3]ANDA=Abbreviated New Drug Application

BA/BE Study Safety Reporting Requirements

BA/BE studies conducted under an IND

- Must meet safety reporting requirements under 21 CFR 320.31 and 312.32
- Must submit an IND safety report(s) for an event(s) that meet(s) the following conditions: 1) serious, 2) unexpected and 3) suspected adverse reaction(s) => SUSARs
- Include individual case safety reports and aggregate reports

BA/BE studies NOT conducted under an IND

- Must meet IND exemption under 21 CFR 320.31
- Must meet expedited safety reporting requirements under 21 CFR 320.31(d)(3)-

  The person conducting a BA or BE study, including any contract research organization, must notify FDA and all participating investigators of any serious adverse event [SAE] observed during conduct of the study, **regardless of whether the event is considered drug related**, as soon as possible but no later than 15 calendar days after becoming aware of its occurrence.

Generic Drug Premarket vs. Postmarket Safety Report Submission & Review Prior to 4/1/24

Report Type		Premarket		Postmarket Safety Reports
		Bio-IND Safety Reports	**IND-exempt BA/BE Safety Reports**	
Submission	Source	Sponsors *conducting* ***BA/BE studies conducted under an IND***	Drug companies or CROs conducting ***BA/BE studies NOT conducted under an IND***	Drug companies, healthcare professionals, consumers, etc.
	Format	Form FDA 3500A	Form FDA 3500A	E2B
	Route	via eCTD	via OGD Premarket email inbox, which is manually entered into the Panorama project tracking system. Initial and Follow-up also linked manually.	via database-to-database (E2B) transmission electronically or Safety Reporting Portal to the FDA Adverse Event Reporting System (FAERS)
Review		OGD/OSCE/DCSS reviews SUSARs.	OGD/OSCE/DCSS reviews SAEs. When ANDA is submitted, SAE reviews are linked to ANDA.	OGD/OSCE/DCSS analyzes and reviews safety reports in FAERS

FAERS enhancements enabled electronic submission of adverse events from premarket BA/BE studies for generic drugs!

Electronic IND Safety Reporting Requirement

- IND safety reports as Individual Case Safety Reports (ICSRs) under 745A(a) of the Federal Food Drug and Cosmetic (FD&C) Act
  - April 1, 2024: Final Guidance for Industry- *Providing Regulatory Submissions in Electronic Format: IND Safety Reports*
  - Sponsors of commercial INDs required to submit specified IND safety reports to FAERS have two options:
    - Electronic Submissions Gateway (E2B Transmission)
    - Safety Reporting Portal
  - Begin voluntary submissions in E2B(R3) format (April 1, 2024)
  - Requirement 24 months after **Final** Guidance publication (April 1, 2026)

- Bio-IND Safety Reports (from **BA/BE studies conducted under an IND**) must meet the electronic ICSR reporting requirement under 745A(a) of the FD&C Act.

IND-exempt BA/BE Safety Reporting

A. Options for submission:

1. May continue to email Form FDA 3500A to OGD-PremarketSafetyReports@fda.hhs.gov.

2. FAERS enhancements for premarket safety reports are available:
   - E2B format is a new option available to notify the FDA of an SAE(s) from **BA/BE studies NOT conducted under an IND** **required** under 21 CFR 320.31(d)(3).

   - Options for submitting IND-exempt BA/BE Safety Reports as ICSRs in E2B(R3) format
     - **Electronic Submission Gateway (E2B Transmission)** **<- Today's Focus**
     - Safety Reporting Portal

Voluntary Electronic Submission of IND-exempt BA/BE Safety Reports

B. Electronic Submission Gateway (E2B Transmission) Option:

1. Understand requirements[4,5]

- *FDA Regional Implementation Guide for E2B(R3) Electronic Transmission of Individual Case Safety Reports for Drug and Biological Products Guidance for Industry Technical Specifications Document* (hereafter referred as Technical Specifications Document)
- ***Final*** *Guidance for Industry*: *Electronic Submission of Expedited Safety Reports from IND-exempt BA/BE studies (April 2024)*

Additional resources:

- *Specifications for Preparing and Submitting Electronic ICSRs and ICSR Attachments*
- *E2B(R3) Electronic Transmission of Individual Case Safety Reports (ICSRs) Implementation Guide –Data Elements and Message Specification*
- *FDA E2B(R3) Core and Regional Data Elements and Business Rules*

[4] Search for FDA Guidance Documents (https://www.fda.gov/regulatory-information/search-fda-guidance-documents).

[5] FAERS Electronic Submissions-standards (https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions-e2br3-standards).

Voluntary Electronic Submission of IND-exempt BA/BE Safety Reports

2. Prepare IT system

- FAERS started accepting **premarket ICSRs in E2B (R3) format on April 1, 2024.**
- Learn the **specifications for preparing and submitting electronic submission** of ICSRs.
- Need an account with FDA to submit ICSRs electronically.
- Notify the FAERS electronic submission coordinator at faersesub@fda.hhs.gov to create an account.

3. Obtain pre-assigned ANDA number ('Pre-ANDA')[6,7]

- Request using CDER NextGen Portal prior to:
  -> Submitting an SAE(s) from the BA/BE study **or**
  -> Starting subject recruitment for the BA/BE study

[6] Requesting a Pre-Assigned Application number (https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/requesting-pre-assigned-application-number).
[7] CDER NextGen Portal (https://cdernextgenportal.fda.gov/Login_CDER?ec=302&startURL=%2Fs%2F).

Voluntary Electronic Submission of IND-exempt BA/BE Safety Reports

4. Identify ICSRs from IND-exempt BA/BE studies

a. Include submission path business rules

		AS2 Header	Routing ID	N.1.4 Value	N.2.r.3 Value
Premarket	CDER IND ICSR	Destination: "CDER" XML Files: AERS_PREMKT_CDER	XML Files: FDA_AERS_PREMKT_CDER	ZZFDA_PREMKT	CDER_IND
	CBER IND ICSR	Destination: "CBER" XML Files: AERS_PREMKT_CBER	XML Files: FDA_AERS_PREMKT_CBER	ZZFDA_PREMKT	CBER_IND
	CDER IND-exempt BA/BE ICSR	**Destination: "CDER" XML Files: AERS_PREMKT_CDER**	**XML Files: FDA_AERS_PREMKT_CDER**	**ZZFDA_PREMKT**	**CDER_IND_EXEMPT_BA_BE**
Postmarket	Postmarket ICSR	Destination: "CDER" XML Files: AERS	XML Files: FDA_AERS	ZZFDA	CDER

Message receiver identifier: N.2.r.3 & Batch receiver Identifier: N.1.4

b. Choose element value=2 for 'Report from study' as the 'Type of Report' in Data Element C.1.3

Data element	Title	Element value
C.1.3	**Type of Report**	**2=Report from study**

Voluntary Electronic Submission of IND-exempt BA/BE Safety Reports

4. Identify ICSRs from IND-exempt BA/BE studies

c. Submit Pre-assigned ANDA ('Pre-ANDA')[8] number

Data element	Title	Element values
FDA.C.5.5b	**Pre-ANDA Number where AE Occurred**	**Numeric**

- Max Length: 10
- Data Type: Numeric (N) (For example, "234567")
- **Conformance: Conditional-Required**
- Business Rule:
  - If *Type of Report (C.1.3)* is 2=Report from study and

    Message Receiver Identifier (N.2.r.3) = "CDER_IND_EXEMPT_BA_BE"

    then *Pre-ANDA Number where AE Occurred (FDA.C.5.5b)* is required.
  - Required to be a valid Pre-ANDA number for processing and routing

[8]Although these are pre-assigned ANDA numbers and the term 'Pre-ANDA' is being used with these numbers, each submission may or may not be associated with the Office of Generic Drug's Pre-ANDA Program (https://www.fda.gov/drugs/generic-drugs/pre-anda-program) for complex drug products .

Voluntary Electronic Submission of IND-exempt BA/BE Safety Reports

5. Identify drug substance

Data element	Title	Element values
G.k.2.2	Medicinal Product Name as Reported by the Primary Source	Medicinal product name (free text)
G.k.2.3.r.1	Substance/Specified Substance Name	Drug substance name (free text)

- Report medicinal product name (proprietary name) using data element G.k.2.2 if available.
- Report drug substance name in data element G.k.2.3.r.1
- Report only drug substance name if medicinal product name (proprietary name) is not available.

6. Characterize drug's role

Data element	Title	Element values
G.k.1	Characterization of Drug Role	1 = Suspect 2 = Concomitant 3 = Interacting 4 = Drug not administered

Voluntary Electronic Submission of IND-exempt BA/BE Safety Reports

7. Inform Test vs. Reference* Unique to generic drugs

Data element	Title	Element values
FDA.G.k.10.a.r	**FDA Additional Information on Drug**	**1 = Test** **2 = Reference** **nullFlavor=NA**

- Max Length: 2
- Data Type: Numeric (N)
- **Conformance: Conditional-Required**
- Business Rule:
  - If *Pre-ANDA Number where AE Occurred (FDA.C.5.5b) is present, then the Observation Code: (Value allowed: 1, 2) must be used to describe the drug's role in the IND-Exempt BA/BE study.*
  - *Use nullFlavor: NA for all other drugs or if information is not available.*

Voluntary Electronic Submission of IND-exempt BA/BE Safety Reports

8. **Other considerations**
   - Refer to the Technical Specifications Document for information on:
     - ICH E2B data elements
     - Regional specifications

9. **Check examples if needed**
   - FDA ICSR XML instances with Read Me descriptions are available at the FAERS electronic submission web page[9]

10. **Look for FDA Notification of Receipt**
    - Review Acknowledgements & Notifications indicating the status of submission, successful acceptance or rejection with reason for rejection after submission.
    - Contact the FAERS electronic submission coordinator at faersesub@fda.hhs.gov if the acknowledgements or notifications are not received.

[9] FAERS Electronic Submissions-standards (https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions-e2br3-standards).

Voluntary Electronic Submission of IND-exempt BA/BE Safety Reports

C. Advantages:

1. Non-public space

- FAERS uses specific data fields (such as E2B data element FDA.C.5.5b for IND-exempt BA/BE Safety Reports) to identify pre-market reports and sequester them from postmarket reports that are available in the public portal.

2. Increased efficiencies

- One submission method
  1) IND-exempt BA/BE safety reports
  2) Bio-IND safety reports
  3) Postmarket safety reports
- Automated confirmation of receipt

3. Support generic drug pharmacovigilance

- Improved generic drug signal detection
- Enhanced data management & analytics

Acknowledgements

- Howard Chazin, OGD/OSCE/DCSS Director
- Debra Catterson, OGD/OSCE/DCSS Deputy Director
- James Osterhout, OGD/OSCE/DCSS Senior Data Scientist
- Suranjan De, Office of Surveillance and Epidemiology/ Regulatory Science Staff/Deputy Director

References

Document / Web Page	Accessible At
FDA Adverse Event Reporting System (FAERS) Electronic Submissions –Web page	https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions
FDA Regional Implementation Guide for E2B(R3) Electronic Transmission of Individual Case Safety Reports for Drug and Biological Products (Apr 2024)	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-regional-implementation-guide-e2br3-electronic-transmission-individual-case-safety-reports-drug
FDA E2B(R3) Core and Regional Data Elements and Business Rules v1.6 (Apr 2024)	https://www.fda.gov/media/157982/download
FDA E2B(R3) Forward Compatible Rules (Apr 2022)	https://www.fda.gov/media/157993/download
FDA ICSR XML Instances (Feb 2024)	https://www.fda.gov/media/157983/download
Electronic Submission of IND Safety Reports - Technical Conformance Guide (Apr 2022)	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/electronic-submission-ind-safety-reports-technical-conformance-guide
Electronic Submission of Expedited Safety Reports From IND-Exempt BA/BE Studies - Draft Guidance for Industry (Apr 2024)	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/electronic-submission-expedited-safety-reports-ind-exempt-babe-studies-guidance-industry
Preparing for the electronic exchange of safety reports	https://www.fda.gov/media/177186/download?attachment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