U.S. FOOD & DRUG ADMINISTRATION

Reporting premarket and postmarket safety reports to FDA using ICH E2B(R3) standards

NOVEMBER 7, 2023

Disclosure

- We have no financial relationships to disclose
- We will not discuss any off-label or investigational use

Session Overview

Description

- This session will review 1) updates to requirements for submitting safety reports for INDs, IND-exempt BA/BE studies, and approved drug and therapeutic biologic products (excluding vaccine) using the ICH E2B(R3) format; 2) implementation plan and progress; 3) testing updates; and 4) FDA readiness and submitter preparedness

Objectives

- 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
- Understand updated regional extensions that are key for postmarket, IND, and IND-exempt BA/BE safety reporting
- Communicate implementation status and readiness

Agenda

- **Recap from previous Public Meeting**
- Implementation Plan and Progress
- External and Internal Testing Update

-- BREAK --

- Regional Extension Updates
- FDA Readiness
- Submitter Preparedness
- Summary

Recap from Previous Public Meeting

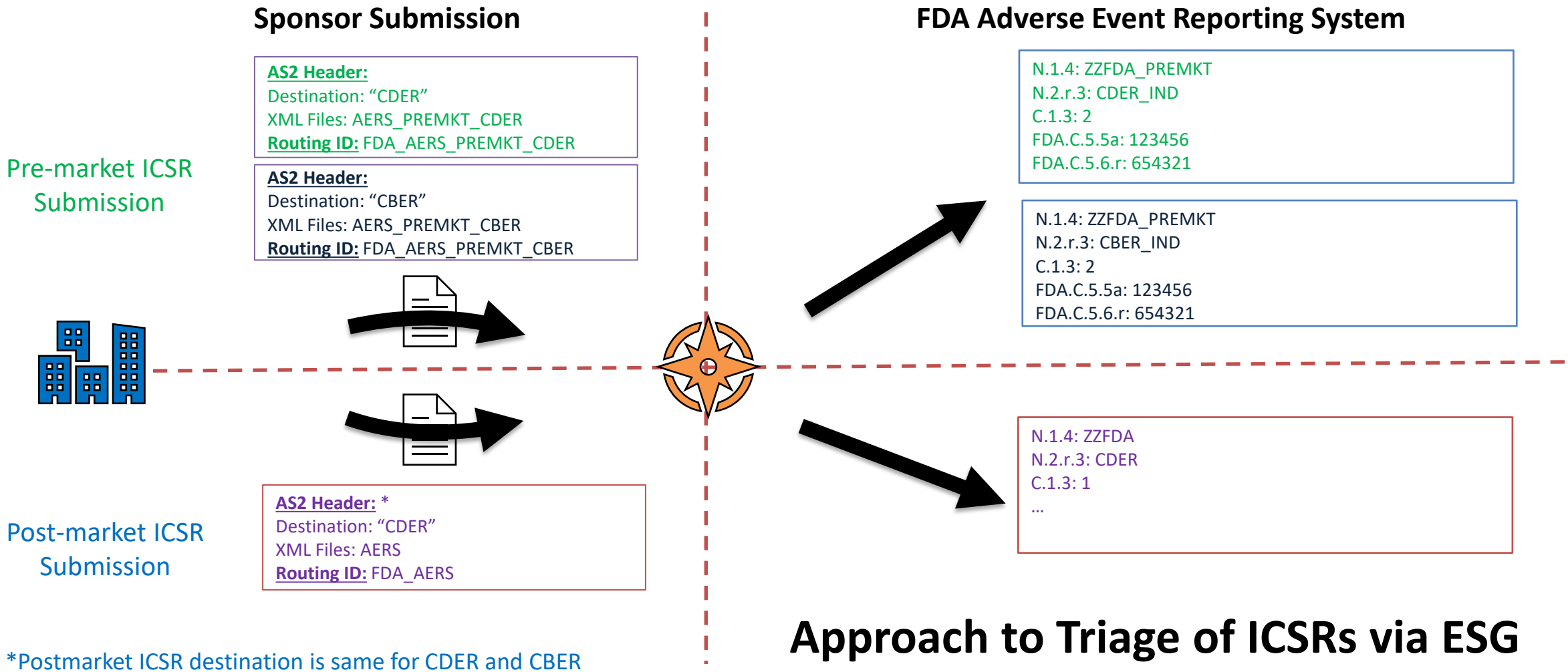
Recap from Previous Public Meeting

- Information on previous meeting
  - Date: April 4 9:00AM – 3:00PM
  - Meeting agenda, presentation slides and recording available at https://www.fda.gov/drugs/news-events-human-drugs/electronic-submission-adverse-event-reports-fda-adverse-event-reporting-system-faers-using

Recap from Previous Public Meeting

- Implement E2B(R3) submission for both **premarket and postmarket** safety report **at the same time**
- **New date for voluntary reporting** will be communicated on FAERS Electronic Submission web page (https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions)
- Refer to **FDA E2B(R3) Core and Regional Data Elements and Business Rules** document for all core ICH and regional extension
- Use of **Controlled Terminology** (e.g., EVS, GSRS etc.)
- **Separate** Submission Path and Business Rules (IND vs IND-exempt BA/BE vs post market)
- **Submission Methods and Mechanisms** based AS2 header and Routing ID

Recap from Previous Public Meeting



Approach to Triage of ICSRs via ESG

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

Recap from Previous Public Meeting

Separate Submission Path Business Rules

- Section N.1: ICH ICSR 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

For all *Message Receiver Identifier (N.2.r.3)* = CDER, the *Batch Receiver Identifier (N.1.4)* must be "ZZFDA".

For all *Message Receiver Identifier (N.2.r.3)* = CDER_IND or CBER_IND or CDER_IND_EXEMPT_BA_BE, the *Batch Receiver Identifier (N.1.4)* must be "ZZFDA_PREMKT"

Recap from Previous Public Meeting

- Discussed **regional extensions** for IND, IND-exempt BA/BE, and postmarket safety reporting
- Plan for **validation and implementation** – E2B validator will be posted on FAERS Electronic Submission web page
- Regional specific **rejection and warning rules**
- Use of **FDA OIDs** in regional extensions
- **R2 to R3 forward compatibility** on regional elements – applicable to postmarket safety reports

Information on ESG NextGen

ESG NextGen offers **Application Programming Interface (API)** assistance with tasks including initial and subsequent submissions, status inquiries, and other service functions as part of the File Submission process. All of the ESG NextGen APIs are built using the RESTful standard for ease of integration. ESG NextGen's API platform provides security enforcement to ensure data exchange is secure

- ❑ With ESG NextGen, industry can
  - use API to generate an API submission ID
  - create submission payload, and
  - submit the payload for FDA to process

- ❑ The combination client ID and secret key is a unique identifier that each industry partner will use to submit data to the FDA.

- ❑ FDA will publish more details in the future, but the draft specifications info can be found here: ESG NextGen Draft API Specification | FDA (https://www.fda.gov/industry/esg-next-generation/esg-nextgen-draft-api-specification)

- ❑ FDA will also disseminate testing information in advance so industry partners can update their respective process/system and be prepared for the testing

Comments and Questions

1. Question: The latest MedWatch form has new elements (for example, gender versus sex at birth). The current proposed R3-regional implementation guide (or technical specification - preference?) does not have this data element. Are there plans to update the R3-regional implementation guide (or technical specification) to add the new gender data element?

   Response: FDA is considering updating the E2B(R3) regional implementation guide (or technical specifications document) to include gender data. Guidance documents represent the Agency's current thinking on a particular subject, and once further guidance is published, gender may be incorporated into the data elements

2. Question: Once 7-day or 15-day IND safety reports are submitted via either submission method, the ESG or the SRP, does the sponsor still need to submit in eCTD format or notify the FDA project manager?

   Response: Once the IND safety reports are submitted electronically via Safety Reporting Portal (SRP) or Electronic Submissions Gateway (ESG), submitters do not need to submit them in eCTD format or notify FDA project manager.

3. Question: For a small business sponsor that has an ESG account but does not have inhouse XML capability, are they able to submit ICSRs through the SRP?

   Response: Yes, they can submit using the Safety Reporting Portal (SRP).

Comments and Questions

4. Question: If we are cross-reporting ICSRs, which IND# should be in the header? The IND for the study in which the event occurred or the IND for which we are submitting to?

   Response: Sponsors should use the IND number under which the clinical trial where the event occurs is conducted as the primary IND number in the indicated E2B data field

5. Question: Can we upload an xml file in SRP instead of entering data manually?

   Response: No, data in an ICSR must be entered manually into the SRP.

6. Question: Is there any work being done to sync the required fields between FAERS, VAERS, and MedWatch?

   Response: Yes, FAERS has harmonized the data elements between FAERS, VAERS, and MedWatch to the extent possible.

7. Question: Please confirm if FDA.C.1.7.1 must be set to the value 6 (7-Day) when submitting follow-up information to an unexpected fatal or life-threatening adverse reaction report from a clinical study?

   Response: Yes, that is correct

Comments and Questions

8. Question: Regarding the Medicinal Product Name as Reported, presumably it would be preferred to use the coded Product Description/Local Tradename from a Company Product Library rather than the verbatim Medicinal Product Name as Reported. Is this correct?

   Response: Please refer to the FDA Regional Implementation Guide (or technical specifications document) Section 4.2.5.3, Data Element G.k.2.2: Medicinal Product Name as Reported by the Primary Source. FDA would prefer to receive the United States local medicinal product name which would be the same name submitted in SPL format as the standard format for the exchange of drug listing information. This supports product auto coding of the submitted safety reports.

9. Question: Regarding the data element FDA.G.k.13.r, FDA Specialized Product Category, for combination products, would this be entered for any combination product ICSR (not just malfunction or 5-day)? Also, would this be provided in addition to the FDA Procode?

   Response: Yes, the FDA Specialized Product Category for combination product is applicable to all ICSRs for combination products.

Comments and Questions

10. Question: Could you please confirm that when cross reporting IND Safety Reports to FAERs, sponsors need only to submit one report to the primary IND and provide a list all other affected INDs?

    Response: Yes, that is correct. Sponsors should use the Data Element FDA C.5.5a: IND Number Where AE Occurred to report the IND number under which the clinical trial where the event occurred. Sponsors should also use the indicated repeatable Data Element FDA.C.5.r.6: IND Number of Cross-Reported IND to submit individually other relevant INDs.

11. Question: Is the mechanism to validate E2B(R3) available only for WebTrader accounts? Will anyone with a gateway-to-gateway connection be able to access the validator tool?

    Response: The FDA E2B(R3) validator tool is independent of the submission mechanism. Submitters may validate XML files prior to submitting ICSRs to the Agency. If rejected, submitters may adjust their XML generator and then submit the ICSR via WebTrader or ESG

12. Question: Does the E2B(R3) Validator show both soft validation and hard validation? Suppose if we receive validation error, does this mean it will fail the transmission of the case?

    Response: The E2B(R3) Validator show both rejection and warning. Any rejection will send a negative acknowledgement to the submitter and the ICSR will not transmit to FDA.

13. Question: Can premarket ICSRs be submitted via ESG database to database during the voluntary submission period?

    Response: Yes, during the voluntary period premarket ICSRs can be submitted via ESG in E2B(R3) format.

Comments and Questions

14. Question: What do you mean when saying a single batch must have the same sender? Can you please provide an example since all ICSRs will be sent by sponsors (i.e., same sender)?

    Response: This applies to a Contract Research Organization (CRO) submitting reports for multiple sponsors or application holders. When more than one ICSR is sent in one batch then all the ICSRs must have the same Message Sender Identifier information (Data Element N.2.r.2).

15. Question: Regarding sending Literature attachments, many times we do not have the final Literature document ready at the time of submission due to various reasons e.g., translation required. When we would send the final Literature attachment, would this be sent as an amendment?

    Response: Please send the final literature attachment as a follow-up ICSR. For more information about reporting follow-up postmarketing ICSRs, please refer to the Guidance for Industry: Providing Submissions in Electronic Format—Postmarketing Safety Reports.

16. Question: Can we still submit FDA codes for devices or IMDRF codes only?

    Response: You can submit either FDA codes or International Medical Device Regulators Forum (IMDRF) codes for the Device Problem Code.

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- **Implementation Plan and Progress**
- External and Internal Testing Update

-- BREAK --

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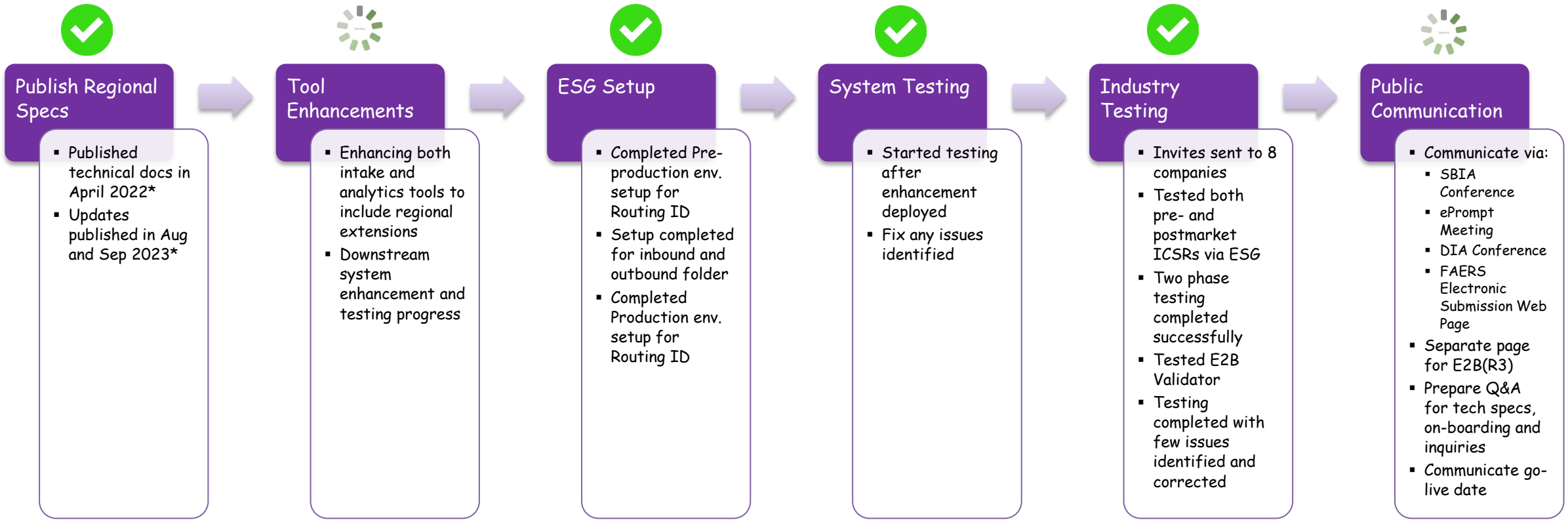
Implementation Plan and Progress

Implementation Plan and Progress



*FDA Adverse Event Reporting System (FAERS) Electronic Submissions | FDA

Completed In Progress

Sponsors should continue to submit premarket ICSRs in the eCTD format and postmarket ICSRs to FAERS in E2B(R2) format until FAERS is ready for E2B(R3) submissions

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U.S. FOOD & DRUG ADMINISTRATION

External and Internal Testing Update
FAERS E2B(R3) Industry Testing

External and Internal Testing Updates

- Internal Testing - Multiple scenario testing conducted
  - Premarket
    - IND safety reports including aggregate safety reports and reports with cross referenced INDs and
    - IND-exempt BA/BE safety reports
  - Postmarket
    - Safety reports including combination products and attachments
    - Postmarket study reports
  - Tested for both positive and negative acknowledgements

External and Internal Testing Updates

- External Testing conducted in 2 Phases
- Phase I testing - Submit E2B(R3) ICSRs along with regional extensions
- Testing Participants and File Submissions
  - Industry testing started on July 5th, 2023, with 7 companies as participants
  - We received 169 E2B(R3) XML files (premarket and postmarket ICSRs) from four (4) companies.

External and Internal Testing Updates

❑ Findings During Phase I Testing

- External connection URL issue with E2B(R3) validator tool for Industry Users
- ESG Routing ID and AS2 Header changed to receive industry file successfully – Use TST prefix
- Dose Units not accepting UCUM codes
- Updating the rejection to warning for xml tag C.1.10.r for non-aggregate reports
- Country code EU not accepted for few country tags
- Currently only 6 digits IND numbers are accepted. We will update system to accept 5 digits IND numbers soon.
- Ability to download to the list of warnings and rejections shown in E2B Validator tool to excel.

External and Internal Testing Updates

❑ Recommendations from Phase I testing

- **FAERS Test Environment Availability:** FDA's ESG Gateway and FAERS Testing environment will remain open for use. You can continue to submit E2B(R3) files for your internal testing and development efforts
- **Data Setup in FAERS :** FAERS team is available to provide data setup
- **Communication:** If you have any questions or need further clarification, please do not hesitate to reach out to us via email to faersesub@fda.hhs.gov and the subject line to start with "**E2B(R3) Testing**"
- **1:1 meetings:** If needed, we are available to setup 1:1 meetings for further discussion and clarification
- **Findings addressed** for retesting in Phase II

External and Internal Testing Updates

- Phase II testing – Retest issues reported and performance testing
  - **Retest** the issues reported
  - **Use the same ESG Routing IDs/AS2 Headers** setting during file submission process
  - **Rigorous testing -** Submit files for the below scenarios:
    - Batch files with multiple ICSRs (batch files can include multiple cases)
    - Attachments in all R3 supported format
    - Large size files
  - **Test E2B Validator Tool** updated with recommendations

Issues resolved from Phase I testing

The requested changes and issues were resolved for Phase II Testing	Change Requests: **1. Updated rejection "R0028" to warning "W0010"** Changed the existing rejection to a warning, if • Type of Report (C.1.3) = 2 (Report from study) and • IND Number where AE Occurred (FDA.C.5.5a) is provided and • Identification Number of the Report Which Is Linked to This Report (C.1.10.r) is populated then • Patient (name or initials) (D.1) must have the value 'AGGREGATE'". **2. System must allow submission of IND numbers with less than 6 digits** System rejected the pre-market reports if the IND number was less than 6 digits. The change now will accept a valid IND number up to 10 numeric characters.

Issues resolved from Phase I testing

The requested changes and issues were resolved for Phase II Testing	Change Requests: **3. Post market study report logic – submit 2 reports** <u>Premarket report:</u> • Batch Receiver Identifier (N.1.4) = ZZFDA_PREMKT • Message Receiver Identifier (N.2.r.3) = CDER_IND or CBER_IND • Type of Report (C.1.3) = 2 (Report from study) • Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4) = 1 (Clinical trials) <u>Postmarket report:</u> • Batch Receiver Identifier (N.1.4) = ZZFDA • Message Receiver Identifier (N.2.r.3) = CDER • Type of Report (C.1.3) = 2 (Report from study) • Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4) = 1 (Clinical trials)

Issues resolved from Phase I testing

The requested changes and issues were resolved for Phase II Testing	Change Requests: **4. FDA.G.k.12.r.11.r Remedial Action Initiated tag update** Earlier system was providing warning for Remedial Action Initiated [FDA.G.k.12.r.11.r] when Malfunction [FDA.G.k.12.r.1] is 'true' and Local Criteria Report Type is '4 (5 Day)'. System will now generate a warning if Remedial Action Initiated [FDA.G.k.12.r.11.r] is not provided when Malfunction [FDA.G.k.12.r.1] is 'true' and Local Criteria Report Type is '5 (30 Days)'.

Issues resolved from Phase I testing

The requested changes and issues were resolved for Phase II Testing	Defects or Issues: 1. **UCUM codes not accepted for Dose units (G.K.4.R.1b)** FAERS has been updated to accept UCUM codes for Dose units (G.K.4.R.1b). 2. **Date of Death (D.9.1) null flavor not accepted when Results in Death (E.i.3.2a) is true** Based on the data rule for pre-market report, "If Results in Death (E.i.3.2a) is true then Date of Death (D.9.1) is required". FAERS has been updated to accept nullFlavor for Date of Death (D.9.1) when Results in Death (E.i.3.2a) is true. 3. **EU country code not accepted country tags** FAERS not accepting country code EU for few tags. FAERS has been updated to accept value “EU”.
E2B Validator Tool update	E2B Validator UI Changes: Added indicator “Severity” to indicate if the XML file has any warning or rejection.

External and Internal Testing Updates

❑ Frequently Asked Questions (FAQ)

- **When will FDA start accepting ICSRs in E2B(R3) format?**
  Response: Yes, during the voluntary period you may begin submitting both pre and post market reports in R3-format. We anticipate that companies may begin to accept postmarketing ICSRs using E2B(R3)-format in January 2024. We hope the final Guidance for Industry: Providing Regulatory Submissions in Electronic Format: IND Safety Reports is published around March 2024, and we will begin accepting premarketing ICSRs at that time.

- **Will I be able to submit R3 files for both pre and post market reports prior to the mandatory reporting start date?**
  Response: Yes, during the 2-year voluntary period you be able to submit both pre and post market reports.

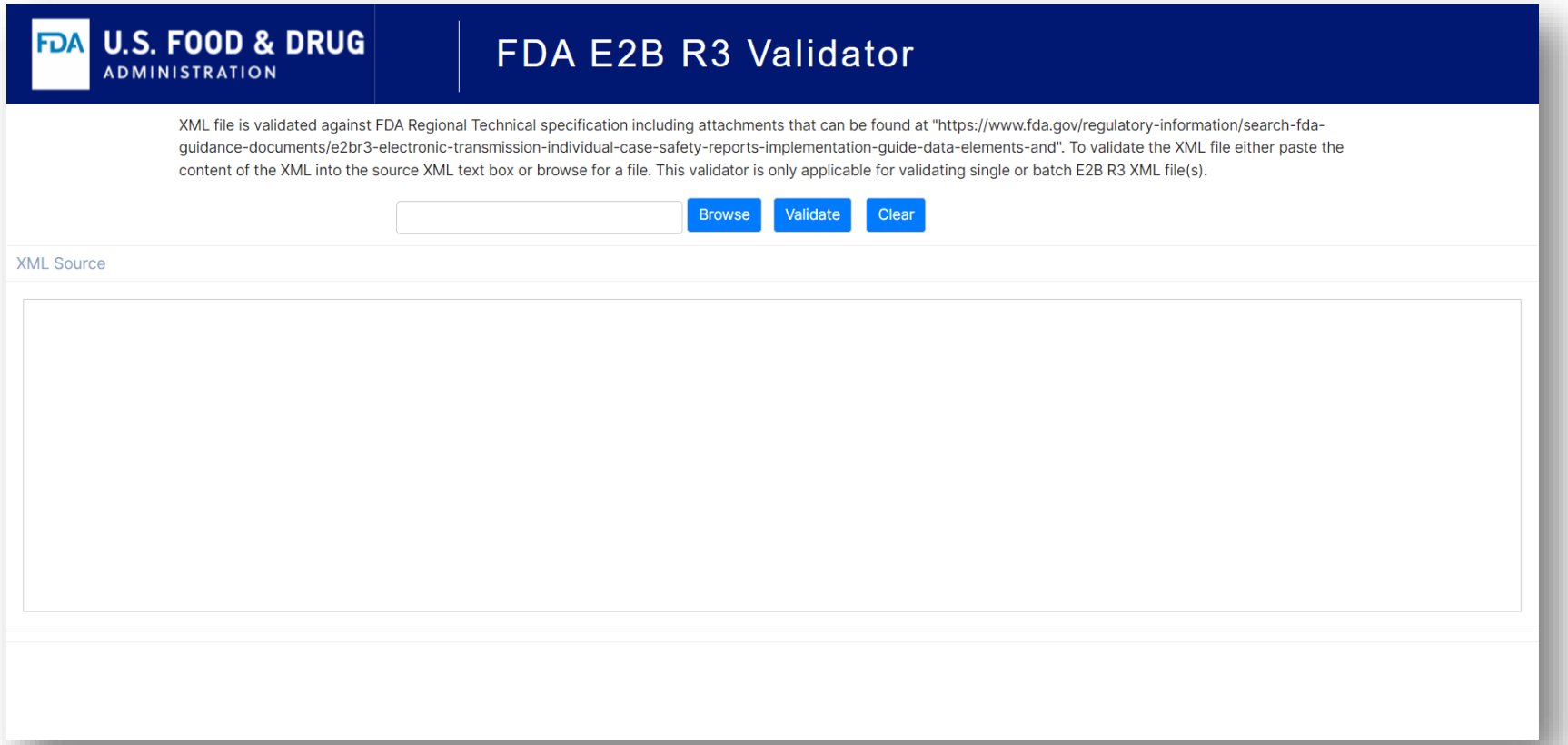
- **Can a company choose to submit post market report in R3 and paper for premarket reports prior to compliance date?**
  Response: Yes, a company can choose to submit postmarket safety reports in R3 format and premarket safety report using eCTD format prior to the compliance date.

- **When will the E2B(R3) Validator tool be available**
  Response: The E2B(R3) Validator tool will be available starting Nov 20, 2023.

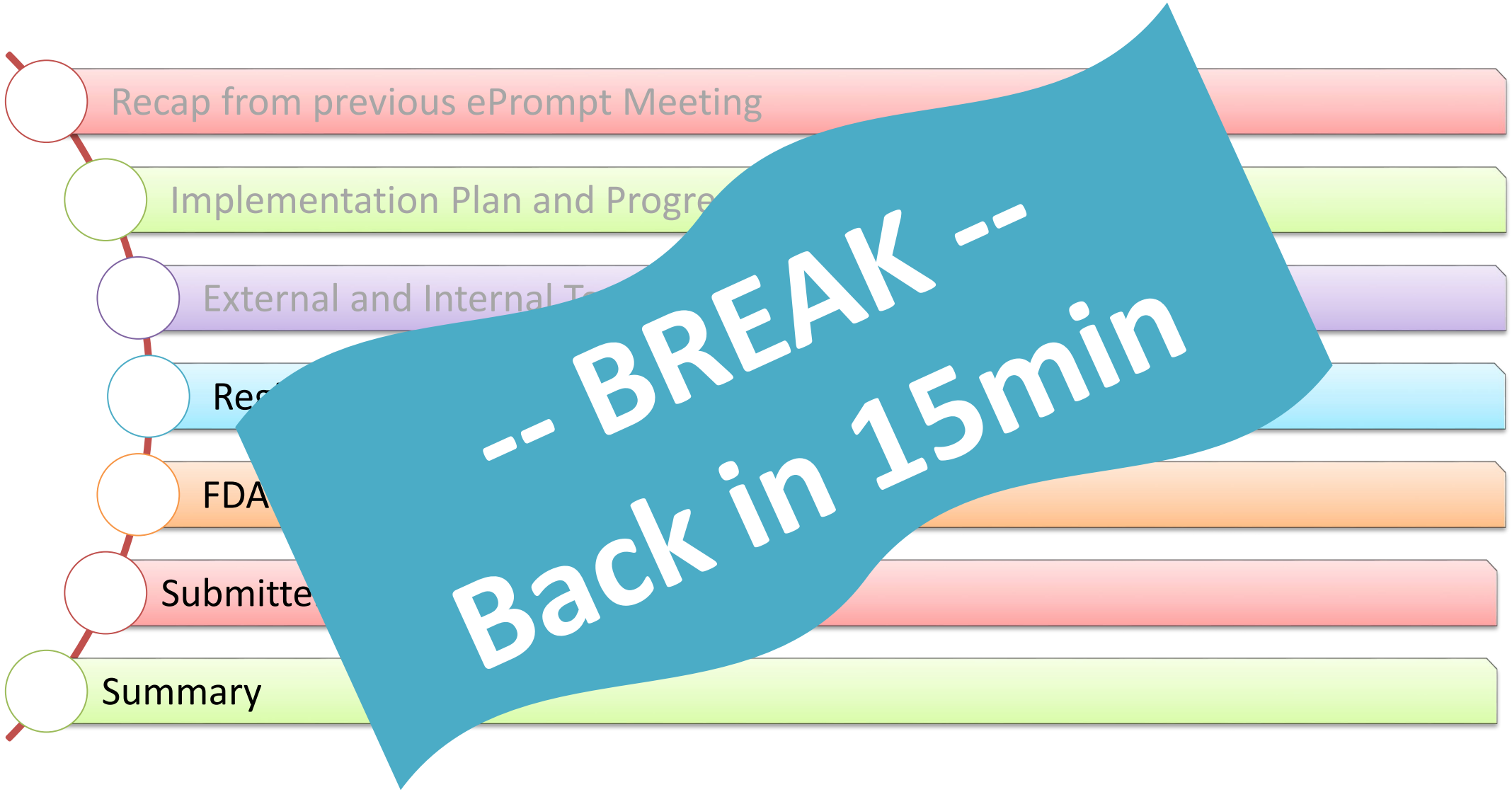
FDA General Comment: FDA will update the FAERS Electronic Submissions web page with a FAQ document to address questions

Mechanism to validate E2B(R3) XML files

- FDA will provide the FDA E2B(R3) Validator tool to facilitate validation of the E2B(R3) XML files generated from your safety database during your pilot testing phase.
- This validator will provide 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.



Agenda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External and Internal Te
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Summary
-- BREAK --
Back in 15min

Agenda

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Regional Extension Updates

Regional Extension Updates

- Corrected OID value in XPath for data element FDA.G.k.12.r.11.r, FDA.G.k.12.r.10, FDA.G.k.12.r.8, FDA.G.k.12.r.2.r, G.k.4.r.10.2a, G.k.2.1.1a, G.k.2.1.1b, D.8.r.2a, D.8.r.2b, D.10.8.r.2a, D.10.8.r.2b
- Corrected XPath for FDA.G.k.12.r.9
- Updated FDA.G.k.10a.r to FDA.G.k.10a and the data field is not repeatable
- Updated "Rejection and Warning Rules" tab to shorten the error description

Data Element	Updates
Device Problem Code (FDA.G.k.12.r.3.r)	Added warning rule with error id W0008 Provide valid FDA or IMDRF device problem code
Message Sender Identifier (N.2.r.2)	Added rejection rule with error id R0100 N.2.r.2 provided is not same for all reports and does not match with Batch Sender Identifier (N.1.3)
Report Nullification / Amendment (C.1.11.1)	Added rejection rule with error id R0101 C.1.11.1 must not have the value (1 or 2) for an initial report
IND number of cross reported IND (FDA.C.5.6.r)	Added warning rule with error id W0012 IND number of cross reported IND (FDA.C.5.6.r) must be a valid number registered with the FDA.

Regional Extension Updates

Data Element	Updates
Remedial Action Initiated (FDA.G.k.12.r.11.r)	Original: Warning error id "W0007" said "….Local Criteria Report Type (FDA.C.1.7.1) = 5 (30-Day)" instead of 4 (5-Day) Updated: Remedial Action Initiated (FDA.G.k.12.r.11.r) is requested, if Malfunction (FDA.G.k.12.r.1) is 'true' and Local Criteria Report Type (FDA.C.1.7.1) = **4** (5-Day)
Patient (name or initials) (D.1)	Original: The business rule generated an error and rejected the ICSR. Updated: Error Id "R0028" reduced to warning "W0010" and added additional criteria for data element D.1 If Identification Number of the Report Which Is Linked to This Report (C.1.10.r) **and IND Number where AE Occurred (FDA.C.5.5a)** is populated, then Patient (name or initials) (D.1) must have the value 'AGGREGATE'
Medicinal Product Name as Reported by the Primary Source (G.k.2.2)	Original: For error id W0009, the error description was “G.k.2.2 does not match the registered product name for application# reported in FDA.C.5.5a/FDA.C.5.5b” Updated: Error description updated to now say “G.k.2.2 does not match the registered product name for application# reported in FDA.C.5.5a/FDA.C.5.5b. **Ignore this message for comparator study product**.”

Regional Extension Updates

Data Element	Updates
Test Result (code) (F.r.3.1)	Original: For error id R0065, the error description was “F.r.3.1 must be provided when F.r.3.2 and F.r.3.4 is not provided” Updated: “At least one of test results (F.r.3.1, F.r.3.2, F.r.3.4) must contain a value when F.r.2.2b is provided.”
Test Result (value / qualifier) (F.r.3.2)	Original: For error id R0066, the error description was “F.r.3.2 must be provided when any of the data element in F.r.2 is provided, and F.r.3.1 and F.r.3.4 is not provided” Updated: At least one of test results (F.r.3.1, F.r.3.2, F.r.3.4) must contain a value when F.r.2.2b is provided.
Result Unstructured Data (free text) (F.r.3.4)	Original: For error id R0066, the error description was “F.r.3.2 must be provided when any of the data element in F.r.2 is provided, and F.r.3.1 and F.r.3.4 is not provided” Updated: At least one of test results (F.r.3.1, F.r.3.2, F.r.3.4) must contain a value when F.r.2.2b is provided.
Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4)	Original: Error id R0102, only checked for Message Receiver Identifier (N.2.r.3) ='CDER_IND' or 'CBER_IND’ but not 'CDER_IND_EXEMPT_BA_BE’ Updated: If Type of Report (C.1.3) is 2 (Report from study) and Message Receiver Identifier (N.2.r.3) = 'CDER_IND' or 'CBER_IND' **or 'CDER_IND_EXEMPT_BA_BE'** then Observation Code: (Value allowed: 1) for Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4)

Regional Extension Updates

Data Element	Updates
Characterisation of Drug Role (G.k.1)	Original: For error id R0065, the error description was “G.k.1 must be provided with Observation Code Value of 1, 3 or 4 when C.1.3 = 1 and N.2.r.3 = "CDER” Updated: “G.k.1 must be provided with Observation Code Value of 1, 3 or 4 when N.2.r.3 = "CDER”
Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4)	Added rejection rule with error id R0104 “If Type of Report (C.1.3) is 2 (Report from Study) and Message Receiver Identifier (N.2.r.3) = 'CDER' and Batch Receiver Identifier (N.1.4) = 'ZZFDA' then Observation Code: (Value allowed: 1, 2, 3) for Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4)”
IND Number where AE Occurred (FDA.C.5.5a)	Added rejection rule with error id R0105 The IND Number where AE Occurred (FDA.C.5.5a) must be a valid number registered with the FDA.
Pre-ANDA Number where AE Occurred (FDA.C.5.5b)	Added rejection rule with error id R0106 The Pre-ANDA Number where AE Occurred (FDA.C.5.5b) must be a valid number registered with the FDA.
Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4)	Original: For error id R0103, If Type of Report (C.1.3) is 1=Spontaneous report and Message Receiver Identifier (N.2.r.3) = 'CDER' then Observation Code: (Value allowed: 2, 3) for Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4) Updated: If Type of Report (C.1.3) is 1=Spontaneous report and Message Receiver Identifier (N.2.r.3) = 'CDER' then Study Type Where Reaction(s) / Event(s) Were Observed must not be provided

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U.S. FOOD & DRUG ADMINISTRATION

FDA Readiness

Proposed Timelines to Implementation

JANUARY 2024

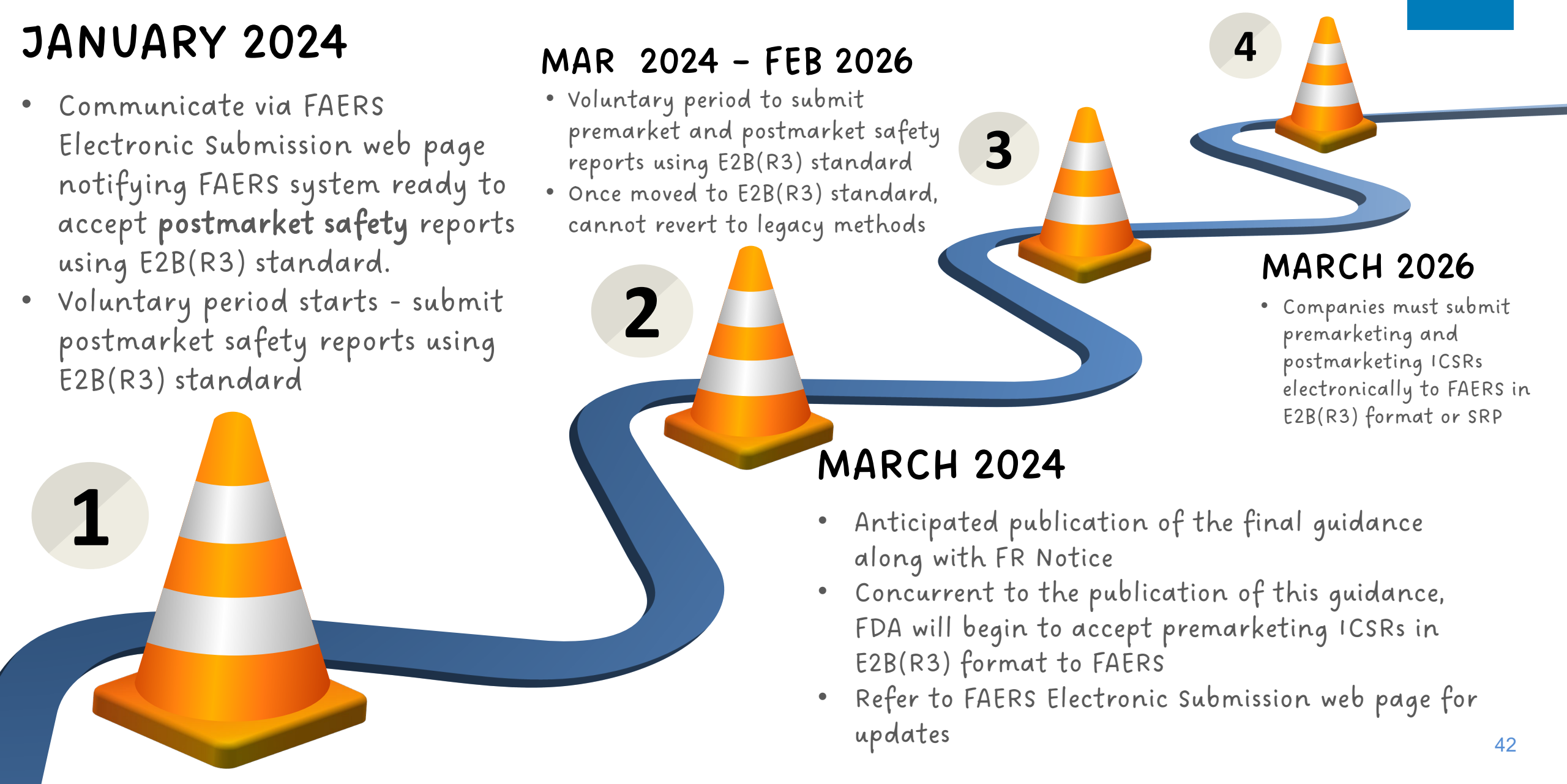
- Communicate via FAERS Electronic Submission web page notifying FAERS system ready to accept **postmarket safety** reports using E2B(R3) standard.
- Voluntary period starts - submit postmarket safety reports using E2B(R3) standard

MAR 2024 – FEB 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

MARCH 2026

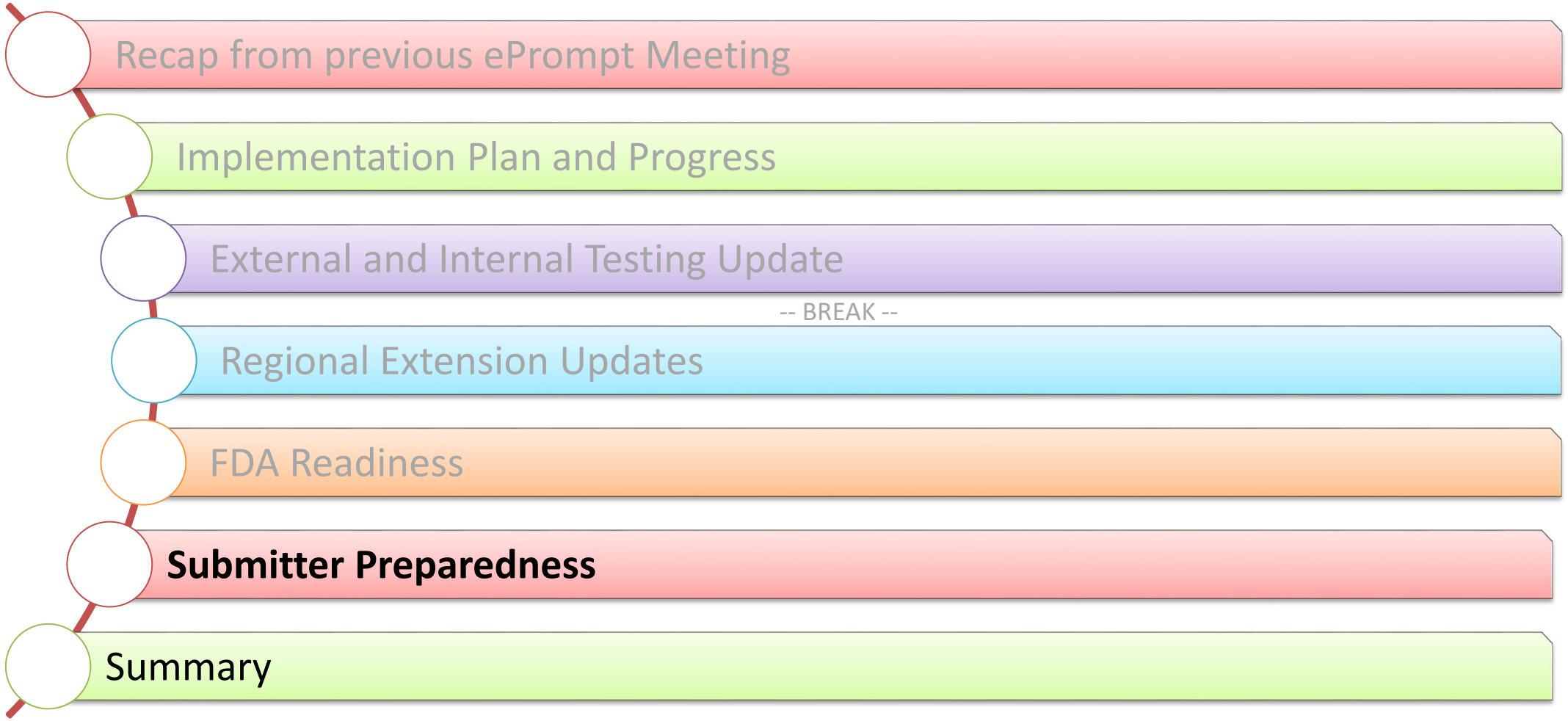
- Companies must submit premarketing and postmarketing ICSRs electronically to FAERS in E2B(R3) format or SRP



MARCH 2024

- Anticipated publication of the final guidance along with FR Notice
- Concurrent to the publication of this guidance, FDA will begin to accept premarketing ICSRs in E2B(R3) format to FAERS
- Refer to FAERS Electronic Submission web page for updates

Agenda


Recap from previous ePrompt Meeting
Implementation Plan and Progress
External and Internal Testing Update
-- BREAK --
Regional Extension Updates
FDA Readiness
Submitter Preparedness
Summary

U.S. FOOD & DRUG ADMINISTRATION

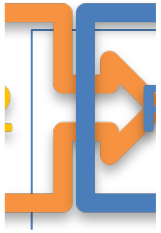
Submitter Preparedness

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

Submitter Preparedness

- Send files via the pre-production Gateway to test the following:
  - Premarket safety reports, including IND aggregate safety reports and cross-referenced INDs
  - Postmarket safety reports, including combination product safety reports
  - Safety reports with attachment
  - Large size safety reports
  - Batch submission of safety reports
  - Test for both positive and negative acknowledgements

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

Submitter Preparedness

Scenario 1: Premarket report on an IND or IND-Exempt BA/BE study
Batch Sender Identifier (N.1.4) = ZZFDA_PREMKT
Message Receiver Identifier (N.2.r.3) = CDER_IND or CBER_IND or CDER_IND_EXEMPT_BA_BE
Type of Report (C.1.3) = 2 (Report from study)
Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4) = 1 (Clinical trials)
IND Number where AE Occurred (C.5.5a) = <IND Number> OR Pre-ANDA Number where AE Occurred (C.5.5b) = <Pre-ANDA Number>

Scenario 2: Solicited reports or reports from Organized Data Collection System
Batch Sender Identifier (N.1.4) = ZZFDA
Message Receiver Identifier (N.2.r.3) = CDER
Type of Report (C.1.3) = 2 (Report from study)
Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4) = 2 (Individual patient use) or 3 (Other studies)

Submitter Preparedness

Scenario 3: Premarket AGGREGRATE report
Batch Sender Identifier (N.1.4) = ZZFDA_PREMKT
Message Receiver Identifier (N.2.r.3) = CDER_IND or CBER_IND
Type of Report (C.1.3) = 2 (Report from study)
Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4) = 1 (Clinical trials)
IND Number where AE Occurred (C.5.5a) = <IND Number>
Patient (name or initials) (D.1) = AGGREGATE
Identification Number of the Report Which Is Linked to This Report (C.1.10.r) = <list of Sender's (case) Safety Report Unique Identifier (C.1.1)>

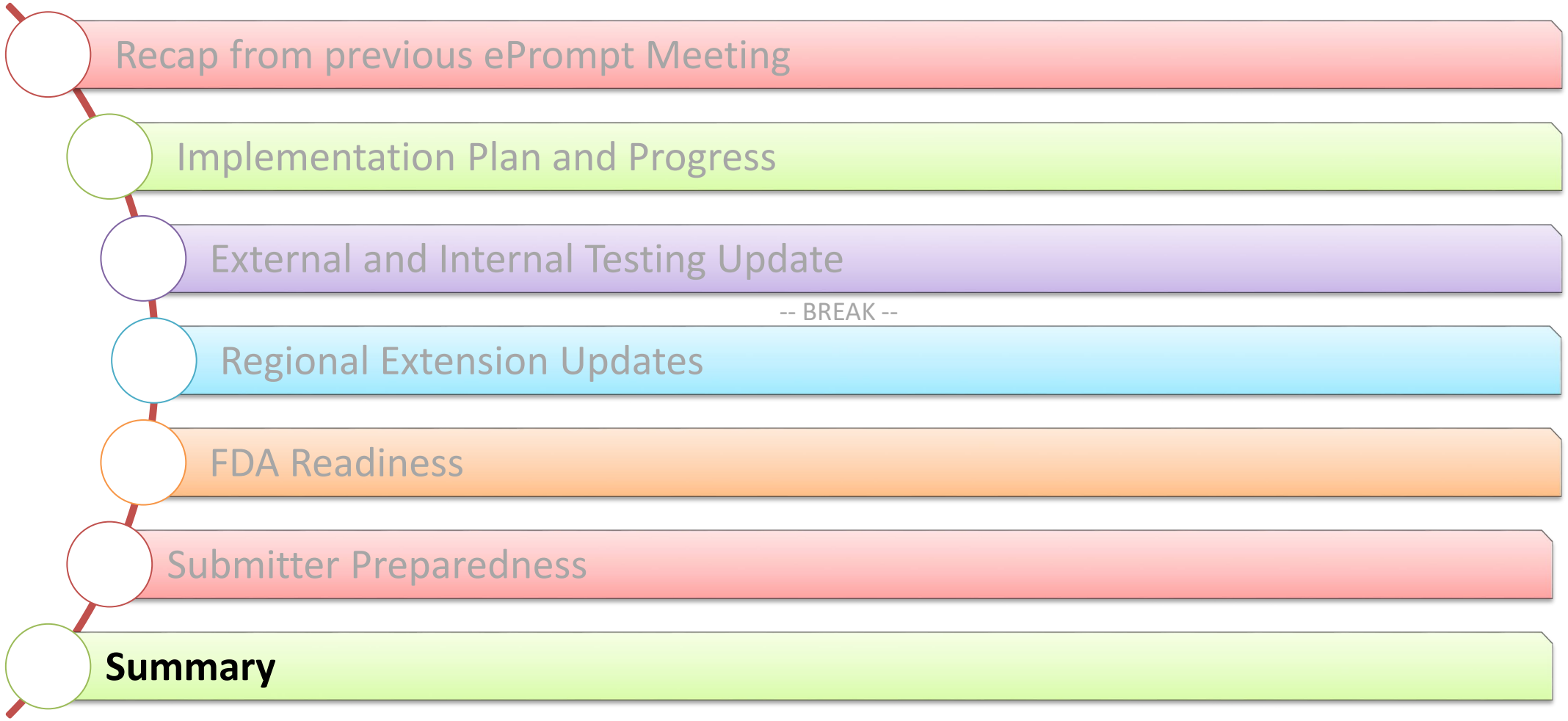
Submitter Preparedness

Scenario 4: Premarket report with cross referenced INDs
Batch Sender Identifier (N.1.4) = ZZFDA_PREMKT
Message Receiver Identifier (N.2.r.3) = CDER_IND or CBER_IND
Type of Report (C.1.3) = 2 (Report from study)
Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4) = 1 (Clinical trials)
IND Number where AE Occurred (C.5.5a) = <IND Number>
IND number of cross reported IND (FDA.C.5.6.r) = <list the cross-referenced INDs>

Submitter Preparedness

Scenario 5: Postmarket study report - Must submit two (2) reports 1) on the IND and 2) on the NDA or BLA	
Report 1	Batch Sender Identifier (N.1.4) = ZZFDA_PREMKT
	Message Receiver Identifier (N.2.r.3) = CDER_IND or CBER_IND
	Type of Report (C.1.3) = 2 (Report from study)
	Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4) = 1 (Clinical trials)
	IND Number where AE Occurred (C.5.5a) = <IND Number>
Report 2	Batch Sender Identifier (N.1.4) = ZZFDA
	Message Receiver Identifier (N.2.r.3) = CDER
	Type of Report (C.1.3) = 2 (Report from study)
	Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4) = 1 (Clinical trials)

Agenda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Summary

- ❑ Recap from the **previous public meeting**
- ❑ Discuss the **implementation plan and progress** showing the activities completed and in-progress
- ❑ Conducted **external and internal testing** for different scenarios
- ❑ Issues identified were **fixed, implement and re-tested**
- ❑ Update to **regional extensions** are posted (v 1.5)
- ❑ Discussed **FDA readiness** with planned dates
- ❑ Update **FAERS Electronic submission** web page
- ❑ Communicated what **submitters can do to prepare** themselves
- ❑ Recommended scenarios to test

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 (Aug 2022)	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 v1.5 (Oct 2023)	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 (Sep 2023)	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 (Aug 2022)	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/electronic-submission-expedited-safety-reports-ind-exempt-babe-studies-guidance-industry

Thank You