Specifications for Preparing and Submitting Postmarket Individual Case Safety Reports (ICSRs) for Vaccines

Technical Specifications Document

Associated Guidance Document(s):

Guidance for Industry: E2B (R3) Electronic Transmission of Individual Case Safety Reports (ICSRs) Implementation Guide – Data Elements and Message Specification (February 2014)

Guidance for Industry: Providing Submissions in Electronic Format - Postmarketing Safety Reports for Vaccines (August 2015)

Guidance for Industry: Postmarketing Safety Reporting for Combination Products (July 2019)

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Draft Revision History

Version	Date	Description
1.0	May, 2016	Substantial revisions as a result of pilot testing with industry September 2014 – March 2015. New document appendices have been added and replaced the term “attribute” with the term “data element” throughout the document.
2.0	May, 2019	Substantial revisions to implement the Combinations Products Post-Market Safety Reporting Rule and to address gaps and inconsistencies identified since Version 1.0. Furthermore, the document has been streamlined to reduce text that is available in the ICH E2B(R3) Implementation Guide.
2.1	June, 2020	Revisions made from feedback received from industry following the May 2019 publish and changes discussed during working group meetings with the FDA Adverse Event Reporting System (FAERS) team and CDC regarding Device Lot Number and Characterization of Drug Role *Similar Device*.
2.2	November, 2020	Revisions made to implement the Geopolitical Entities, Names, and Codes (GENC) Standard Edition 3, Update 11 country codes. See Table 4 for a complete list of the affected data elements.
2.3	December, 2023	Revisions made to provide guidance on submitting challenge information, to correct the Vaccination Facility Type code, and to ensure that modifications to regional data element FDA.C.1.6.1.r.3 are accurately recorded.

Table of Contents

Specifications for Preparing and Electronically Submitting Individual Case Safety Reports (ICSRs) and ICSR Attachments for Vaccines

I. Introduction

The purpose of this technical specifications document is to assist senders submitting post-market ICSRs and ICSR attachments for vaccines in electronic format to the Vaccine Adverse Event Reporting System (VAERS). Please note that throughout this document, VAERS and eVAERS are used interchangeably. Vaccine ICSRs must be submitted to VAERS using the International Council on Harmonization's (ICH) E2B ICSR (R3) standard as described in the ICH E2B (R3) Implementation Guideline (IG).[1] The IG describes the harmonized, core set of ICH E2B (R3) data elements and business rules for creating ICSR files. This document clarifies certain aspects of the IG for reporting to VAERS and defines additional Food and Drug Administration (FDA) regional data elements not addressed in the IG. FDA regional data elements have been added by FDA to support vaccine ICSR reporting to VAERS.

This document does not apply to the following Center for Biologics Evaluation and Research (CBER) regulated products:

- CBER-regulated drug products marketed for human use with approved New Drug Applications (NDAs) and Abbreviated New Drug Applications (ANDAs)
- CBER-regulated therapeutic biological products marketed for human use with approved Biologic License Applications (BLAs)
- Whole blood or blood components
- Human cells, tissues, and cellular and tissue-based products (HCT/Ps) regulated solely under section 361 of the Public Health Service Act

Stakeholders interested in submitting ICSRs in ICH E2B (R3) format or with questions about this document or technical difficulties with submissions to eVAERS should contact the CBER ICSR Submissions Coordinator at: CBERICSRSubmissions@fda.hhs.gov.[2]

A. Individual Case Safety Reports

For purposes of this technical specification, an ICSR is a description of an adverse experience related to an individual patient or subject that is associated with the use of a vaccine. More specifically, an ICSR is made up of data elements, such as the date and time of the adverse experience, the name of the suspect vaccine and the name of the manufacturer of a vaccine. The data elements presented here include those listed in the relevant regulation at § 21 Code of Federal Regulations (CFR) 600.80, most notably § 600.80(g).

ICSR attachments provide submitters with the ability to include supporting information for ICSRs, such as relevant hospital discharge summaries and autopsy reports or death certificates. ICSR attachments may also include published articles for ICSRs gathered from scientific literature (§ 600.80(d)).

Postmarket ICSRs and ICSR attachments for vaccines are to be submitted to FDA through the FDA Electronic Submission Gateway (ESG). ICSRs for vaccines are to be prepared in accordance with FDA regional extensions to the ICH E2B (R3) Extensible Markup Language (XML[3]) file format. ICSRs are not to be submitted in the electronic Common Technical Document (eCTD) nor submitted in a Portable Document File (PDF) format.

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[1] Link to the E2B(R3) Individual Case Safety Report (ICSR) Specification and Related Files: https://ich.org/page/e2br3-individual-case-safety-report-icsr-specification-and-related-files

[2] https://www.fda.gov/industry/about-esg/cber-vaccine-icsr-implementation

[3] Extensible Markup Language (XML) is a markup language that defines a set of rules for encoding documents in a format that is both human-readable and machine-readable

B. Updates to this version of the Technical Specification

FDA made revisions in this version of the technical specification to provide guidance on submitting re-challenge information, to correct values for the 'Vaccination Facility Type' (FDA.G.k.4.r.14.8), and to record modifications to the 'Attachment File Name' (FDA.C.1.6.1.r.3). In addition, FDA has updated the eVAERS Business Rules, referenced in Appendix I (previously labeled as "Appendix B: Consolidated Business Rules Document"), which provide additional detail and specific data requirements for each data field. Specifically, the business rules that have been updated in this version of the Technical Specifications/Business Rules are listed in **Table 27** in Appendix I.

II. FDA Regional Implementation of ICH E2B (R3)

A. Regional Data Elements

The use of the term, *"regional extension"* in this document refers to FDA data elements and terminologies supported in the ICSR file in addition to the ICH E2B (R3) data elements. FDA regional extensions for VAERS are specific to vaccine safety surveillance and include data elements required by FDA for post-market safety reporting for vaccines. These FDA regional extensions help support Agency efforts to improve overall ICSR data quality and support other Department of Health and Human Services (HHS) public health initiatives.

B. Data Element Conformance

FDA regional extensions generally follow the ICH E2B (R3) data element conformance (e.g., required/mandatory or optional) described in the IG. However, for certain regional data elements, FDA has changed the data element conformance for ICSRs for VAERS due to regional regulatory requirements not addressed in the IG, and these exceptions are noted in the relevant sections of this document. More information on data element conformance is available in the eVAERS Business Rules which are referenced in Appendix I of this document. The eVAERS Business Rules list the validation rules used to process incoming eVAERS ICSRs for all ICH and FDA regional data elements.

C. Regional Controlled Terminology

Controlled terminologies used for VAERS regional data elements are supported by the US National Cancer Institute's (NCI) Enterprise Vocabulary Service (EVS) as well as other terminologies listed in **Table 1**. Information about the NCI EVS is available at the NCI website at: http://evs.nci.nih.gov/. Reference links to these controlled terminologies are provided in the relevant sections of this document. The System Object Identifiers (OIDs) are also listed in **Table 1**.

Table 1: System Object Identifiers Implemented by FDA ICSR for Vaccines

Object Identifier	Reference Source	Description
2.16.840.1.113883.3.26.1.1	National Cancer Institute Thesaurus	Primary NCI OID which supports multiple FDA controlled terminologies such as Structured Product Labeling (SPL) Dosage Forms and VAERS Primary Source Reporter codes.
2.16.840.1.113883.6.69	Food and Drug Administration Drug Registration and Listing System	FDA internal system used to generate and maintain the National Drug Code (NDC) Directory.

Object Identifier	Reference Source	Description
2.16.840.1.113883.4.9	Food and Drug Administration Substance Registration System	FDA internal system used to generate and store regional Unique Ingredient Identifiers (UNII).
1.3.6.1.4.1.519.1	Dun and Bradstreet	Data Universal Numbering System, commonly known as the DUNS Number, is a business identification system that identifies, validates and links to more than 225 million businesses worldwide.

D. Data Elements that are designed to use International Organization for Standardization (ISO) Identification of Medicinal Product (IDMP) Compliant Terminologies

These ISO IDMP related data elements are listed in **Table 2**. FDA currently uses regional terminology to support certain ISO IDMP data elements:

- Substance/Specified Substance Identifiers (ISO 11238:2012): Supported using FDA Unique Ingredient Identifiers (UNII); and
- Medicinal Product Identifiers (ISO 11615:2012): Supported using the three-segment FDA National Drug Code

Table 2: VAERS Data Elements with Regional Controlled Terminology

Data Element ID	E2B(R3) Name	Controlled Terminology
D.8.r.2b ; D.10.8.r.2b ; G.k.2.1.1b ; FDA.G2.K.2b	Medicinal Product Identifier (MPID)	FDA NDC
D.8.r.3b ; D.10.8.r.3b ; G.k.2.1.2b	Pharmaceutical Product Identifier (PhPID)	*(Currently not in use)*
G.k.2.3.r.2b	Substance/Specified Substance TermID	FDA Substance Registration System (SRS) Unique Ingredient Identifier (UNII)
G.k.4.r.9.2b	Pharmaceutical Dose Form TermID	FDA SPL Dosage Form or EDQM codelist
G.k.4.r.10.2b ; G.k.4.r.11.2b ; FDA.G2.k.4b	Route of Administration TermID	FDA SPL or EDQM codelist
G.k.2.3.r.3b ; G.k.4.r.1b ; G.k.5b	Dose and Strength Unit	FDA SPL or E2B codelist
Various country fields (see Table 5 below)	(See Table 5 below)	GENC 2-character codelist

E. Use of the *DisplayName* Data Element

FDA has implemented and recommends the use of the XML data element *displayname* to facilitate

human and computer system identification and understanding of coded regional data elements in the ICSR file. The example below demonstrates how *displayname* is used:

EXAMPLE:

<subjectOf2 typeCode="SBJ">
<observation classCode="OBS" moodCode="EVN">
<code code="C102468" **displayName="Illness at time of vaccination**"
codeSystem="2.16.840.1.113883.3.26.1.1"/>

F. FDA Regional Implementation of Unified Codes for Units of Measurement (UCUM)

FDA follows the E2B IG concerning the use of the UCUM for coding units of measure. The complete UCUM value set can be downloaded from the Regenstrief Institute website at: http://unitsofmeasure.org/trac/.

For product 'Strength (unit)', 'Dose (unit)' and 'Cumulative Dose to First Reaction (unit)', FDA accepts units of measure from either the FDA SPL Units of Measure list available here: https://www.fda.gov/industry/structured-product-labeling-resources/units-measure, or the Units of Measure codelist provided by ICH (i.e., "E2B codelist"), available here: http://estri.ich.org/e2br3/index.htm.

For 'Test Result (unit)', select the most appropriate UCUM code.

Table 3: UCUM related VAERS Data Elements

Data Element ID	E2B(R3) Name	Controlled Terminology
G.k.2.3.r.3b	Strength (unit)	FDA SPL or E2B codelist
G.k.4.r.1b	Dose (unit)	FDA SPL or E2B codelist
G.k.5b	Cumulative Dose to First Reaction (unit)	FDA SPL or E2B codelist
F.r.3.3	Test Result (unit)	Not constrained to any specific codelist but use of a valid UCUM code is expected

G. FDA Regional Implementation of Country Code-Related Data Elements

US Public Law 80-242 (1947) requires the US Government to use geographic names that have been approved by the U.S. Board on Geographic Names (BGN). The Geopolitical Entities, Names, and Codes (GENC) Standard is the US Government implementation of ISO 3166 that is approved by BGN (for additional information, visit website https://www.fgdc.gov/standards/news/GENC). The FDA Data Standards Advisory Board (DSAB) adopted GENC as the Agency standard to represent countries and their principal subdivisions (e.g., state/province).

VAERS accepts the GENC two-character code as adopted by the FDA DSAB. This version of the GENC Standard is GENC Standard Edition 3 Update 11 (i.e., the latest, June 2019, edition), which is available at https://evs.nci.nih.gov/ftp1/GENC/. Note that the GENC 2-character Code adopted by FDA is slightly different from the ISO-3166-1 alpha-2 version used by the ICH E2B guideline. For a complete list of GENC 2-character codes, please refer to https://evs.nci.nih.gov/ftp1/GENC/About.html. See **Table 4** for a list of VAERS data elements related to country code.

Table 4: VAERS Data Elements related to Country Code

Data Element ID	E2B(R3) Name	Controlled Terminology
C.2.r.3	Reporter's Country Code	GENC Edition 3, Update 11 nullFlavor: MSK, ASKU, NASK, UNK
C.3.4.5	Sender's Country Code	GENC Edition 3, Update 11
C.5.1.r.2	Study Registration Country	GENC Edition 3, Update 11 nullFlavor: ASKU, NASK
FDA.D.1j	Patient address country	GENC Edition 3, Update 11 nullFlavor: MSK, ASKU, NASK, NI
E.i.9	Identification of the Country Where the Reaction / Event Occurred	GENC Edition 3, Update 11
G.k.2.4	Identification of the Country Where the Drug Was Obtained	GENC Edition 3, Update 11
G.k.3.2	Country of Authorization / Application	GENC Edition 3, Update 11
FDA.G.k.4.r.14.4	Vaccination Facility Country	GENC Edition 3, Update 11 nullFlavor: NI
FDA.G.k.12.r.7.1e	Device Manufacturer Country	GENC Edition 3, Update 11

Please note that in the ICH E2B(R3) IG instruction, the data element C.1.1 is preferably represented by a combination of country code and two other fragments of ID information, however, the IG instruction does not explicitly require the incorporation of country code into this data element value. Similarly, FDA eVAERS does not pose any validation rule requiring a country code, regardless of format or standard, on this data element.

III. General Data Completion Instructions

A. Required and Optional Data Elements

A required data element is one that must be present (i.e., not to be omitted) either in the ICSR message or an instance of a repeating data element section within the ICSR message.

A required data element may or may not allow a nullFlavor, depending on the data validation rules associated with the data element.

An optional data element generally does not have to be included in the message if it does not have a value. But in some cases, a referential data validation rule may require an optional data element be indicated with a nullFlavor under certain circumstances.

The eVAERS Business Rules, included as Appendix I to this document, list all VAERS data elements, including ICH and FDA regional data elements, and the validation rules used to process incoming eVAERS ICSRs. The Business Rules provide detailed information on the conformance, format, and where applicable, allowed values, null flavors, and controlled terminologies for each data element.

Custom data elements not described in the eVAERS Business Rules are not allowed.

B. Description in English

All ICSR data elements should be completed in English with the exceptions of the following elements:

- 'Reaction/Event as Reported by the Primary Source in Native Language' (E.i.1.1a);
- 'Case Summary and Reporter's Comments in Native Language' (H.5.r)

C. Date/Time Data Elements

Actual local dates and times should be used and offset (i.e., +/-ZZzz) is attached where appropriate. A single format (CCYYMMDDhhmmss.UUUU[+/-ZZzz]) is used to represent dates and times. The minimum level of precision for the date data elements is specified in the Business Rules, however, as much information as is available (e.g., known) should be provided. Future dates are not acceptable in an ICSR message.

D. Use of Metric Units

Metric units should be used for measurement values.

E. Version of Medical Dictionary of Regulatory Activities (MedDRA)

A single version of MedDRA should be used for all MedDRA coding data elements within the same ICSR. Therefore, the same MedDRA version should be reflected in all the populated data elements concerning MedDRA version information. However, within a safety message (i.e., a batch of ICSRs), different ICSRs can refer to different MedDRA versions.

F. Standard Terminologies and Codelists

If a data element is defined with a specific codelist (in the "Values" column of the Business Rules), the associated codelist must always be used. Also, when the codelist code is captured as the value of a data element, its text name should be provided in *displayname* to make the XML code human readable.

G. Use of nullFlavors

NullFlavors are used to explain the reason for the lack of data on required elements. The following definitions of nullFlavors are from the E2B IG and can be used as appropriate.

Table 5: nullFlavor Codes

Code	Name	Definition
NI	No Information	No information whatsoever can be inferred from this exceptional value. This is the most general exceptional value. It is also the default exceptional value.
MSK	Masked	There is information on this item available, but it has not been provided by the sender due to security, privacy or other reasons. There could be an alternate mechanism for gaining access to this information. Note: using this nullFlavor can provide information considered to be a breach of confidentiality, even though no detail data is provided. Its primary purpose is for those circumstances where it is necessary to inform the receiver that the information does exist without providing any detail.
UNK	Unknown	A proper value is applicable, but not known.
NA	Not Applicable	No proper value is applicable in this context (e.g., last menstrual period for a male).
ASKU	Asked But Unknown	Information was sought but not found (e.g., patient was asked but did not know)
NASK	Not Asked	This information has not been sought (e.g., patient was not asked)
NINF	Negative Infinity	Negative infinity of numbers.
PINF	Positive Infinity	Positive infinity of numbers.

H. ICSR Attachment(s)

To facilitate ICSR attachment file processing, the data element "*Attachment file name*" must be included using the <reference value> data element in the XML file, which must be placed after the <text mediaType> tag.

EXAMPLE:

```
<reference typeCode="REFR">
<document classCode="DOC" moodCode="EVN">
<code code="1" codeSystem="2.16.840.1.113883.3.989.2.1.1.27"
displayName="documentsHeldBySender"/>
<title>Sample Autopsy Report</title>
<text mediaType="text/plain" representation="B64">
<reference value="SUMMARY OF CLINICAL HISTORY.txt"/>
VGhlIHBhdGllbnQgd2FzIGEgMzUgeWxlIHdpdGggbm8gc==
</text>
</document>
</reference>
```

Special Note: the "*attachment file name*" must follow the naming convention for a valid 'url'. Letters, digits and special characters "a"--"z", "A"--"Z", digits, and the characters plus ("+"), period ("."), hyphen ("-"), underscore ("_"), space (" "), parentheses ("()"), and hash ("#") are allowed.

If the file type in the reference value tag does not match the file extension in the file name, the file will be rejected. For example a file with <reference value="SAMPLE FILE.txt"/> must have a text file media type reported.

For more information about restrictions please see http://www.ietf.org/rfc/rfc1738.txt.

I. ICSR and ICSR Attachment File Size Limitations

The FDA ESG supports the receipt of electronic regulatory submissions of up to 100 GB in size; however, the recommended eVAERS ICSR submission size is less than 100 MB. ICSRs and ICSR attachments should not be compressed.

The following attachment file types are supported:

- Portable document format (.pdf)
- Image file formats (.jpeg, .jpg)
- Bitmap image format (.bmp)
- Portable Network Graphics (.png)
- Graphics Interchange Format (.gif)
- Tagged image file format (.tif, .tiff)
- Rich text format (.rtf.)
- Text format (.txt)
- Spreadsheet file format (.xls, .xlsx)
- Word processing document format (.doc, .docx, .wpd)

In accordance with E2B ICH guidance, ICSR attachments should be sent inline as embedded files using base 64 encoding (refer to ICH E2B (R3) IG Section 3.5 for further information).

IV. The Structure of an ICSR Message for VAERS

A safety message includes the ICSR Transmission Identification (i.e., batch wrapper) and one or more ICSR messages. Each ICSR message contains one and only one ICSR, including a message wrapper and structured ICSR sections.

The FDA has adapted the base E2B ICH ICSR for reporting ICSRs to VAERS. This document presents information on FDA specific fields or deviations from the E2B IG within the relevant E2B ICH ICSR Section. Sections that are not hyperlinked do not have FDA specific fields or deviations from the E2B IG.

In each of the following sections, there is a table that lists the FDA regional data elements and/or data elements that deviate from the base E2B IG. For additional information please refer to the eVAERS business rules document (**Appendix I: eVAERS Business Rules**).

The following illustrates how ICSR information is organized in a safety message:

(*)=Required section (#)=Repeatable section

N.1 **Transmission Identification (Batch Wrapper) (N.1)** ***(*)***

N.2.r **ICSR Message Header (Message Wrapper) (N.2.r)** ***(*) (#)***

C.1 **Identification of the Individual Case Safety Report (Section C.1)** ***(*)***

C.2.r **Primary Source(s) of Information (Section C.2.r)** ***(*) (#)***

C.3 **Information on the Sender of Case Safety Report (Section C.3)** ***(*)***

C.4.r **Literature References (C.4.r)** ***(#)***

C.5 STUDY IDENTIFICATION ***(#)***

D. **Patient Characteristics (Section D)** ***(*)***

E.i **Reactions/Events (Section E.i)** ***(*) (#)***

F.r RESULTS OF TESTS & PROCEDURES RELEVANT TO THE INVESTIGATION OF THE PATIENT ***(#)***

G.k **Drug(s) Information (Section G.k)** ***(*) (#)***

FDA.G2 **VAERS Vaccines Given Within 4 Weeks (FDA.G2)** ***(#)***

H. NARRATIVE CASE SUMMARY AND FURTHER INFORMATION ***(*)***

A. Transmission Identification (Batch Wrapper) (N.1)

Individual and batch ICSR files are supported using the HL7 batch message wrapper using the message interaction identifier **MCCI_IN200100UV01**. ICSR sender and receiver information is captured in the batch wrapper using specific data elements to distinguish ICSR sender and receiver information. For more information about HL7 Batch and Generic Message Transmission wrappers, refer to the ISO/HL7 27953-2 Annex A: Transmission Infrastructure topic.

Table 6: Data Elements that deviate from the base E2B IG, section N.1

Data Element	Field Name	Values	Modification to ICH E2B (R3)
ICH N.1.3	Batch Sender Identifier	Free Text	Change in Business Rule
ICH N.1.4	Batch Receiver Identifier	CBER VAERS, CBER_VAERS	Change in Business Rule and Values

1. Batch Sender Identifier (N.1.3)

The Batch Sender Identifier can be the Data Universal Numbering System (DUNS) number (9 Digit Identifier using the Dun and Bradstreet (D&B) Object Identifier (OID) 1.3.6.1.4.1.519.1) or another Identifier.

For more information about how to obtain a DUNS number, refer to the FDA Business Entity Webpage at: https://www.fda.gov/industry/structured-product-labeling-resources/business-entity-identifiers.

2. Batch Receiver Identifier (N.1.4)

The VAERS program uses the FDA ESG Routing ID for test and production submissions. These identifiers correspond to the FDA ESG connection (e.g., WebTrader or Application Standard 2 (AS2) B2B) used to send the ICSR submission to VAERS. Please refer to Section VI.B: FDA ESG Transaction Partners of this document for more information about VAERS routing IDs.

B. ICSR Message Header (Message Wrapper) (N.2.r)

Each ICSR within a batch includes a transmission wrapper in conformance to the HL7 rules for forming a message. Transmission wrapper information includes an identifier for the transmission, sender information, and receiver information.

Table 7: Data elements that deviate from the base E2B IG, section N.2.r

Data Element	Field Name	Values	Modification to ICH E2B (R3)
ICH N.2.r.2	Message Sender Identifier	Pre-approved Sender ID	Change in Business Rule
ICH N.2.r.3	Message Receiver Identifier	CBER VAERS, CBER_VAERS	Change in Business Rule and Values
ICH N.2.r.4	Date of Message Creation	CCYYMMDDhhmmss[+/-ZZzz]	Change in Business Rule and Values

1. Message Sender Identifier (N.2.r.2)

Senders must receive FDA approval of their Message Sender Identifier before beginning VAERS Submissions. All ICSRs must use the agreed upon Message Sender Identifier. See the instructions for Batch Sender Identifier (Section IV, C, 1).

2. Message Receiver Identifier (N.2.r.3)

The VAERS program uses the FDA ESG Routing ID for test and production submissions. These identifiers correspond to the FDA ESG connection (e.g., WebTrader or AS2 B2B) used to send the ICSR submission to VAERS. Please refer to Section VI.B: FDA ESG Transaction Partners of this document for more information about VAERS routing IDs.

V. ICSR Content

This section identifies the data elements where FDA has deviated from the ICH E2B (R3) and/or added FDA regional data elements. For additional information, please refer to the eVAERS business rules document (Appendix I). Data elements that do not deviate from the E2B IG are not presented below; these elements can be found in the E2B IG and in the eVAERS business rules document.

A. Identification of the Individual Case Safety Report (Section C.1)

Table 8: Data elements that deviate from the base E2B IG, section C.1

Data Element	Field Name	Values	Modification to ICH E2B (R3)
ICH C.1.1	Sender's (case) Safety Report Unique Identifier	Free text (country code-company or regulator name-report number)	Additional Guidance
ICH C.1.6.1.r.2	Included Documents	Media type: e.g., Application/PDF, image/jpeg, application/DICOM, text/plain Representation: e.g., B64	Change in Business Rules and Data Type
FDA.C.1.6.1.r.3	Attachment File Name	Free Text	FDA Regional Element
ICH C.1.7	Does This Case Fulfil the Local Criteria for an Expedited Report?	false, true nullFlavor: NI	Additional Guidance
FDA.C.1.7.1	Local Criteria Report Type	<Observation><code>= C54588. 1=15 Day 2=Non-Expedited AE 4=5 Day 5=Malfunction only (No AE)	FDA Regional Element
ICH C.1.8.1	Worldwide Unique Case Identification	Free text (See C.1.1 user guidance for format)	Additional Guidance
ICH C.1.9.1.r.1	Source(s) of the Case Identifier(s)	Free Text	Change in Conformance
ICH C.1.9.1.r.2	Case Identifier(s)	Free text (See C.1.1 user guidance for format)	Change in Conformance
ICH C.1.11.1	Report Nullification / Amendment	1=Nullification 2=Amendment	Change in Conformance
FDA.C.1.12	Combination Report Flag	<Observation><code>= C156384. false, true nullFlavor: NI	FDA Regional Element

1. Sender's (case) Safety Report Unique Identifier and Worldwide Unique Case Identification (C.1.1 and C.1.8.1)

The IG specified format for C.1.1 is a 3-component term composed of: country code- company name-report number. VAERS ICSRs should generally follow the IG guidance for both C.1.1 and C.1.8.

However, FDA supports use of alternative formats for C.1.1 (Sender's (case) Safety Report Unique Identifier) and C.1.8.1 (Worldwide Unique Case Identification) for initial reports previously submitted to FDA in paper format (e.g., VAERS-1 form).

While the ICH E2B(R3) IG instruction, preferably recommends that C.1.1 is represented by a combination of country code and two other fragments of ID information, the IG instruction does not explicitly require the incorporation of country code. Similarly, FDA eVAERS does not pose any validation rule requiring a country code, regardless of format or standard, on this data element. For foreign ICSRs, senders should be cognizant of local and regional requirements regarding confidentiality and personal privacy concerns.

2. Linking of Initial and Follow up ICSRs ICH using C.1.1 and C.1.8.1

In follow-up reports, use the same identifier for C.1.8.1 that was assigned to the initial ICSR when both versions were submitted electronically. If the initial ICSR was submitted on paper but its follow-up ICSR is to be submitted electronically, include the Sender's (case) Safety Report Unique Identifier (also called Manufacturer Control Number (MCN)) from the initial report in C.1.10.r in the follow-up electronic submission.

3. Included Documents (C.1.6.1.r.2)

When including document attachments with an ICSR, the <title> data element should include a short description of the type of document being sent as an ICSR attachment (e.g., Autopsy Report). Compression is not used for U.S. reporting and encoding is limited to B64. The regional data element, *Attachment file name*, is used to automate ICSR file attachment identification and processing in the CBER document repository. This data element is supported using the <reference value=> element and attribute in the XML file. The attachment file name (C.1.6.1.r.3) must be provided in this data element and the location of the attachment file name must follow the <text mediaType> XML tag as follows:

EXAMPLE:

```
<reference typeCode="REFR">
        <document classCode="DOC" moodCode="EVN">
                <code code="1" codeSystem="2.16.840.1.113883.3.989.2.1.1.27"
                        displayName="documentsHeldBySender"/>
                <title>Autopsy Report</title>
                        <!--  Documents Held by Sender (repeat as necessary -->
                                <text mediaType="text/plain" representation="B64">
                                <reference value="Final_Report013115.pdf"/>
                                </text>
                        <!-- : Included Documents #1 -->
        </document>
</reference>
```

4. Does This Case Fulfil the Local Criteria for an Expedited Report (C.1.7) and Local Criteria Report Type (FDA.C.1.7.1)?

FDA follows the E2B IG for the values allowed for C.1.7: "true, "false", or "NI". VAERS ICSRs that meet the FDA reporting criteria for a 15-day alert report or for a 5-day report are expedited reports, and a value of "true" should be applied for C.1.7.

FDA has also applied a regional rule requiring a coded response for "Local Criteria Report Type" (FDA.C.1.7.1), which specifies the type of expedited or non-expedited report. The 'Local Criteria Report Type' is dependent on the selections made on the FDA regional data element 'Combination Product Report Indicator' (FDA.C.1.12) (see more information in section 5) and C.1.7. If the Combination Product Report Indicator (FDA.C.1.12) is answered as true, and the case is an Expedited Report, then the Local Criteria Report Type value must be '1=15 Day' or '4=5 Day'. If the Combination Product Report Indicator is true and the case is not an Expedited Report, then the allowed 'Local Criteria Report Type' value options are '2=Non-Expedited AE' or '5=Malfunction only (No AE)'.

If an ICSR is not a combination product report and it is expedited, then the 'Local Criteria Report Type' is '1=15 Day'; if it is not expedited, then the 'Local Criteria Report Type' is '2=Non-Expedited AE'.

Table 9: Relationship Between Data Elements FDA.C.1.12, ICH C.1.7 and FDA.C.1.7.1

Combination Product? (FDA.C.1.12)	Expedited Report? (ICH C.1.7)	Local Criteria Report Type (FDA.C.1.7.1)
true	true	1=15 Day, 4=5 Day
true	false	2=Non-Expedited AE, 5=Malfunction only (No AE)
false or nullFlavor: NI	true	1=15 Day
false or nullFlavor: NI	false	2=Non-Expedited AE

5. Combination Production Report Indicator (FDA.C.1.12)

For FDA reporting, if the ICSR includes a suspect vaccine that is a combination product and for which the sender is the applicant, then the value selected should be "true."

For additional guidance on submitting ISCRs for Combination Products, refer to the "Postmarketing Safety Reporting for Combination Products Guidance for Industry and FDA Staff" available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products.

B. Primary Source(s) of Information (Section C.2.r)

Each ICSR shall have one primary reporter (primary source) identified in conformance with regional confidentiality requirements. For FDA reporting, whenever a reporter is marked as the Primary Source for Regulatory Purposes, then all data elements used to identify the Reporter (i.e., Reporter's given name, family name, street, city, state, zip, and phone), become mandatory and either a value or a nullFlavor must be provided for each data element. Additionally, the reporter's email address is added as a mandatory FDA regional data element. The nullFlavor MSK is not allowed for U.S. cases.

Table 10: Data elements that deviate from the base E2B IG, section C.2.r

Data Element	Field Name	Values	Modification to ICH E2B (R3)
ICH C.2.r.1.2	Reporter's Given Name	Free text nullFlavor: MSK, ASKU, NASK	Change in Conformance
ICH C.2.r.1.4	Reporter's Family Name	Free text nullFlavor: MSK, ASKU, NASK	Change in Conformance
ICH C.2.r.2.3	Reporter's Street	Free text nullFlavor: MSK, ASKU, NASK	Change in Conformance

Data Element	Field Name	Values	Modification to ICH E2B (R3)
FDA.C.2.r.2.3.1	Reporter's Street Address - Line 2	Free text	FDA Regional Element
ICH C.2.r.2.4	Reporter's City	Free text nullFlavor: MSK, ASKU, NASK	Change in Conformance
ICH C.2.r.2.5	Reporter's State or Province	Free text; 2 characters for US Cases nullFlavor: MSK, ASKU, NASK, NI	Change in Conformance and field length
FDA.C.2.r.2.5.1	Reporter's County	Free text or NCI US Counties Terminology Subset Code nullFlavor: MSK, ASKU, NASK, NI	FDA Regional Element
ICH C.2.r.2.6	Reporter's Postcode	Free text nullFlavor: MSK, ASKU, NASK	Change in Conformance
ICH C.2.r.2.7	Reporter's Telephone	Free text nullFlavor: MSK, ASKU, NASK	Change in Conformance
FDA.C.2.r.2.8	Reporter's Email	Free text nullFlavor: MSK, ASKU, NASK	FDA Regional Element
ICH C.2.r.3	Reporter's Country Code	GENC two-letter code nullFlavor: MSK, ASKU, NASK, UNK	Change in Conformance

Data Element	Field Name	Values	Modification to ICH E2B (R3)
ICH C.2.r.4	Qualification	1=Physician 2=Pharmacist 3=Other health professional 4=Lawyer 5=Consumer or other non health professional nullFlavor: UNK C16960=Patient C42709=Parent	Additional Guidance

1. Reporter's County and Reporter's Country (FDA.C.2.r.2.5.1 and C.2.r.3)

For FDA reporting, if the Patient is the Primary Source Reporter (C.2.r.5), then Reporter's County and Reporter's Country are also mandatory, in order to help capture the patient's complete contact information (see "Primary Source Reporter for Regulatory Purposes (C.2.r.5)" below).

2. Reporter Qualification (C.2.r.4)

The reporter's relationship to the patient is captured with the Reporter Qualification data element. The ICH E2B (R3) Reporter Qualification codes "1" or "3" are used for healthcare professionals, and values for patient and parent have been added as regional expansions (see **Table 11**).

Table 1: Regional VAERS Reporter Qualification Codes

NCI Concept Identifier	Description
C16960	Patient
C42709	Parent

3. Primary Source Reporter for Regulatory Purposes (C.2.r.5)

In cases where the patient is identified as the Primary Source Reporter for Regulatory Purposes (C.2.r.5), additional FDA regional data elements are used in C.2.r to capture the patient's full contact information and complete address (including the US State and County) and email address. The patient's name and address information are required and correspond to the person who received the vaccine or that person's legal representative as required by the National Childhood Vaccine Injury Act (NCVIA). For foreign cases, if the identification of the patient is prohibited by national or regional confidentiality laws or directives, the null flavor code MSK should be used. In any case, name and address information, including email address, are redacted from VAERS data made available to the public.

When the patient or parent is not a primary source reporter, information about these individuals should be provided using the appropriate ICH guidance for the patient (D.1) or parent (D.10); However, the ICH data elements, D.1.1 Patient Name and D.1.10 Parent Name, are expanded to support capture of additional details (Section D).

C. Information on the Sender of Case Safety Report (Section C.3)

For FDA reporting, the data elements listed in the table below, which are used to identify the person responsible for sending the ICSR, are mandatory. Additionally, an FDA Regional Data Element, Sender's Street Address - Line 2, is added an optional data element.

Table 12: Data elements that deviate from the base E2B IG, section C.3.3

Data Element	Field Name	Values	Modification to ICH E2B (R3)
ICH C.3.3.1	Sender's Department	Free Text	Change in Conformance
ICH C.3.3.2	Sender's Title	Free Text	Change in Conformance
ICH C.3.3.3	Sender's Given Name	Free Text	Change in Conformance
ICH C.3.3.5	Sender's Family Name	Free Text	Change in Conformance
ICH C.3.4.1	Sender's Street Address	Free Text	Change in Conformance
FDA.C.3.4.1.1	Sender's Street Address - Line 2	Free Text	FDA Regional Element
ICH C.3.4.2	Sender's City	Free Text	Change in Conformance
ICH C.3.4.3	Sender's State or Province	Free Text	Change in Conformance
ICH C.3.4.4	Sender's Postcode	Free Text	Change in Conformance
ICH C.3.4.5	Sender's Country Code	GENC two-letter code	Change in Conformance
ICH C.3.4.6	Sender's Telephone	Free Text	Change in Conformance
ICH C.3.4.7	Sender's Fax	Free Text	Change in Conformance
ICH C.3.4.8	Sender's E-mail Address	Free Text	Change in Conformance

D. Literature References (C.4.r) and Study Registration (C.5)

When literature articles are provided as ICSR attachments, FDA has limited encoding to B64, and compression cannot be used. The regional data element, *Attachment file name* (FDA.C.1.6.1.r.3) is used to automate ICSR file attachment identification and processing. This data element is supported using the <reference value='…'> element/attribute in the XML file. The attachment file name must be provided in this element and the location of the *Attachment file name* must follow the <text mediaType> XML tag. Refer to the XML snippet example for ICH C.1.6.1.r.2 for more information.

Table 13: Data elements that deviate from the base E2B IG, section C.4.r

Data Element	Field Name	Values	Modification to ICH E2B (R3)
ICH C.4.r.2	Included Documents	Media type: e.g. Application/PDF, image/jpeg, application/DICOM, text/plain Representation: e.g., B64	Change in Data Type and Additional Guidance

1. Included Documents (C.4.r.2)

The location of the attachment file name must follow the <text mediaType> attribute based upon the following example:

<text mediaType="text/plain" representation="B64">
<reference value="SUMMARY OF CLINICAL HISTORY.txt"/>
VGhlIHBhdGllbnQgd2FzIGEgMzUgeWVhciBvbGQgQWZyaWNhbiBBbWVyaWNhbiBtYWxlIHdpdGggbm8gc2lXJnZSBzYWRkbGUgdGhyb21idXMgcmVz</text>

If the file extension in the filename does not match the media type, the ICSR file will be rejected.

2. Study Registration (C.5.1.r.2)

FDA accepts GENC country codes only, which does not include “EU.”

Table 14: Data elements that deviate from the base E2B IG, section C.5

Data Element	Field Name	Values	Modification to ICH E2B (R3)
C.5.1.r.2	Study Registration Country	GENC two-letter code nullFlavor: ASKU, NASK	Change in Business Rules

E. Patient Characteristics (Section D)

Table 15: Data elements that deviate from the base E2B IG, section D

Data Element	Field Name	Values	Modification to ICH E2B (R3)
ICH D.1.	Patient (name or initials)	Use expanded Patient Name fields	Change in Business Rules and Conformance
FDA.D.1a	Patient Name Prefix	Free Text nullFlavor: MSK, ASKU, NASK, UNK	FDA Regional Element
FDA.D.1b	Patient First Name	Free Text nullFlavor: MSK, ASKU, NASK	FDA Regional Element
FDA.D.1c	Patient Middle Name	Free Text nullFlavor: MSK, NASK, UNK	FDA Regional Element
FDA.D.1d	Patient Last Name	Free Text nullFlavor: MSK, NASK, UNK	FDA Regional Element
FDA.D.1e	Patient Address Line 1	Free Text nullFlavor: MSK, NASK, UNK	FDA Regional Element
FDA.D.1f	Patient Address Line 2	Free Text	FDA Regional Element
FDA.D.1g	Patient Address City	Free Text nullFlavor: MSK, NASK, UNK	FDA Regional Element
FDA.D.1h	Patient Address State or Foreign Province Name	Free Text; 2 characters for US cases nullFlavor: MSK, ASKU, NASK, NI	FDA Regional Element
FDA.D.1i	Patient Address County	Free Text nullFlavor: MSK, ASKU, NASK, NI	FDA Regional Element
FDA.D.1j	Patient Address Country	GENC two-letter code nullFlavor: MSK, ASKU, NASK, NI	FDA Regional Element

Data Element	Field Name	Values	Modification to ICH E2B (R3)
FDA.D.1k	Patient Address Postal Code	Free Text nullFlavor: MSK, ASKU, NASK	FDA Regional Element
FDA.D.1l	Patient Telephone	Free Text nullFlavor: MSK, ASKU, NASK	FDA Regional Element
FDA.D.1m	Patient Email	Free Text nullFlavor: MSK, ASKU, NASK	FDA Regional Element
ICH D.2.1	Date of Birth	See Appendix II of the ICH IG for further guidance on formatting date/time fields. nullFlavor: MSK	Change in Business Rules
FDA.D.2.1a	Age at Time of Vaccination	Numeric	FDA Regional Element
FDA.D.2.1b	Age at Time of Vaccination (unit)	UCUM code: a (Year), mo (Month), wk (Week), d (Day), h (Hour), 10.a (decade)	FDA Regional Element
ICH D.2.2a	Age at Time of Onset of Reaction / Event (number)	Numeric	Change in Business Rules
ICH D.2.2b	Age at Time of Onset of Reaction / Event (unit)	UCUM code: a (Year), mo (Month), wk (Week), d (Day), h (Hour), 10.a (decade)	Change in Business Rules
ICH D.2.2.1a	Gestation Period When Reaction / Event Was Observed in the Foetus (number)	Numeric	Change in Business Rules
ICH D.2.2.1b	Gestation Period When Reaction/Event Was Observed in the Foetus (unit)	UCUM code: mo (Month), wk (Week), d (Day), {Trimester}	Change in Business Rules
ICH D.2.3	Patient Age Group (as per reporter)	0=Foetus 1=Neonate (Preterm and Term newborns) 2=Infant 3=Child 4=Adolescent 5=Adult 6=Elderly nullFlavor: MSK, UNK, ASKU, NI	Change in Business Rules, Conformance, and Values
ICH D.7.1.r.1b	Medical History (disease / surgical procedure / etc.) (MedDRA code)	Numeric	Change in Business Rules
FDA.D.7.4a	Illness at Time of Vaccination MedDRA Version	N.N	FDA Regional Element
FDA.D.7.4b	Illness at time of Vaccination MedDRA Code	Numeric	FDA Regional Element

Data Element	Field Name	Values	Modification to ICH E2B (R3)
ICH D.8.r.2a	MPID Version Date/Number	Free Text	Change in Business Rules and Conformance
ICH D.8.r.2b	MPID	MPID: two or three segment NDC Code separated by hyphens	Change in Business Rules and Conformance
ICH D.8.r.3a	PhPID Version Date/Number	Not in use for FDA reporting	N/A
ICH D.8.r.3b	Pharmaceutical Product Identifier (PhPID)	Not in use for FDA reporting	N/A
FDA.D.8.r.8a	Patient Age at Vaccination (number)	Numeric	FDA Regional Element
FDA.D.8.r.8b	Patient Age at Vaccination (unit)	UCUM code: h (Hour), d (Day), wk (Week), mo (Month), a (Year), 10.a (decade)	FDA Regional Element

1. Patient Name and Contact Information (D.1)

If the primary source reporter is the Patient, then section D.1 is optional and can be omitted from the XML file (because the data elements for reporter name and contact information will capture this information for the patient). When this section is included in VAERS ICSRs, full patient name and contact information (e.g., first and last name, address, phone, email) is required. Provide expanded FDA regional data elements for the patient's name (Patient Name Prefix, Patient First Name, Patient Middle Name, and Patient Last Name) as nested parts in the Patient Name field (D.1) using the <name> element. Additionally, provide expanded FDA regional data elements for the patient's address (Address Line 1&2, City, County, State, Country, Zip Code, Phone and Email) as nested data elements within the <addr> data element. In general, an identifiable patient is required in order to submit an ICH ICSR. However, when the local criteria report type is Malfunction Only (No AE), and there was no patient involved in the malfunction, then all of the mandatory nested name and address fields in D.1 should be populated with "None". For foreign cases, if the identification of the patient is prohibited by certain national or regional confidentiality laws or directives, the null flavor code MSK should be used. In any case, name and address information, including email address, are redacted from VAERS data made available to the public.

2. Patient Address State or Foreign Province Name (FDA.D.1h)

US Postal Service (USPS) two-letter state abbreviations or foreign province names are supported for the <State/Province> data element. USPS state abbreviations can be obtained from the USPS website site: https://pe.usps.com/text/pub28/28apb.htm.

3. Patient Address County (FDA.D.1i)

FDA supports free text descriptions and regional terminology in the <county> address data element to support consistent capture of US county names. If the county information is provided as free text, the full county name and USPS state abbreviation should be provided when known to help ensure uniqueness across US states. If the county information is provided as coded information, use the reference sections 4.6 and 4.7 of the American National Standards Institute (ANSI) International Committee for Information Technology Standards (INCITS) specification standard 31-2009, which is entitled, "Codes for the Identification of Counties and Equivalent Areas of the United States, Puerto Rico, and the Insular Areas".[4]

[4] The U.S. Census Bureau is the maintenance agency for setting the codes for counties under ANSI/INCITS 31-2009.

NCI has pre-coordinated this data for FDA and has placed this data in an NCIt subset named "US Counties Terminology" which has an NCI code of C111076. The terminology subset is available for download from the NCI EVS website at: http://evs.nci.nih.gov/ftp1/FDA/ICSR. The FDA preferred term (PT) from this subset (rather than the NCIt Code) should be used. In the example below, the county code of TN187 should be used to represent Williamson County in the state of Tennessee (rather than C110209).

NCIt PT: Williamson County, TN
NCIt SY: Williamson County
NCIt SY: Williamson County, Tennessee
FDA PT: TN187

4. Patient Age Information (D.2)

FDA requires that at least one of the data elements in the Age Information section (Date of Birth (D.2.1), Age at Time of Vaccination (FDA.D.2.1a/b), Age at time of Onset of Reaction (D.2.2a/b), and Patient Age Group (D.2.3)) be populated, preferably Date of Birth and/or Age at the Time of Vaccination. "Patient Age Group" is required if no other age field is available (unless the Local Criteria Report Type is Malfunction Only (No AE)). Applicants should distinguish the *Age at the Time of Vaccination* concept from Age at time of Reaction/Event (ICH D.2.2) in vaccine ICSRs by using a separate <observation> code=3. The FDA regional terminology code for *Age at the Time of Vaccination* is C103173. If Local Criteria Report Type = Malfunction Only (No AE), then all age fields are optional.

5. VAERS Illness at the Time of Vaccination (FDA.D.7.4)

The FDA regional data element, *Illness at the Time of Vaccination*, is captured as a separate data element, which has a relationship with the suspect vaccine product(s) listed in the ICH Drug Information Section G.K. This regional data element is supported as an additional <observation> using the FDA terminology code C102468 to distinguish the data element from other patient medical history items in the Relevant Medical History and Concurrent Conditions Section (D.7). Applicants should provide information about any short-term illness, condition or symptom present at or about the time of vaccination (e.g., cold, fever, ear infection), and should follow ICH guidance concerning the use of MedDRA coding. Information for start date and end date for this data element is not required.

6. Relevant Past Drug History (D.8)

FDA regional extensions to ICH section D.8 are needed to support regional terminology and the VAERS data element "Age at Time of Vaccination" (FDA.D.8.r8a/b) for past vaccination history. This data element is captured as an additional <observation> using the regional terminology code C88065 and the value is captured as an HL7 PQ datatype with coded units of measure using UCUM.

a) Name of Drug as Reported (D.8.r.1)

To help ensure simple and consistent product identification, applicants should provide the names of vaccines exactly as listed in the Purple Book: https://purplebooksearch.fda.gov/.

Published by FDA and updated periodically, the Purple Book lists biological products, including biosimilar and interchangeable biological products, licensed by FDA under the Public Health Service Act (the PHS Act). The proprietary names listed in the Purple Book should be used whenever possible; proper names can be used if insufficient information is available to identify the specific product.

For vaccines, the MPID should be used, if known. When MPID is unknown, applicants may use the regional vaccine abbreviation as the US product trade name in the <kindOfProduct><name> data

These ANSI/INCITS 31-2009 county codes are not unique across all U.S. states, and as a result ANSI/INCITS 31-2009 sections 4.6 and 4.7 sets forth a format to permit unique representation of each county. ANSI/INCITS 31-2009 sections 4.6 and 4.7 state that unique representation is achieved by concatenating the two-character U.S. Postal Service representation of the state or state equivalent in which the county or county equivalent is located with the three-digit ANSI/INCITS 31-2009 county code

element.

b) MPID (D.8.r.2)

FDA has modified the ICH E2B (R3) Medicinal Product Identifier (MPID) to accommodate use of the FDA NDC code. FDA accepts the two-segment NDC (labeler code + product code) or three-segment NDC (labeler code + product code + package type) as the regional MPID. FDA NDC codes are available for download at: https://www.fda.gov/drugs/drug-approvals-and-databases/national-drug-code-directory. If the MPID is provided (D.8.r.2b), then MPID Version Date and Number (D.8.r.2a) is required.

F. Information Concerning the Parent (Section D.10)

In cases where a fetus or breast-feeding infant is exposed to one or more vaccines through the parent and experienced an adverse event, information on both the parent and the child/fetus should be provided. Reports of these cases are referred to as parent-child/fetus reports. Please see E2B IG (Section D) for principles to be used for filing these reports. Note that Section D.10 should be used in the case of a parent-child/fetus report where the parent had no reaction/event. Otherwise, this section should not be used.

Table 16: Data elements that deviate from the base E2B IG, section D.10

Data Element	Field Name	Values	Modification to ICH E2B (R3)
FDA.D.10.2.2.1a	Parent Age at Vaccination (number)	Numeric	FDA Regional Element
FDA.D.10.2.2.1b	Parent Age at Vaccination (unit)	UCUM code: h (Hour), d (Day), wk (Week), mo (Month), a (Year), 10.a (decade)	FDA Regional Element
ICH D.10.8.r.2a	MPID Version Date/Number	Free Text	Change in Business Rules and Conformance
ICH D.10.8.r.2b	MPID	MPID: two or three segment NDC Code separated by hyphens	Change in Business Rules and Conformance
ICH D.10.8.r.3a	PhPID Version Date/Number	Not in use for FDA reporting	N/A
ICH D.10.8.r.3b	Pharmaceutical Product Identifier (PhPID)	Not in use for FDA reporting	N/A

1. Parent Contact Information (D.10.1)

D.10 data elements (including FDA regional data elements) apply only when the child/fetus has an adverse reaction/event (other than early spontaneous abortion/fetal demise), and the parent is the source of exposure to the suspect product. For FDA reporting, when the parent is the source of exposure, provide the parent's contact information (address, phone and email) in the relevant ICSR section (e.g., Primary Source(s) of Information or Patient Information). The HL7 role code PRN is used to distinguish the parent information in the XML file. Additional data elements such as <name> and regional <observation> codes are used.

2. Parent Age at Time of Vaccination (FDA.D.10.2.2.1)

In addition to the ICH data elements of Parent Date of Birth and Parent Age, the FDA regional data element, *Parent Age at Time of Vaccination*, is provided in Section D.10. *Parent Age at Time of Vaccination* is captured using the <observation> data element and regional terminology code C103173

when known. The age value and unit should be captured using the HL7 PQ data type and coded units of measure using UCUM.

G. Parent Relevant Past Drug History (D.10.8.r)

FDA regional extensions and terminology are used in this section for ICH D.10.8.r.1 (Name of Drug as Reported) and D.10.8.r.2 (MPID).

Table 17: Data elements that deviate from the base IG, section D.10.8.r

Data Element	Field Name	Values	Modification to ICH E2B (R3)
FDA.D.11	Patient Race Code	<Observation><code>= C17049. C16352=African American C41259=American Indian or Alaska Native C41260=Asian C41219=Native Hawaiian or Other Pacific Islander C41261=White nullflavor: UNK, MSK, OTH	FDA Regional Element and Change in Business Rules
FDA.D.12	Patient Ethnicity Code	<Observation><code>= C16564. C17459=Hispanic or Latino C41222=Non Hispanic or Latino nullflavor: UNK, MSK, NI	FDA Regional Element and Change in Business Rules
FDA.D.13	Pregnant at time of Vaccination	<Observation><code>= C162844. false, true nullFlavor: UNK	FDA Regional Element
FDA.D.14	Patient Military Status	<Observation><code>= C114855. C114854=Active Duty C114857=Reserve C114858=National Guard C114859=TRICARE Beneficiary	FDA Regional Element

1. FDA Patient Race and Ethnicity Information (FDA.D.11 and FDA.D.12)

FDA is improving its ability to collect and analyze patient race and ethnicity data using structured data elements and controlled terminology. Applicants should provide patient race and ethnicity information using the regional terminology codes listed in **Table 18**. The race <observation> code is C17049, and multiple race classification codes can be used for a person. The ethnicity <observation> code is C16564, and only one (1) ethnic group code can be used. If the patient race or ethnicity information is not available or unknown, use the appropriate nullFlavor values for Unknown (UNK), No information (NI) or Masked (MSK) within these data elements. If the Local Criteria Report Type=Malfunction Only (No AE), then this field is optional.

Table 18: FDA Race and Ethnicity Codes

NCI Concept Identifier	Description

C1704	Race
C16352	African American
C41259	American Indian or Alaska Native
C4126	Asian
C41219	Native Hawaiian or Other Pacific Islander
C41261	White
C1656	**Ethnicity**
C1745	Hispanic or Latino
C41222	Not Hispanic or Latino

2. Pregnant at Time of Vaccination (FDA.D.13)

For this FDA regional data element, select "true" to identify vaccine recipients that were pregnant at the time of vaccination.

3. Patient Military Status (FDA.D.14)

The FDA regional data element, *Patient Military Status,* is used for U.S. Military or Department of Defense related reports to indicate the patient's military status (or association with military health services) at the time of vaccination. This data element is supported using an additional <observation> code C114855 with coded values as reflected in **Table 19**.

Table 19: Patient Military Status

NCI Concept Identifier (OID 2.16.840.1.113883.3.26.1.1)	Description
C114855	Patient Military Status ICSR Terminology
C114854	Active Duty
C114857	Reserve
C114858	National Guard
C114859	TRICARE Beneficiary

H. Reactions/Events (Section E.i)

FDA regional extensions to ICH Section E.i support additional patient outcome options for specifying hospitalization required versus prolonged, the number of days hospitalized, and the hospital name, city, and state as well as information about a doctor or other healthcare professional visit, and Emergency Department (ED) or urgent care visit related to the event.

Table 20: Data elements that deviate from the base E2B IG, section E.i

Data Element	Field Name	Values	Modification to ICH E2B (R3)
FDA.E.i.1.3	Reaction Identifier	UUID/GUID format: 32 Hexadecimal digits with hyphen grouping 8-4-4-4-12	FDA Regional Element
FDA.E.i.3.2c.1	Hospitalization Required	True, nullFlavor: NI	FDA Regional Element
FDA.E.i.3.2c.1a	Number of days hospitalized	Numeric nullFlavor: NI	FDA Regional Element

Data Element	Field Name	Values	Modification to ICH E2B (R3)
FDA.E.i.3.2c.1b	Hospital Name	Free Text, nullFlavor: NI	FDA Regional Element
FDA.E.i.3.2c.1c	Hospital City	Free Text, nullFlavor: NI	FDA Regional Element
FDA.E.i.3.2c.1d	Hospital State	Free Text, nullFlavor: NI	FDA Regional Element
FDA.E.i.3.2c.2	Resulted in Prolongation of Hospitalization	True, nullFlavor: NI	FDA Regional Element
FDA.E.i.3.3a	Emergency Department or urgent care	<Observation><code>= C53513 True, nullFlavor: NI	FDA Regional Element
FDA.E.i.3.3b	Doctor or other healthcare professional Office/Clinic Visit	<Observation><code>= C16988 True, nullFlavor: NI	FDA Regional Element
FDA.E.i.3.2g	AE Outcome None of the Above	Data element is used to support VAERS value "Other" using an additional <Observation> <code>=C17649. True, nullFlavor: NI	FDA Regional Element
FDA.E.i.3.4	Best doctor/healthcare professional title or prefix	Free Text	FDA Regional Element
FDA.E.i.3.4a	Best doctor/healthcare professional Last Name	Free Text	FDA Regional Element
FDA.E.i.3.4b	Best doctor/healthcare professional First Name	Free Text	FDA Regional Element
FDA.E.i.3.4c	Best doctor/healthcare professional Middle Name	Free Text	FDA Regional Element
FDA.E.i.3.4d	Best doctor/healthcare professional Telephone and extension	HL7 <telecomm> format	FDA Regional Element
FDA.E.i.3.4e	Best doctor/healthcare professional Email	HL7 <telecomm> format	FDA Regional Element

Data Element	Field Name	Values	Modification to ICH E2B (R3)
ICH E.i.4	Date of Start of Reaction / Event	See Appendix II of the ICH IG for further guidance on formatting date/time fields. nullFlavor: MSK, ASKU, NASK	Change in Business Rules and Conformance
ICH E.i.5	Date of End of Reaction / Event	See Appendix II of the ICH IG for further guidance on formatting date/time fields. nullFlavor: MSK, ASKU, NASK	Change in Business Rules and Conformance
ICH E.i.6a	Duration of Reaction / Event (number)	Numeric	Change in Business Rules
ICH E.i.9	Identification of the Country Where the Reaction / Event Occurred	GENC two-letter code	Change in Business Rules

For FDA reporting, event seriousness should be determined based on the occurrence of death, life-threatening event, hospitalization, and other criteria listed in 21 CFR 600.80 (a). With regards to the "*Otherwise Medically Important Condition*" (ICH E.i.3.2f), applicants should judge events to be otherwise medically important based on the description provided in 21CFR600.80(a) and associated guidance and their medical judgment. FDA Regional extensions support additional patient outcomes of ED/urgent care visit and doctor or other healthcare professional visit. AEs which are treated or evaluated in these settings may or may not be considered medically important conditions; applicants should judge seriousness based on 21CFR600.80 (a).

1. Hospital Information (FDA.E.i.3.2.c.1)

A VAERS regional terminology code for distinguishing between *Hospitalization Required* and *Resulted in Prolongation of Hospitalization* is required when the Boolean value for ICH E.i.3.2c *Caused / Prolonged Hospitalization* is "true". The regional data elements should be completed in accordance with ICH guidance by using the allowable values of "true" or the nullFlavor "NI" for the regional Boolean data elements. The FDA OID and value set are provided in **Table 21**.

Table 21: VAERS Reaction/Event Outcome Terminology

NCI Concept Identifier (OID 2.16.840.1.113883.3.26.1.1)	Description
C53513	Emergency Room
C16988	Physician Office
C17649	AE Outcome None of the Above
C50414	Hospitalization Required
C102450	Resulted in Prolongation of Hospitalization
C102443	Number of Days Hospitalized

The *Number of Days Hospitalized* and the *Hospital Name, City, and State* are required when the data element *Hospitalization Required* is true. The *Hospital Name, City, and State* should be provided using the <representedOrganization> data element. This data element is associated as the organization scoping role for the <AssignedEntity> data element as the performer of the hospitalization act. The <organization.name> data element captures the name of the facility and the <address> data element

captures the city and state information. U.S. State information should be captured using free text or USPS two letter state abbreviations. If the information is unknown, the nullFlavor "NI" should be used.

2. Other VAERS AE Treatment Outcomes (FDA.E.i.3.3)

The FDA regional data element, *Doctor/healthcare professional Office,* should be selected as an AE Outcome when the patient's adverse event was evaluated and/or treated at a doctor's office or other healthcare professional's office or clinic. The FDA regional data element, *Emergency Department or urgent care,* should be selected when the patient's adverse event was evaluated and/or treated at an emergency department or urgent care. The information in these FDA regional data elements is a separate and distinct concept from the ICH reaction/event seriousness criteria (E.i.3.2a, b, c, d, e, and f).

The FDA regional data element, *AE Outcome None of the Above*, is captured using the <observation> data element and regional terminology code C17649. This data element should only be "true" when none of the above seriousness criteria (E.i.3.2a, b, c, d, e, and f) apply and the AE was not treated or evaluated in an ED/urgent care (FDA.E.i.3.3a) or healthcare professional office/clinic (FDA.E.i.3.3b).

3. Best doctor/healthcare professional information (FDA.E.i.3.4)

The FDA regional data elements, *Best doctor/healthcare professional title, last name, first name, middle name, telephone, and email,* are used to capture contact information for the best physician or other healthcare professional to contact about the adverse event.

The additional <prefix> name part data element is used to capture the provider's professional title information (e.g., Doctor, Registered Nurse (RN), etc.). Other <name> part data elements are used to capture the first, middle, and last name of the provider. The <address> data element is used to capture the provider's telephone number and email address.

I. Drug(s) Information (Section G.k)

This section aligns with the ICH Section G.k to capture the drug information. The data elements discussed in this section also help to identify device components of combination products.

Table 22: Data elements that deviate from the base E2B IG, section E.i

Data Element	Field Name	Values	Modification to ICH E2B (R3)
ICH G.k.1	Characterization of Drug Role	1=Suspect 2=Concomitant 3=Interacting 4=Drug Not Administered	Change in Business Rules
FDA G.k.1.a	FDA Other Characterization of Drug Role	1=Similar Device	Change in Business Rules and Conformance
ICH G.k.2.1.1a	MPID Version Date/Number	Free text	Change in Business Rules and Conformance
ICH G.k.2.1.1b	Medicinal Product Identifier (MPID)	MPID: two or three segment NDC Code separated by hyphens	Change in Business Rules and Conformance
ICH G.k.2.1.2a	Pharmaceutical Product Identifier (PhPID) Version Date/Number	Not in use for FDA reporting	N/A
ICH G.k.2.1.2b	PhPID	Not in use for FDA reporting	N/A
FDA.G.k.2.2.1	U.S. generic name	Free Text	FDA Regional Element

Data Element	Field Name	Values	Modification to ICH E2B (R3)
ICH G.k.2.3.r.1	Substance/Specified Substance Name	Free Text	Change in Business Rules
ICH G.k.2.3.r.2a	Substance/Specified Substance TermID Version Date/Number	Free Text	Change in Business Rules
ICH G.k.2.3.r.2b	Substance/Specified Substance TermID	SubstanceID	Change in Business Rules
ICH G.k.2.4	Identification of the Country Where the Drug Was Obtained	GENC two-letter code	Change in Business Rules
ICH G.k.3.1	Authorization / Application Number	Free Text	Change in Business Rules
ICH G.k.3.2	Country of Authorization / Application	GENC two-letter code	Change in Business Rules and Conformance
ICH G.k.4.r.9.2a	Pharmaceutical Dose Form TermID Version Date / Number	Free Text	Change in Business Rules
ICH G.k.4.r.9.2b	Pharmaceutical Dose Form TermID	FDA SPL Dosage Form or EDQM codelist	Change in Business Rules
ICH G.k.4.r.10.1	Route of Administration (free text)	Free text nullFlavor: ASKU, NASK, UNK	Change in Conformance
ICH G.k.4.r.10.2a	Route of Administration TermID Version Date / Number	Free Text	Change in Business Rules and Conformance
ICH G.k.4.r.10.2b	Route of Administration TermID	FDA SPL or EDQM codelist	Change in Business Rules
ICH G.k.4.r.11.2a	Parent Route of Administration TermID Version Date / Number	Free Text	Change in Business Rules and Conformance
ICH G.k.4.r.11.2b	Parent Route of Administration TermID	FDA SPL or EDQM codelist	Change in Business Rules
FDA.G.k.4.r.12	Vaccine Anatomical Approach Site	See Table 22 nullFlavor: MSK, ASKU, NASK	FDA Regional Element
FDA.G.k.4.r.13	Dose Number in Series	Numeric	FDA Regional Element
FDA.G.k.4.r.14	Vaccination Facility Name	Free Text nullflavor: NI	FDA Regional Element
FDA.G.k.4.r.14.1a	Vaccination Facility Address Line 1	Free Text nullflavor: NI	FDA Regional Element
FDA.G.k.4.r.14.1b	Vaccination Facility Address Line 2	Free Text nullflavor: NI	FDA Regional Element
FDA.G.k.4.r.14.2	Vaccination Facility City	Free Text nullflavor: NI	FDA Regional Element

Data Element	Field Name	Values	Modification to ICH E2B (R3)
FDA.G.k.4.r.14.3	Vaccination Facility State	Free Text or USPS two letter abbreviation. nullFlavor: NI	FDA Regional Element
FDA.G.k.4.r.14.4	Vaccination Facility Country	GENC two-letter code nullFlavor: NI	FDA Regional Element
FDA.G.k.4.r.14.5	Vaccination Facility Postal Code	Free Text nullFlavor: NI	FDA Regional Element
FDA.G.k.4.r.14.6	Vaccination Facility Telephone	HL7 <telecomm> format nullFlavor: NI	FDA Regional Element
FDA.G.k.4.r.14.7	Vaccination Facility Fax	HL7 <telecomm> format nullFlavor: NI	FDA Regional Element
FDA.G.k.4.r.14.8	Vaccination Facility Type	See Table 23 nullflavor: UNK, OTH	FDA Regional Element
FDA.G.k.4.r.14.9	Vaccination Facility Military Flag	true, false nullFlavor: NI	FDA Regional Element

1. Characterization of Drug Role (ICH G.k.1)

The first product in Section G (Drug(s) Information) must be either *Suspect* or *Interacting*, unless the product has at least one device constituent part where Malfunction = "True", in which case the value can be *Suspect, Interacting,* or *Drug Not Administered*.

2. FDA Other Characterization of Drug Role (FDA G.k.1.a)

The "FDA Other Characterization for Drug Role" of *Similar Device* applies to scenarios where an applicant is aware of a malfunction that occurred with one product ("vaccine A"), which has a device constituent part that is the same or similar to the device part of a second product ("vaccine B") also marketed by the applicant. If the applicant determines that the malfunction observed with vaccine A would be likely to occur with vaccine B, then the applicant must submit a malfunction report for vaccine B. For example, if applicants market, outside of the U.S. (OUS), a combination product with a device constituent part that is similar to the device constituent part of a product marketed by the applicant within the U.S., and a malfunction is observed with the OUS product that would be likely to occur with the U.S. product, then, consistent with the approach for device products, the applicant should submit a malfunction report for the U.S. product. For additional information on reporting for "similar devices", including additional example scenarios, see the FDA Guidance "Postmarketing Safety Reporting for Combination Products Guidance for Industry and FDA Staff" available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products.

For FDA reporting of this scenario, the U.S.-marketed product, with the device constituent part that is similar to the device part of the OUS product, should be assigned the drug role (G.k.1) of *drug not administered* and the "FDA Other Characterization for Drug Role" (G.k.1.a) of *similar device*. Similar device is allowed in G.k.1.a when Combination Product (FDA.C.1.12) is *true*, Malfunction (FDA.G.k.12.r.1) is *true*, and G.k.1 is *Drug Not Administered.*

3. FDA MPID (G.k.2.1.1b)

The FDA regional extensions described in this section are the same regional extensions described in the Past Drug History Section (see V.E.6: Relevant Past Drug History ICH D.8). The FDA NDC should be used as the regional MPID when known. FDA accepts the two-segment NDC (labeler code + product code) or three-segment NDC (labeler code + product code + package type) as the regional MPID. FDA NDC codes are available for download at the FDA Structured Product Labeling (SPL) Resources webpage at: https://www.fda.gov/industry/structured-product-labeling-resources/nsde.

Questions concerning these identifiers should be addressed to spl@fda.hhs.gov. Foreign MPIDs are also allowed when available. The NDC code is captured using the <kindOfProduct><code> data element, and the regional MPID Version Date/Number (ICH G.k.2.1.1a) is the date and time of the modified file downloaded from the FDA website.

4. Medicinal Product Name as Reported by the Primary Source (ICH G.k.2.2)

To help ensure simple and consistent product identification, applicants should provide the names of vaccines exactly as listed in the Purple Book: https://purplebooksearch.fda.gov/.

Published by FDA and updated periodically, the Purple Book lists biological products, including biosimilar and interchangeable biological products, licensed by FDA under the Public Health Service Act (the PHS Act). The proprietary names listed in the Purple Book should be used whenever possible; proper names can be used if insufficient information is available to identify the specific product.

When foreign vaccine trade names are used, the information should be provided as free text in the <name> data element. Additionally, the U.S. generic name (FDA.G.k.2.2.1) should also be provided using an additional <genericMedicine><name> data element which links the foreign trade name to the non-proprietary, generic substance.

For FDA reporting, if the report involves a Malfunction of the device component of a vaccine combination product, then this field should still be populated with the name of the vaccine. Information on the device components of the product is collected in separate fields (see Device Fields in **Table 24)**.

5. Substance/Specified Substance (G.k.2.3.r)

FDA supports regional and ISO IDMP value sets for G.k.2.3.r when available. If an ISO IDMP 'Substance Name TermID' (G.k.2.3.r.2b) is not available, the substance/specified substance name (G.k.2.3.r.1) should be drawn from the FDA Substance Registration System's (SRS) Unique Ingredient Identifiers (UNII) when appropriate. FDA UNIIs can be obtained from the FDA Substance Registration System website. SRS files are made available for download at: http://fdasis.nlm.nih.gov/srs/jsp/srs/uniiListDownload.jsp. The regional Substance/Specified Substance TermID Version Date/Number (G.k.2.3.r.2a) is the date and time of the modified file downloaded from the FDA website. Questions concerning these identifiers should be addressed to fda-srs@fda.hhs.gov.

FDA requires at least one of: MPID (G.k.2.1.1), Substance TermID (G.k.2.3.r.2b), or Substance Name (G.k.2.3.r.1). If neither the MPID (i.e., NDC code) or the Substance TermID is provided, and only the active substance name is known (G.k.2.3.r.1), then use the name of the active substance as it appears in the FDA SRS. FDA recommends that applicants proactively validate substance information with primary source reporters before preparing the ICSR submission.

6. Authorization / Application Number (G.k.3.1)

For U.S. source reports, if Application Number is provided for the first product under section G, then it must be a BLA number. Please see Business Rules for format and length requirements.

7. Pharmaceutical Dosage Form (G.k.4.r.9.2b)

FDA accepts either the EDQM codelist for Pharmaceutical Dose Form Term ID or the FDA SPL Dosage Form list.

Please refer to ICH and EDQM guides for specific user instructions on EDQM: https://www.edqm.eu/sites/default/files/standard_terms_introduction_and_guidance_for_use.pdf

The list of FDA SPL dosage forms is available at: https://www.fda.gov/industry/structured-product-labeling-resources/dosage-forms

8. Route of Administration Term ID (G.k.4.r.10.2b)

FDA accepts either the EDQM codelist for Route of Administration Term ID or the FDA SPL Route of Administration list.

Please refer to the ICH and EDQM guides for specific user instructions on EDQM:
https://www.edqm.eu/sites/default/files/standard_terms_introduction_and_guidance_for_use.pdf

The list of FDA SPL Route of Administration Terms is available at:
https://www.fda.gov/industry/structured-product-labeling-resources/route-administration

9. Parent Route of Administration Term ID (G.k.4.r.11.2b)

FDA accepts either the EDQM codelist for Route of Administration Term ID or the FDA SPL Route of Administration list.

Please refer to the ICH and EDQM guides for specific user instructions on EDQM:
https://www.edqm.eu/sites/default/files/standard_terms_introduction_and_guidance_for_use.pdf

The list of FDA SPL Route of Administration Terms is available at:
https://www.fda.gov/industry/structured-product-labeling-resources/route-administration

10. VAERS Anatomical Approach Site (FDA.G.k.4.r.12)

The *Vaccine Anatomical Approach Site* is an FDA regional data element. This data element is captured using the substance administration <approachSite> data element and is coded using the FDA ICSR Vaccination on Body Site Terminology value set provided in **Table 22** below.

Table 22: FDA ICSR Vaccination on Body Site Terminology

NCI Concept Identifier (OID 2.16.840.1.113883.3.26.1.1)	Description
C105633	Left Arm
C105634	Left Deltoid
C105638	Left Gluteus Medius
C105642	Left Lower Forearm
C105632	Left Thigh
C105640	Left Vastus Lateralis
C105636	Right Arm
C105635	Right Deltoid
C105639	Right Gluteus Medius
C105643	Right Lower Forearm
C105637	Right Thigh
C105641	Right Vastus Lateralis

11. VAERS Dose Number in Series (FDA.G.k.4.r.13)

The *VAERS Dose Number in Series* data element is captured using the <outboundRelationship2 typeCode="FLFS"> data element and the <sequenceNumber> data element is used to capture the dose number.

12. Vaccination Facility Information (FDA.G.k.4.r.14)

The FDA regional data elements for vaccination facility information are required for US cases; the HL7 null flavor code NI (No Information) should be used if facility information is not available. The facility information, such as the name, address, telephone, fax and email, should be provided using the appropriate data elements in the <substanceAdministration> <performer> participation (e.g.,

<representedOrganization> data element. Refer to the Business Rules for more information about how to capture this data element in the XML file.

13. Vaccination Facility Type (FDA.G.k.4.r.14.8)

The FDA regional data element, *Vaccination Facility Type,* is required for U.S. source reports and supported using regional terminology. The facility type information is captured using the <performer><assignedEntity> code. The NCI EVS OID and NCI regional concept IDs are provided in **Table 23**.

Table 23: VAERS Vaccination Facility Type

NCI Concept Identifier (OID 2.16.840.1.113883.3.26.1.1)	Description
C16988	Physician Office
C16696	Hospital
C51282	Clinic
C53528	Urgent Care Center
C114860	Public Health Department
C114861	Workplace Clinic
C114862	School/Student Health Clinic
C114863	Pharmacy/Drug store
C53533	Nursing Home
C16801	Long term care for elderly

Facility type choices for: Other and unknown are supported using the appropriate HL7 null flavor values (OTH and UNK).

14. Vaccination Facility Military Flag (FDA.G.k.4.r.14.9)

The FDA regional data element, Vaccination Facility Military Flag, is used to further specify whether the Vaccination Facility is a Department of Defense (DOD)/military site. This data element is supported using a Boolean response to an additional <observation> code for Military Site: C114865.

15. Reaction Re-Occurance (G.k.9.i.4)

If a reaction recurred on re-administration of a product, then this data element may be provided. When including this data element, the reaction identifier is required when providing challenge causality assessment for reactions. The values for this field are listed below:

J. Combination Product Information (FDA.G.k.10.r and FDA.G.k.12.r)

FDA has provided additional regional extensions to accommodate reports for Combination Products as required by the “Postmarketing Safety Reporting for Combination Products Rule”, issued on December 20, 2016. For proper ICSR submissions for vaccine combination products, the information in **Table 24** should be provided, as applicable.

Combination products are regulated products that are each comprised of any combination of a drug, device, and/or a biological product. For vaccines, the most common example of a combination product is a vaccine supplied as a pre-filled syringe (i.e., a “single entity” combination composed of a biologic and a device).

Table 24: Information on Combination Products

Data Element	Field Name	Values	Modification to ICH E2B (R3)
FDA.G.k.10.r.1	FDA Specialized Product Category	See Table 25	FDA Regional Element
FDA.G.k.12.r.1	Malfunction	<Observation><code> =C54026. true, false	FDA Regional Element
FDA.G.k.12.r.2.r	Follow-up Type	<Observation><code> =C54592. 1=Correction 2=Additional Information 3=Response to FDA request 4=Device evaluation	FDA Regional Element
FDA.G.k.12.r.3.r	Device Problem Code	<Observation><code> =C54451. FDA Device Problem Codelist	FDA Regional Element
FDA.G.k.12.r.4	Device Brand Name	Free Text nullFlavor: NI	FDA Regional Element
FDA.G.k.12.r.5	Common Device Name	Free Text nullFlavor: NI	FDA Regional Element
FDA.G.k.12.r.6	Device Product Code	FDA Device Component Code	FDA Regional Element
FDA.G.k.12.r.7.1a	Device Manufacturer Name	Free Text	FDA Regional Element
FDA.G.k.12.r.7.1b	Device Manufacturer Address	Free Text	FDA Regional Element
FDA.G.k.12.r.7.1c	Device Manufacturer City	Free Text	FDA Regional Element
FDA.G.k.12.r.7.1d	Device Manufacturer State	Free Text	FDA Regional Element
FDA.G.k.12.r.7.1e	Device Manufacturer Country	GENC two-letter code	FDA Regional Element
FDA.G.k.12.r.8	Device Usage	1=Initial Use of Device 2=Reuse 3=Unknown	FDA Regional Element
FDA.G.k.12.r.9	Device Lot Number	Free Text	FDA Regional Element
FDA.G.k.12.r.10a	Operator of the Device	1=Health Professional 2=Lay User/Patient 3=Other	FDA Regional Element

Data Element	Field Name	Values	Modification to ICH E2B (R3)
FDA.G.k.12.r.11.r	Remedial Action Initiated	<Observation><code> =C54594 1=Recall 2=Repair 3=Replacement 4=Relabeling 5=Notification 6=Inspection 7=Patient Monitoring 8=Modification or Adjustment 9=Other	FDA Regional Element

1. Specialized FDA Product Categories (FDA.G.k.10.1)

FDA extensions are used in ICH G.k.10.r to support the identification of specialized FDA product categories of combination products. The FDA regional data element <characteristic.code> is used to support coding of specialized FDA product categories in the drug information section using NCI concept identifier C94031. Note that the "Combination Product Report Flag", data element FDA.C.1.12 is used to indicate that an ICSR includes a combination product; FDA.G.k.10.r is used to indicate which product(s) are combination products and the type of combination product. FDA regional codes for combination product types are listed in **Table 25** below:

Table 25: FDA Specialized Product Categories

NCI Concept Identifier C94031 (OID 2.16.840.1.113883.3.26.1.1)	Product Type Description
C102834	Type 1: Convenience Kit of Co- Package
C102835	Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)
C102836	Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)
C102837	Type 4: Device Coated/Impregnated/Otherwise Combined with Drug
C102838	Type 5: Device Coated or Otherwise Combined with Biologic
C102839	Type 6: Drug/Biologic Combination
C102840	Type 7: Separate Products Requiring Cross Labeling
C102841	Type 8: Possible Combination Based on Cross Labeling of Separate Products (Temporary Type)
C102842	Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)

2. Malfunction (FDA.G.K.12.r.1)

Malfunction is captured as a Boolean value (true or false) and should be provided for all combination products in an ICSR when the Combination Product Report Flag is "true". When the value for FDA.C.1.7 "Local Criteria Report Type=Malfunction Only (no AE), then the value for a malfunction must be "true" for at least one product.

3. Device Problem Codes (FDA.G.K.12.r.3.r)

FDA maintains a list of device problem codes available at: https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/MDRAdverseEventCodes/default.htm.

If there is no device problem associated with the ICSR, use the device problem code for "No Known Device Problem". At least one device problem code must be provided when malfunction=true.

4. Device Brand Name, Common Device Name, Device Product Code (FDA.G.k.12.r.4/5/6)

Provide the names or Device Product Code ("ProCode") for the device constituent part of the combination product (e.g., the syringe component of a vaccine supplied as a pre-filled syringe). At least one of these three data elements should be provided for each combination product.

At least one of the 3 must be reported with a non-null value for the device constituent part when Malfunction=true.

There will always be two <name> elements present – the first being the brand name, and the second being the common device name. Either can be null however, if both are null a value for FDA.G.k.12.r.6 is required.

The list of device product codes is available at: https://www.fda.gov/medical-devices/classify-your-medical-device/product-code-classification-database

5. Device Manufacturer Name, Address, City, State, Country (FDA.G.k.12.r.7.1a-)

Provide the name and location of the manufacturer of the device constituent part of the product.

6. Device Usage (FDA.G.k.12.r.8)

Indicate the usage of the device as the initial use, reuse, or unknown.

7. Device Lot Number (FDA.G.k.12.r.9)

Provide the lot number of the device.

8. Device Operator (FDA.G.k.12.r.10a)

Indicate the operator of the device.

9. Remedial Action Initiated (FDA.G.k.12.r.11.r)

Indicate the applicable action(s). This data element is required for 5-day reports (i.e., FDA.C.1.7 "Local Criteria Report Type='5-day'). See the FDA regulations concerning remedial action (21 CFR Parts 7, 803 and 806) for additional information.

K. VAERS Vaccines Given Within 4 Weeks (FDA.G2)

An FDA regional extension is required to support the *VAERS* data section *Vaccines Given within 4 Weeks*. This organizer section is used to capture relevant information about other vaccines received within one month prior to the date of the suspect vaccine(s) described in the ICH G.k Drug Information section. The FDA regional organizer section should be included to distinguish this information from the suspect vaccine(s) in the XML file using the regional <observation> code C102467. Data elements within this organizer section are summarized below.

Table 26: Vaccines given within 4 weeks

Data Element	Field Name	Values	Modification to ICH E2B (R3)
FDA.G2.k.1	Vaccine Type	Free Text or VAERS Vaccine type abbreviations nullFlavor: NI	FDA Regional Element
FDA.G2.k.2a	MPID Version Date / Number	Free Text	FDA Regional Element
FDA.G2.k.2b	MPID	MPID: two or three segment NDC Code separated by hyphens	FDA Regional Element
FDA.G2.k.3	Date Given	Date is captured as the low value of xsi:type IVL_TS for effectiveTime Date nullFlavor: NI, UNK	FDA Regional Element
FDA.G2.k.4a	Route of Administration TermID Version Date / Number	Free Text	FDA Regional Element
FDA.G2.k.4b	Route of Administration TermID	FDA SPL or EDQM codelist	FDA Regional Element
FDA.G2.k.5	Vaccine Anatomical Approach Site	See Table 22 nullFlavor: UNK, ASKU, NI	FDA Regional Element
FDA.G2.k.6	Dose Number in Series	Numeric	FDA Regional Element
FDA.G2.k.7	Lot Number	Free Text	FDA Regional Element
FDA.G2.k.8	Manufacturer Name	Free Text	FDA Regional Element

1. Vaccine Type (FDA.G2.k.1)

To help ensure simple and consistent product identification, applicants should provide the names of vaccines exactly as listed in the Purple Book: https://purplebooksearch.fda.gov/.

Published by FDA and updated periodically, the Purple Book lists biological products, including biosimilar and interchangeable biological products, licensed by FDA under the Public Health Service Act (the PHS Act). The proprietary names listed in the Purple Book should be used whenever possible; proper names can be used if insufficient information is available to identify the specific product.

2. Medicinal Product Identifier and Version Number (FDA.G2.k.2b)

The FDA NDC should be used as the regional MPID when known. Refer to section **V.I.2 FDA MPID ICH G.k.2.1.1b** of this document for more information about the use of FDA NDC codes.

3. Date Given (FDA.G.k.2.3)

The VAERS data element, *Date Given*, is captured within the <effectiveTime> data elements as the low value using the <xsi:type IVL_TS> data element. Note that at least **one** of the available date/time data elements in the ICH G.k Drug Information section must be provided. Nullflavor values of NI or UNK are accepted for this field. Refer to the ICH E2B (R3) IG for more information about the use of available product administration date/time data elements that can be used.

4. Route of Administration Term ID (FDA.G2.k.4b)

The vaccine route of administration should be provided in accordance with the information provided in section **V.I.8 Route of Administration TermID (G.k.4.r.10.2b)** of this document.

5. Vaccine Anatomical Approach Site (FDA.G2.k.5)

The vaccination site of administration should be provided in accordance with the information provided in section **V.I.9 VAERS Anatomical Approach Site** of this document.

6. Route of Administration TermID (FDA.G2.k.4b)

FDA accepts either the EDQM codelist for Route of Administration Term ID or the FDA SPL Route of Administration list.

Please refer to ICH and EDQM guides for specific user instructions on EDQM:
https://www.edqm.eu/sites/default/files/standard_terms_introduction_and_guidance_for_use.pdf

The list of FDA SPL Route of Administration Terms available at:
https://www.fda.gov/industry/structured-product-labeling-resources/route-administration

7. Dose Number in Series (FDA.G2.k.6)

The VAERS data element, *Dose Number in Series,* is captured using the <outboundRelationship2 typeCode="FLFS"> data element and the <sequenceNumber> data element is used to capture the dose number.

8. Lot Number (FDA.G2.k.7)

The VAERS data element, *Lot Number,* is captured in accordance with the ICH E2B (R3) guidance for ICH G.k.4.r.7 Batch / Lot Number. Refer to the ICH E2B (R3) IG for more information about this data element.

9. Manufacturer Name (FDA.G2.k.8)

The vaccine *Manufacturer Name* data element is captured using the <playingOrganization> data element for the <asManufacturedProduct> information in the XML file. Refer to the FDA ICSR Instance Example (Appendix II: FDA ICSR Instance Example) for an example of how to populate this information in the XML file.

VI. The Electronic Submission

Prepare your ICSR for electronic submission as follows:

- Provide a unique filename for the submission
- Add a file header and file extension
- Populate the elements of the ICSR file
- If applicable, add ICSR attachments to the ICSR file

ICSR attachments should be submitted to FDA at the same time that the associated ICSR file is submitted or as an attachment to a follow-up report. General information on electronic submission of vaccine postmarket ICSR reports to CBER can be viewed at CBER web page:
https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/electronic-submission-postmarket-safety-reports

A. Options for Electronic Submission into eVAERS

The FDA Electronic Submissions Gateway (ESG) is the central point of entry for sending various submission types including eVAERS ICSRs electronically to the FDA.

FDA provides two options for electronic submission of ICSRs and ICSR attachments involving vaccine products for processing via ESG:

- **FDA ESG Web Interface**: The FDA ESG Web Interface sends submissions via Hyper Text

Transfer Protocol Secure (HTTPS) through a web browser per AS2 standards. This method is intended primarily for small volume submitters.

- **Applicability Statement 2 Business-to-Business (AS2 B2B) Gateway-to-Gateway**: An electronic submission protocol that uses HTTP/HTTPS for communications.

Either or both options can be selected by a submitter to send eVAERS submissions to the FDA. The direct database-to-database submission method is described on FDA's Electronic Submissions Gateway (ESG) Web page[5]. Companies that normally use the direct database-to-database method to submit reports to FDA could use the eSubmitter tool[6] as a backup method for eVAERS submissions as appropriate. Additional information about FDA ESG connection options is described in the FDA ESG User Guide and is available for download from the FDA ESG website at:

https://www.fda.gov/industry/about-esg/user-guide

B. FDA ESG Transaction Partners

If not already obtained, vaccine manufacturers that intend to submit E2B (R3) ICSRs to eVAERS must apply for a Transaction Partner account (i.e., FDA ESG Web Interface submission account, and/or AS2 submission account) and complete the corresponding registration process.

Step-by-Step instructions from getting a test account to final approval of production readiness are included in the FDA ESG User Guide; and the most up-to-date information (e.g., announcement of system maintenance schedule, process update, etc.) can be found at the FDA ESG website.

If you have any problems with your account registration, please contact ESG Help Desk at ESGHelpDesk@fda.hhs.gov. When ready to conduct eVAERS production submission readiness testing (i.e., testing submission of guidance-compliant ICSR files), contact CBER ICSR Submissions Coordinator (mailto:CBERICSRSUBMISSIONS@fda.hhs.gov) to confirm your Sender ID information and testing date(s).

C. FDA ESG Routing Identifier

The ESG header information is separate from the ICSR file and is unique to the type of FDA ESG connection. Specific to eVAERS submissions, submitters must use the following ESG header value to ensure that the submission is routed to eVAERS:

- ESG Web Interface Submissions: CBER VAERS
- AS2 Gateway-to-Gateway Submissions: CBER_VAERS

D. Creating Electronic ICSRs using the FDA eSubmitter Software

The FDA eSubmitter is a free software that supports the creation of multiple submission types including eVAERS ICSR. eSubmitter is a stand-alone application and not connected to the FDA system. The software and any output files reside locally on your computer, allowing you to work on a submission offline, save, and continue later. Once you package a submission in eSubmitter, you can securely submit it through FDA ESG as discussed above.

CBER has implemented an eSubmitter data entry template (XML form) which supports data entry and submission of vaccine ICSRs and ICSR attachments. Information about the CBER ICSR eSubmitter template is available on the FDA eSubmitter website at:
http://www.fda.gov/forindustry/fdaesubmitter/default.htm.

[5] The FDA ESG Web page is available at:
http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/default.htm

[6] The FDA eSubmitter webpage is available at: https://www.fda.gov/industry/fda-esubmitter/icsr-reporting-vaers

E. Sending in Submissions

Before submitting an ICSR in electronic format to FDA for the first time, you should submit your request to CBER via email at CBERICSRSUBMISSIONS@fda.hhs.gov. For subsequent submissions in electronic format, it is not necessary to contact the VAERS Coordinator before submitting the ICSR. For additional information on providing submissions using the ESG, refer to FDA's ESG Web page at: http://www.fda.gov/esg.

F. eVAERS Acknowledgements

Once a submission (one or more ICSRs and ICSR attachments) reaches the ESG and is successfully recognized and decrypted, an ESG Message Delivery Notice (MDN, also called ACK1) will be sent to the inbox of the account from which the submission was received. The name of receipt message includes the file/folder name of the submission that was sent. The MDN message contains the message ID of the submission and a date stamp for when the submission was received by the FDA ESG. The Message ID is a unique alphanumeric string that identifies each submission, and critical for tracking of the submission (see ACK2 below). The date stamp will serve as the official FDA receipt date of each successfully transmitted ICSR and ICSR attachment in the submission. See FDA's ESG Web page for further information about receipt of submissions through the ESG.

After receipt of the submission, CBER will process the ICSRs and ICSR attachments and a second automated acknowledgement message (CBER receipt acknowledgment, also called ACK2) will be sent to the sender via the ESG. The CBER receipt acknowledgement informs the sender that the ICSR submission(s) have successfully reached CBER. This file is named with a unique alphanumeric string known as the Core ID. The date and time stamp contained in this acknowledgment conveys when CBER received your submission from the ESG. The Message ID, which is copied into the ACK2 file, can be used to track the submission upstream.

FDA expects that you will receive your ESG MDN and CBER receipt acknowledgement within 24 hours after you have submitted an ICSR, including any associated ICSR attachments to the ESG.

A third automated acknowledgment message (VAERS file validation and load acknowledgment, also called ACK3) will be sent to the sender to provide file validation and load status for each ICSR submission. The ACK3 provides the acceptance or rejection status of the safety message by eVAERS, and the detail of any validation errors and warning messages for each of the ICSRs within the safety mesage. The sender should ensure that the ACK3 message indicates that the submission is a valid submission (i.e., accepted by eVAERS). If a submitted message has a "Rejection" status, the submitter needs to make corrections and re-transmit the ICSR file. Refer to section VI.G of this document for more information about Failed ICSR Submissions.

G. Issue Resolution

For each submission, if you do not receive the ACK1 and ACK2 within 24 hours post submission, or do not receive ACK3 within 24 hours of ACK1, contact the CBER ICSR Submissions Coordinator at CBERICSRSUBMISSIONS@fda.hhs.gov. You may also check the ESG system operational status through the ESG System Status Web page at:

https://www.fda.gov/industry/about-esg/planned-maintenance-and-status-history.

1. Rejected ICSR Submissions

If you receive an FDA ACK3 response of an unsuccessful (rejected) ICSR submission, the following instructions should be followed:

- For a safety message containing a single ICSR message, re-submit the corrected ICSR with a new unique batch identifier

- For a safety message containing more than one ICSR messages, separate the failed ICSR(s) from the successfully submitted ICSRs, correct the failed ICSRs, and resubmit them as a new

submission with a unique batch identifier

  - The resubmission must not contain any of the successfully processed ICSRs

- Warnings in an ACK3 should be investigated and addressed

  - It is not required that safety messages with only Warnings be re-submitted unless a correction and/or provision of follow-up information is deemed necessary

- Both the Rejection and Warning messages in the ACK3 will identify what data element is involved and which validation rule is violated

2. Contingencies If the ESG Is Temporarily Unavailable

As stated previously, we expect that you will receive your ESG MDN and CBER receipt acknowledgement within 24 hours after you have submitted an ICSR or ICSR attachment(s) to the ESG. If you do not receive these messages within 24 hours, we recommend that you first check the FDA ESG Web page to determine whether we are experiencing any problems with the ESG.

- If the ESG is functional, and you have not received the CBER receipt acknowledgement within 24 hours after the end of the transmission, contact ESGHelpDesk@fda.hhs.gov for assistance

  - Please be prepared to provide the Core ID, which is the ID assigned by the FDA ESG for submission tracking, as well as the company name on the account and the date and time the submission was sent

- If the ESG is not functional for more than 24 hours, FDA will post a notice on the FDA ESG Web page to provide further guidance concerning alternative submission methods

  - If the ESG is not functional for more than 48 hours, the FDA ESG email distribution list (listserv) will be used to communicate procedures on how to proceed with your submission

  - If you follow these procedures, it is important that you do not re-submit the ICSRs or ICSR attachment(s) to FDA using the ESG when it becomes functional

  - Note that when you follow the alternate submission method, the official FDA receipt date of the ICSRs or ICSR attachment(s) will be the date when the submission is received by FDA or the VAERS program (for example, if the submission is faxed, the receipt date will be the date on the timestamp of the successful fax)

If you submit ICSRs or ICSR attachment(s) that we are unable to load into the VAERS database because you did not use the correct data elements or an electronic transport format that CBER supports, the third automated VAERS acknowledgement message will indicate that we could not load these ICSRs (or ICSR attachment(s)) into VAERS. The acknowledgement also will indicate which, if any, ICSRs or ICSR attachment(s) that you sent to the ESG at the same time were processed into VAERS. You should re-submit to us only those ICSRs or ICSR attachment(s) that were not processed into VAERS. Your re-submission should be given a different file name (batch identifier) than the original submission and should take place within the required reporting timeframe. The date of the ESG MDN acknowledgement for the resubmission will serve as the official FDA receipt date of the ICSR or ICSR attachment(s).

VII. Appendix I: eVAERS Business Rules

The eVAERS Business Rules spreadsheet provides technical information about VAERS data elements including field lengths, datatypes, and business rule validations. Due to the length and evolving content of the XML file, the regional business rules will be periodically updated to align with technical and business program requirements over time. The spreadsheet is available as a separate document on CBER Vaccine ICSR Implementation page on FDA's website at: https://www.fda.gov/industry/about-esg/cber-vaccine-icsr-implementation

As discussed in Section 1.B, the business rules that have been updated in this version are listed in **Table 27**.

Table 27: Updated Business Rules

Data Element ID	E2B (R3) Name	FDA Business Rules
C.1.1	Sender's (case) Safety Report Unique Identifier	While the ICH E2B(R3) IG instruction preferably recommends that C.1.1 is represented by a combination of country code and two other fragments of ID information, the IG instruction does not explicitly require the incorporation of country code. Similarly, FDA eVAERS does not pose any validation rule requiring a country code, regardless of format or standard, on this data element. For foreign ICSRs, senders should be
C.2.r.3	Reporter's Country Code	This field is required when C.2.r.5 = 1 Note: MSK is not allowed for US cases when C.2.r.3 Reporter's Country Code = "US" Note: FDA accepts GENC country codes only, which does not include "EU"

Data Element ID	E2B (R3) Name	FDA Business Rules
C.2.r.4	Qualification	The reporter's relationship to the patient is captured with the Reporter Qualification data element. The ICH E2B (R3) Reporter Qualification codes "1" or "3" are used for healthcare professionals, and values for patient and parent have been added as regional expansions.
C.2.r.5	Primary Source for Regulatory Purposes	This data element is used to flag one Primary Source of Information (C.2) as the Primary Source for Regulatory Purposes. When it is populated as 1 (='Primary'), the patient's name and address information are both required and correspond to the person who received the vaccine or that person's legal representative as required by the NCVIA. For foreign cases, if the identification of the patient is prohibited per national or regional confidentiality laws or directives, the null flavor code MSK should be used. In any case, name and address information, including email address, are redacted from VAERS data made available to the public. When the patient or parent is not a primary source reporter, information about these individuals should be provided using the appropriate ICH guidance for the patient (D.1) or parent (D.10); However, the ICH data elements, D.1.1 Patient Name and D.1.10 Parent Name, are expanded to support capture of additional details (Section D).

Data Element ID	E2B (R3) Name	FDA Business Rules
C.3.4.5	Sender's Country Code	Regionally required for all reports. Note: FDA accepts GENC country codes only, which does not include "EU"
C.5.1.r.2	Study Registration Country	Note: FDA accepts GENC country codes only, which does not include "EU"
D.7.3	Concomitant Therapies	N/A
E.i.9	Identification of the Country Where the Reaction / Event Occurred	Note: FDA accepts GENC country codes only, which does not include "EU"
FDA.C.1.6.1.r.3	Attachment file name	This field is required when C.1.6.1.r.2 has a file. The location of the attachment file name must follow the <text mediaType> attribute based upon the following example: text mediaType="text/plain" representation="B64"> <reference value="SUMMARY OF CLINICAL HISTORY.txt"/>. If the file extension in the filename does not match the media type reported in C.1.6.1.r.2, the ICSR file will be rejected. Special Note: the "attachment file name" must follow the naming convention for a valid 'url'. Letters, digits, and special characters "a"--"z", "A"--"Z", digits, and the characters plus ("+"), period ("."), hyphen ("-"), underscore ("_"), space (" "), parentheses ("()"), and hash ("#") are allowed.
FDA.D.1j	Patient address country	(1) This field is required when the patient is not the primary source reporter (i.e. C.2.r.4 does not equal C16960 for the Primary Source Reporter for Regulatory Purposes) (2) This field should be populated with "None" when Local Criteria Report Type = Malfunction Only (No AE), and there was no patient involved in the malfunction.

Data Element ID	E2B (R3) Name	FDA Business Rules
		(3) MSK and NI are not allowed for U.S. cases Note: FDA accepts GENC country codes only, which does not include "EU"
FDA.E.i.3.3a	Emergency room/department or urgent care	N/A
FDA.G.k.4.r.14.4	Vaccination Facility Country	For U.S. Source Reports: This field is required for the first product (under section G). Note: FDA accepts GENC country codes only, which does not include "EU"
FDA.G.k.4.r.14.8	Vaccination Facility Type	For U.S. Source Reports: This field is required for the first product (under section G). This field is required when c.2.r.3 = US.
FDA.G.k.12.r.7.1e	Device Manufacturer Country	Note: FDA accepts GENC country codes only, which does not include "EU"
F.r.3.3	Test Result (unit)	N/A
G.k.1.a	FDA Other Characterisation of Drug Role	Similar Device is only allowed if Combination Product (C.1.12) ='true', Malfunction (G.k.12.r.1) ='true' and Characterisation of Drug Role (G.k.1) = '4' (=Drug Not Administered)
G.k.2.4	Identification of the Country Where the Drug Was Obtained	Note: FDA accepts GENC country codes only, which does not include "EU"
G.k.3.2	Country of Authorization / Application	Note: FDA accepts GENC country codes only, which does not include "EU"
G.k.9.i.4	Did Reaction Recur on Re-administration?	Optional data element; however, when the value is 1 (yes - yes (rechallenge was done, reaction recurred) or 2 (yes - no (rechallenge was done, reaction did not recur)), Reaction Identifier (FDA.E.i.1.3) is required when providing rechallenge causality assessment for reactions captured in Section E and drugs in Section G
G.k.2.3.r.2b	Substance/Specified Substance TermID	FDA requires at least one of: MPID (G.k.2.1.1), Substance TermID (G.k.2.3.r.2b), or Substance Name (G.k.2.3.r.1)

Data Element ID	E2B (R3) Name	FDA Business Rules
		This field is required if G.k.2.3.r.2a is populated

VIII. Appendix II: FDA ICSR Instance Examples

Due to the length and evolving content of the XML files, regional instance examples are provided as separate documents on CBER Vaccine ICSR Implementation page on FDA's website (Appendix A) at: https://www.fda.gov/industry/about-esg/cber-vaccine-icsr-implementation