FDA Regional Technical Specifications for ICH E2B (R3) Implementation

Postmarket Submission of Individual Case Safety Reports (ICSRs) for Vaccines

Draft Technical Specifications Document

This Document is incorporated by reference into the following Guidance Document(s):

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

Guidance for Industry: Providing Submissions in Electronic Format — Postmarketing Safety Reports for Vaccines

For questions regarding this technical specifications document, contact the CBER Office of Communication, Outreach and Development at 301-827-1800 or 800-835-4709.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (CBER)

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Document Revision History

Page Number	Section	Description
	Global Document Change	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. A detailed document revision history is provided in Appendix D.

Table of Contents

FDA Regional Technical Specifications for ICH E2B (R3)

I. INTRODUCTION

The purpose of this technical specifications document is to assist senders submitting vaccine individual case safety reports (ICSRs) and ICSR attachments in electronic format to the Center for Biologics Evaluation and Research (CBER) in the Food and Drug Administration (FDA). This document describes how additional FDA regional data elements not addressed in the International Conference on Harmonisation's (ICH) E2B (R3) Implementation Guideline (IG) are supported in the ICSR file.

This technical specifications document does not apply to the following CBER-regulated biological products:

- CBER-regulated drug products marketed for human use with approved new drug applications (NDAs) and abbreviated new drug applications (ANDAs)
- CBER-regulated 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

Note: For drug and therapeutic biologics ICSR submissions, please refer to the FAERS electronic reporting website at: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm.

ICSRs and ICSR attachments should be submitted to FDA using the FDA Electronic Submission Gateway (ESG) and be prepared in accordance with the ICH E2B (R3) XML[1] file format. ICSRs should **not** be submitted to the electronic Common Technical Document (eCTD)[2] in a portable document file (PDF) format. Agency information about electronic submissions will be updated as necessary to reflect the evolving nature of the technology and the experience of those using this technology.

II. BACKGROUND

The ICH E2B Expert Workgroup (E2B EWG) released their revised pharmacovigilance reporting guideline: *E2B (R3) Clinical Safety Data Management: Data Elements for*

[1] 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

[2] Electronic Common Technical Document: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm

Transmission of Individual Case Safety Reports in July 2013. The ICH guideline describes the harmonized, core set of ICH E2B (R3) data elements, ICH business rules and other technical requirements for creating ICH-compliant XML files for ICSR data exchange. FDA data elements described in this document are considered non-harmonized regional data elements that support reporting to the Vaccine Adverse Event Reporting System (VAERS). VAERS reporting requirements are referenced in the National Childhood Vaccine Injury Act of 1986 (NCVIA)[3]. In addition to the regional data elements described in this document, FDA supports use of all the ICH E2B (R3) data elements and related technical specifications to help create compliant ICSR files. A list of the technical specifications and website links are provided as follows:

- International Standards Organization (ISO)/Health Level Seven (HL7) 27953-2 International Standard: Health informatics -- Individual case safety reports (ICSRs) in pharmacovigilance -- Part 2: Human pharmaceutical reporting requirements for ICSR. The ISO/HL7 27953-2 standard describes the HL7 Version 3 XML message specification, schemas and datatypes used to support ICSR data exchange. The standard is available for purchase from the ISO website at: http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_detail.htm?csnumber=53825;

- ICH E2B (R3) IG, associated technical appendices, backward/forward compatibility document and Questions and Answers (Q&A) Document[4], which describes the technical and business requirements for the ICH harmonized core set of data elements used for ICH E2B reporting. The complete ICH E2B (R3) IG and Q&A package is available for download from the ICH website at: http://www.ich.org/products/electronic-standards.html

- FDA ISO/HL7 Individual Case Safety Report Draft Validation Procedures Document, which provides procedures and examples for accommodating ICH and FDA regional data elements in the XML file. ICSR files can be validated using the Pragmatic Data ICSR Validator tool. The ICSR validation tool is accessible from the FDA ICSR Data Standards website at: http://www.fda.gov/ForIndustry/DataStandards/IndividualCaseSafetyReports/default.htm Refer to the entry for File Validation Tools under Schema Files and Validation Procedures on the FDA website

- Appendix A of this technical specifications document is a consolidated XML file example that demonstrates how ICH and FDA regional data elements are supported in the ICSR schema file. Appendix A is available for download from the CBER ICSR Implementation website at: http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/ucm387293.htm;

[3] National Childhood Injury Act of 1986: http://www.nvic.org/Vaccine-Laws/1986-Vaccine-Injury-Law.aspx

[4] Implementers of this technical specifications document should note that the ICH E2B Implementation Working Group (IWG) recently published a Question and Answers (Q&A) document for the ICH E2B (R3) IG package. FDA will align with these changes overtime and will incorporate these changes as necessary and describe in subsequent releases of this technical specifications document

- Appendix B **(New)** of this technical specifications document is a consolidated eVAERS data elements and describes the business rules spreadsheet, which lists all ICH and FDA regional data elements and a description of the business validation rules used to process incoming eVAERS ICSR files. Appendix B is available for download from the CBER ICSR Implementation website at: http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/ucm387293.htm.

- Appendix C **(New)** of this technical specifications document is a reconciliation of the VAERS-1 and VAERS-2 Form data elements to the updated ICH E2B (R3) specification, as well as mapping to new regional data elements.

- Appendix D **(New)** of this technical specifications document is a detailed summary of all changes made to this document as a result of industry pilot testing. Future updates to this document will be summarized in the new Document Revision History section and Appendix D will be deleted.

FDA technical specifications relevant to ICH E2B (R3) adoption and implementation will be updated periodically to reflect the Agency's progress and ability to receive ICH E2B (R3) formatted submissions and will be published on FDA websites. Stakeholders interested in submitting ICSRs in ICH E2B (R3) format should contact the VAERS Electronic Submissions Coordinator at: CBERICSRSUBMISSIONS@fda.hhs.gov for more information about specific program adoption, testing and implementation timelines.

III. FDA REGIONAL IMPLEMENTATION OF ICH E2B (R3)

FDA plans to implement ICH E2B (R3) incrementally over several years. Implementation of ICH E2B (R3) by CBER for VAERS reporting is imminent to help transition vaccine adverse event (AE) reporting from paper-based to automated electronic submissions using a standardized XML file format. Implementation of ICH E2B (R3) aligns the VAERS reporting program with other electronic postmarket submission programs for drugs, biologics, medical devices and animal drugs using the FDA Electronic Submissions Gateway.

A. Technical Approach for Accommodating FDA Regional Data Elements

1. Regional Data Elements

The use of the term, *"regional extension"* in this document refers to additional FDA data elements supported in the ICSR file using available ISO/HL7 27953-2 schema data elements. FDA VAERS regional extensions are specific to vaccine safety surveillance and consistent with information collected on the VAERS reporting form. Additional regional data elements described in this document help support Agency efforts to improve overall ICSR data quality and support other Department of Health and Human Services (DHHS) public health initiatives. Use of the term *"conformance"* in this document refers to data element definitions, formats, and use (e.g., required or optional). Data element conformance is consistent with the ISO/HL7 27953-2

standard, content described in the ICH IG and VAERS regional data elements described in this document.

2. Regional Controlled Terminology

The use of the term, *"controlled terminology"* in this document refers to a finite set of values (terms and codes) that represent the FDA allowed values for a data element. The regionally defined controlled terminologies extend those defined within the ICH documentation. The use of the term, *"value set"* used in this document refers to a list of specific values (terms and their codes) derived from one or more standard vocabularies which define clinical concepts that support effective health information exchange. For example, the ICH E2B (R2) Routes of Administration list is an example of a value set used for ICH data exchange but these concepts are also found in other terminology systems such as the Systematized Nomenclature of Medicine--Clinical Terms (SNOMED CT). FDA regional controlled terminology is supported by the US National Cancer Institute's (NCI) Enterprise Vocabulary Service (EVS) and the FDA Substance Registration System (SRS). Information about the NCI EVS system is available at the NCI website at: http://evs.nci.nih.gov/. Reference links to FDA controlled terminology are provided in the relevant sections of this document and regional code system Object Identifiers (OIDs) are listed in Table 1.

Table 1: FDA Regional Terminology Code System Object Identifiers

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 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
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 D-U-N-S Number, is a unique global business identification system that identifies, validates and links to more than 225 million

		businesses worldwide.

3. Integration of ISO Identification of Medicinal Product (IDMP) Standards

FDA uses regional terminology to support related ISO IDMP data elements (e.g., controlled terms and identifiers) for known US-licensed products. The related ISO IDMP data elements are:

- Substance/Specified Substance Identifiers (ISO 11238:2012): Supported using FDA Unique Substance Ingredient Identifiers (UNII); and

- Medicinal Product Identifiers (ISO 11615:2012): Supported using the three-segment FDA National Drug Code

For more information about FDA regional terminology used to support related ISO IDMP data elements, refer to the relevant sections of this technical specifications document.

4. Use of the Display Name Data Element

FDA has implemented 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 display name 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"/>
```

IV. FDA REGIONAL TECHNICAL REQUIREMENTS

A. Electronic ICSR Submissions using the FDA ESG

1. FDA ESG Connection Options

Connections to the FDA ESG are supported using a gateway-to-gateway or web interface using Hyper Text Transfer Protocol Secure (HTTPS) for transmission according to Applicability Statement 2 Business-to-Business (AS/2 B2B) standards. 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:
http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/ucm334359.htm.

2. 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 temporary eVAERS ICSR submission size is limited to 20 MB. This limit is based upon information described in the European Medicines Agency (EMA) European Union (EU) Individual Case Safety Report Implementation Guide (EMA IG). The EMA IG specifies the

ICSR case size should not exceed 20 MB and embedded ICSR attachments should not exceed 15MB. The EMA IG is available for download from EMA's website at: http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2014/04/WC500165979.pdf. FDA will continue to evaluation eVAERS file and ICSR attachment size limitations based upon implementation experience, and will publish changes in subsequent revisions to this technical specifications document. ICSRs and ICSR attachments should **not** be compressed. Refer to section ***D. ICSR Attachments*** of this document for more information about sending ICSR attachments.

3. FDA Small Business Support for VAERS Reporting

FDA supports small business transactions using the ESG WebTrader Hosted Solution (WTHS) and FDA eSubmitter software. Once a WebTrader account is established with the FDA ESG, small business users can submit electronic vaccine ICSRs to VAERS using FDA's eSubmitter software. CBER has implemented an ICH E2B (R3)-compliant ICSR 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.

4. FDA ESG Transaction Partners and Testing

4.1 ESG Transaction Partners

To submit electronically to the FDA, organizations must apply for a Transaction Partner account (i.e., WebTrader or AS2 B2B). ESG account request procedures and information is available at CBER websites. For information about WebTrader accounts, use the WebTrader checklist link: http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/ucm114831.htm. For information about AS2 B2B accounts, use the AS2 link: http://www.fda.gov/forindustry/electronicsubmissionsgateway/ucm115948.htm.

4.2 ESG Testing

Applicants will need to complete two levels of testing: (1) to establish a successful Transaction Partner account and (2) to confirm the ability to generate VAERS guidance-compliant ICSR files. When testing connectivity, applicants should not send ICSR submissions to the Center's production account. Instead send all connectivity test submissions to the appropriate ESG test account (GW_TEST CONNECTION) using the submission type "CONNECTION TEST".

For more information about ESG connectivity testing, contact: esgprep@fda.hhs.gov.

For more information about VAERS testing, contact: CBERICSRSUBMISSIONS@fda.hhs.gov.

4.3 FDA ESG Routing Identifier

When exchanging ICSRs with the FDA ESG, senders must use the appropriate CBER gateway routing identifier (ID) to insure that the submissions are routed to VAERS. The ESG header information is separate from the ICSR file and is unique to the type of FDA ESG connection used to submit ICSR files (e.g., AS/2 B2B or WebTrader) as follows:

VAERS ESG headers:

WebTrader Accounts: CBER VAERS
AS/2 B2B Accounts: CBER_VAERS

5. ICSR Acknowledgments

5.1 FDA ESG Acknowledgments

The FDA ESG provides two acknowledgments (ACK) for ICSR submissions. These ACKs have a relationship with the official FDA receipt date as indicated in the FDA Receipt Date Guidance available from the CBER wesite at: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm072385.pdf. The FDA ESG acknowledgments are:

- **ACK 1** = FDA Message Delivery Notification (MDN) status
- **ACK 2** = Center Receipt

For more information about FDA submissions tracking, refer to the FDA Receipt Date Guidance. For more information about what to do in case of ESG failures, refer to Section G of the Draft Gudiance to Industry: Providing Submissions in Electronic Format —Postmarketing Safety Reports for Vaccines located on CBER's website at: http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/ucm405477.htm.

5.2 FDA VAERS Program-Level Acknowledgments

The VAERS program is implementing third-level acknowlegments (**ACK 3**) to provide information about ICSR file validation errors. ACK 3 is the VAERS program acceptance acknowledgment, and communicates important information about validation errors and VAERS acceptance of the ICSR file. Failure to meet FDA ICSR file validation may result in the need to correct and retransmit ICSR files. ICSR file validation error codes will be used to communicate important information about processing errors for each ICSR file. Refer to ICH E2B (R3) section 4.0: The ICSR Acknowledgement Transaction, for more information about the format and content of the ACK file.

5.3 Failed ICSR Submissions

If you receive an FDA ACK 3 response of an unsuccessful (failed) ICSR submission, please refere to the following instructions:

- For a single ICSR submission, resubmit the corrected ICSR with a new unique batch identifier. Refer to section B.4 Batch Sender Identifier N.1.3 of this document for more information about ICSR batch identifiers.

- For ICSR submissions containing multiple ICSR files (batch submissions), and one or more ICSRs in the submission fails to process, separate the failed ICSRs from the successfully submitted ICSRs, correct the failed ICSRs, and resubmit them as a new submission with a unique batch identifier. For example, if there were 50 ICSRs in an original batch submission and 15 of them failed to process, then only the failed 15 ICSRs must be corrected and resubmitted with a new unique batch identifier. The resubmission must not contain any of the successfully processed ICSRs.

- If you do not receive an FDA AE program (ACK3) acknowledgement within 24 hours of the ESG message delivery notice of acknowledgement (ACK 1), please resubmit the original ICSR submission without changing the batch identifier.

B. ICSR Batch and Message Transmission Wrappers

The FDA ISO/HL7 27953 Individual Case Safety Report Draft Validation Procedures Document provides XML schema examples and procedures for populating ICSR data elements described in this section. The ICSR Validation Procedures document is accessible from the FDA ICSR Data Standards webpage at: http://www.fda.gov/ForIndustry/DataStandards/IndividualCaseSafetyReports/default.htm.

1. ICSR Batch Wrapper Information

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.

1.1 Type of Messages in Batch N.1.1

ICH E2B (R3) uses one ICSR message type, which is characterized by the HL7 message interaction ID PORR_IN049016UV. FDA does not support the additional HL7 interaction IDs or message types for Follow Up or Withdrawn ICSRs. FDA only accepts the value of “1” for N.1.1 Type of Messages in Batch.

1.2 Batch Number N.1.2

Each electronic submission of ICSRs must have a unique batch identifier (filename or number). You may choose your own format to maintain uniqueness. For more information about the use

of the ICSR batch number in ICSR acknowledgements, refer to ICH E2B (R3) IG Section 4.0: The ICSR Acknowledgment Transaction.

1.3 Batch Sender Identifier N.1.3

Senders should use the Data Universal Numbering System (DUNS) number for N.1.3 using the Dun and Bradstreet (D&B) Object Identifier (OID) 1.3.6.1.4.1.519.1. FDA has begun an initiative to verify facility information that has been provided to FDA electronically including, but not limited to, facilities' DUNS numbers, addresses, and products. The DUNS number datatype is a nine-digit identifier.

For more information about the FDA Business Entity Identifier initiative, refer to the FDA D&B Verification webpage at:
http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/drugregistrationandlisting/ucm307027.htm.

For more information about how to obtain a DUNS number, refer to the FDA Business Entity Webpage at:
http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm162544.htm.

1.4 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 AS2 B2B) used to send the ICSR submission to VAERS. Please refer to section 4: FDA ESG Transaction Partners and Testing of this document for more information about VAERS routing IDs.

2. Message Transmission Wrapper

Each ICSR 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**.**

2.1 Message Identifier N.2.r.1

The Message Identifier will be the same as the ICH C.1.1 Sender's Safety Report Unique Identifier.

2.2 Message Sender Identifier N.2.r.2

The Message Sender Identifier is the same identifier used for the N.1.3 Batch Message Sender Identifier data element.

2.3 Message Receiver Identifier N.2.r.3

The Message Receiver Identifier is the same identifier used for the N.1.4 Batch Receiver Identifier data element.

C. Regional Data Elements and Controlled Terminology

1. Relationship with the VAERS Data Collection Form

VAERS is co-managed by FDA and CDC and therefore it is important that information contained in ICSRs from vaccine manufacturers be consistent with reports received from healthcare providers, patients and consumers. Information about how to collect specific VAERS form data elements is included in the relevant sections of this technical specifications document. However, the Agency recognizes that the VAERS form may undergo revision over time and information concerning reconciliation of new or unsupported data elements will be incorporated in future updates to this technical specifications document. Information about how to reconcile VAERS-1 data elements that are no longer supported is included in **Appendix C**.

2. Data Element Conformance

FDA supports the ICH E2B (R3) data element conformance categories (e.g., required or optional) described in the ICH E2B (R3) IG. However, FDA data element conformance may vary due to regional regulatory requirements not addressed in the ICH E2B (R3) IG (e.g., VAERS specific data elements) and these exceptions are noted in the relevant ICH section headers of this document.

3. ICSR Terminology for Clinical Information and Units of Measurement

FDA supports ICH E2B (R3) recommendations concerning use of the Medical Dictionary for Regulatory Activities (MedDRA)[5] terminology for coding of clinical and laboratory terms. When possible, use the Lowest Level Term (LLT) and record the LLT as the MedDRA numeric code rather than the LLT name (e.g. the LLT name is Rash; the MedDRA numeric code for LLT Rash is 10378444). Applicants should refer to the ICH E2B (R3) IG for data elements that specify the use of MedDRA coding.

FDA supports the use of the Unified Codes for Units of Measurement (UCUM) for coding units of measure. The UCUM value set can be downloaded from the Regenstrief Institute website at: http://unitsofmeasure.org/trac/. Regional data elements that use a constrained set of UCUM codes (e.g., medication dosing units) are available from the FDA SPL website at: http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm168397.htm. Other FDA controlled terminologies are noted in the relevant sections of this technical specifications document and include information about the regional terminology Object Identifiers (OIDs) and allowable value sets.

4. FDA Regional Drug Information Terminology

[5] Companies can license MedDRA from an international maintenance and support services organization (MSSO) (toll free number 877-258-8280; direct 571-313-2574; fax 571-313-2345; e-mail MSSOhelp@mssotools.com).

FDA regional extensions to ICH G.K are needed to support regional product identification and traceability to vaccine supply chain and vaccination facility information. FDA will adopt ISO IDMP terminology when it becomes available. Use of IDMP will be addressed in future updates to this technical specifications document. In the interim, FDA supports use of the regional terminology used in Structured Product Labeling (SPL) submissions to support several ICH and regional data elements. Examples of supported SPL terminology include: Dosage Forms, Route of Administration, Unique Ingredient Identifiers and FDA Specialized Product Codes. Regional terminology accepted for specific drug information data elements is referenced in the relevant sections of this technical specifications document.

D. ICSR Content

1. Identification of the Individual Case Safety Report ICH Section C.1

1.1 Safety Report Identifier Format for ICH C.1.1 and C.1.8

FDA supports use of alternative formats for C.1.1 (Sender's (case) Safety Report Unique Identifier) and C.1.8 (Worldwide Unique Case Identification) for initial reports previously submitted to FDA in paper format (e.g., VAERS-1 form). ICSR senders should not change the safety report ID format and should follow the appropriate ICH guidance concerning reassignment of safety report IDs for electronic ICSRs by including the reassigned ID in the case narrative when applicable.

1.2 Linking of Initial and Follow up ICSRs ICH using C.1.1 and C.1.8

Applicants should follow ICH guidance for C.1.1 Sender's (case) Safety Report Unique Identifier and C.1.8.1 Worldwide Unique Case Identification for electronic ICSRs. 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 referred to as the *Manufacturer Control Number*[6] {MCN} listed in Box 24 of the VAERS-1 form) from the initial report in both C.1.1 and in C.1.8.1 in the follow-up electronic submission.

Always use the same identifier for C.1.1 that was assigned to the initial ICSR when submitting follow-up reports for the lifecycle of that case. If the internal Safety Report Unique Identifier is provided, note the internally reassigned safety report ID in the ICSR narrative section H.1 of the follow-up report (e.g., "*This ICSR has been reassigned the Company ID number COA12345*"). **Do not use the internally reassigned safety report ID for any follow-up reports**.

In the event that an incorrect safety report ID has been used in a follow-up report, contact the VAERS Program Coordinator at CBERICSRSUBMISSIONS@fda.hhs.gov so that the follow-up ICSR can be matched to the initial ICSR in the VAERS database.

[6]The value should be a concatenation of 3 segments separated by a dash/hyphen: 'country code-company or regulator name-report number'. Country code is the 2-letter ISO 3166 part 1 code (ISO 3166-1 alpha-2) corresponding to the country of the primary source of the report (C.2.r.3)

1.3 Additional Available Documents Held by Sender ICH C.1.6

FDA is clarifying the ICH guidance for C.1.6.1.r.1 when C.1.6.1 is set to 'true'. Senders should provide a list of the documents using the repeatable document reference structure and **only** provide the title of the document being held. Senders should **not** include the content of the document in the XML file if it is not provided as an ICSR attachment.

EXAMPLE: A sender conveys that they are *holding* a discharge summary and detailed laboratory report

<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>Hospital Discharge Summary</title>
</document>
</reference>
<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>Labcorp Report</title>
</document>
</reference>

1.4 Included Documents ICH C.1.6.1.r.2

FDA is clarifying the ICH guidance for ICH C.1.6.1.r.2 when documents are sent as ICSR attachments. 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 US reporting and encoding is limited to B64. The regional data element, *Attachment file name*, is used to help facilitate automated ICSR file attachment identification and processing in the CBER document repository. This data element is supported using the <reference value> data element in the XML file. The attachment file name should 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>

1.5 Identification of Expedited and Non-Expedited ICSRs using ICH C.1.7

FDA concurs with ICH E2B (R3) conformance criteria for C.1.7 to specify if the case fulfills regional requirements for expedited reporting; however, FDA **does not** support use of the HL7 null flavor NI for this data element for initial reports. For FDA reporting, if C.1.7 is populated with a "false" value, the ICSR is considered a non-expedited report.

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

2.1 Reporter Qualifications ICH C.2.r.4

FDA supports the use of ICH, regional terminology and constrained HL7 null flavor codes to capture information for the Reporter Qualifications in ICH C.2.r.4. The VAERS-1 form data elements applicable to ICH C.2.r.4 are: Vaccine Administered By, Responsible Physician, Form Completed By, Relation to Patient and Other. Regional reporter qualification terminology is provided in Table 2. The VAERS options for Vaccine Administered By, Form Completed By, and Relation to Patient are no longer supported as separate data elements and do not need to be provided in the XML file. The VAERS option Responsible Physician is supported using the ICH E2B (R3) Reporter Qualification code "1".

The VAERS option "Other" is supported using the HL7 null flavor code: OTH. 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 (ICH D.1) or parent (ICH D.10); However, the ICH data elements, D.1.1 Patient Name and D.1.10 Parent Name, are expanded to support capture of expanded regional name part data elements for the <name> XML tag for last name, first name and middle initial. See sections **IV.D.4: Patient Characteristics** and **IV. D.5 Parent Information** of this document for more information.

Table 2: VAERS Reporter Qualification Codes

NCI Concept Identifier	Description
C16960	Patient
C42709	Parent

2.2 Primary Source Reporter for Regulatory Purposes ICH C.2.r.5

In cases where the patient is identified as the Primary Source Reporter for Regulatory Purposes (ICH C.2.r.5), additional VAERS data elements are used in ICH 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 is required and corresponds 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 by certain national confidentiality laws or directives, the HL7 null flavor code MSK should be used. In any case, no identifying information will be made available to the public.

3 Literature References ICH Section C.4.r

FDA is clarifying the ICH guidance for C.4.r when literature articles are provided as ICSR attachments. Compression is not used for US reporting and encoding is limited to B64. The regional data element, *Attachment file name*, is used to help facilitate automated ICSR file attachment identification and processing. This data element is supported using the <reference value> data element in the XML file. The attachment file name should be provided in this data 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.

4 Patient Characteristics ICH Section D

4.1 Patient Name and Contact Information ICH D.1

For vaccine ICSRs, full patient name and address information (e.g., address, telephone and email address) is required. The <name> data element, including its related nested name parts for <prefix>, <given> and <family> names are used to capture complete patient name information. VAERS supports two additional address part data elements: <streetAddressLine> and <county>. These data elements are additional nested data elements within the<address> data element.

4.1.1 US State County Names

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*".[7]

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

NCI has pre-coordinated this data for FDA and has placed this data in an NCIt subset named "US Counties Terminology" which has an NCIt 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
NCIt Code: C110209

The <telecomm> data element is repeatable and special prefix designations are used to distinguish different telcommunications address types such as telephone and email addresses. 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://www.usps.com/send/official-abbreviations.htm.

For detailed examples on how to capture Patient Name and Contact Information, please refer to Appendix A of this document which can be downloaded from the CBER ICSR Implementtion website. Information about VAERS datatypes and field lengths for this section are provided in Appendix Appendix B is available for download from the CBER ICSR Implementation website.

4.2 Patient Age Information ICH D.2

VAERS patient age information may be supported using the VAERS concept code for *Age at the Time of Vaccination* or ICH D.2.2 Age at Time of Onset of Reaction/Event. For vaccine ICSRs, applicants should to clearly distinguish *Age at the Time of Vaccination* concept from ICH D.2.2 in vaccine ICSRs using a separate <observation> code and value when known. The FDA regional terminology code for *Age at the Time of Vaccination* is C103173. The age value should be provided in accordance with ICH guidance using the HL7 physical quantity (PQ) datatype and UCUM coding for units of measure (e.g., hours, days, weeks, months, years).

4.3 VAER Patient Military Status

The VAERS data element, *Patient Military Status* is used to support verification of the patient's military status (or association with military health services) at the time of vaccination. This data element is supported using and additional <observation> code with coded values as reflected in

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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.

Table 3. The regional terminology is used to capture the patient's military status and relationship with military health services such as TRICARE[8]:

Table 3: VAERS Patient Military Status

FDA Object Identifier	NCI Concept Identifier	Description
2.16.840.1.113883.3.26.1.1	C114855	Patient Military Status ICSR Terminology
	C114854	Active Duty
	C114857	Reserve
	C114858	National Guard

4.4 FDA Patient Race and Ethnicity (Ancestry) Information

FDA is improving its ability to collect and analyze patient race and ethnicity data using structured data elements and controlled terminology. FDA currently captures race information either as free text in Section B, box 7 (Other Relevant History, Including Preexisting Medical Conditions) of the MedWatch 3500A form or as free text descriptions in the case narrative field. To help facilitate consistent data capture of race and ethnicity information, definitions for regional terms are consistent with data standards defined by the US Office of Management and Budget (OMB)[9] and the Department of Health and Human Services (HHS) Office of Minority Health[10]. Applicants should provide patient race and ethnicity information using the regional terminology codes listed in Table 4. The race <observation> code is C17049 and multiple race classification codes can be used. The ethnicity <observation> code is C16564 and only one (1) ethnic group code should be used. If the patient race or ethnicity information is not available or unknown, use the appropriate HL7 null flavor values for Unknown (UNK), No information (NI) or Masked (MSK) within these data elements.

Table 4: FDA Race and Ethnic Group Codes

NCI Concept Identifier	Description
C17049	**Race**
C16352	African American
C41259	American Indian or Alaska Native
C41260	Asian
C41219	Native Hawaiian or Other Pacific Islander

[8] TRICARE® is the health care program serving Uniformed Service members, retirees and their families worldwide: http://www.tricare.mil/

[9] Revisions to the Standards for the Classification of Federal Data on Race and Ethnicity: http://www.whitehouse.gov/omb/fedreg_1997standards/

[10] HHS Office of Minority Health, Explanation of Data Standards for Race, Ethnicity, Sex, Primary Language and Disability: http://www.minorityhealth.hhs.gov/templates/content.aspx?ID=9228

C41261	White
C16564	**Ethnic Group**
C17459	Hispanic or Latino
C41222	Not Hispanic or Latino

4.5 VAERS Illness at the Time of Vaccination

The FDA regional VAERS 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. The 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 listed in the ICH 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. However, at least one of the available date/time data elements in the drug information section should be populated such as, G.k.4.r.4: Date and Time of Start of Drug, G.k.4.r.5: Date and Time of Last Administration, G.k.4.r.6: Duration of Drug Administration or G.k.6: Gestation Period at Time of Exposure.

Refer to **Appendix A** of this technical specifications document for more information about how to populate the XML schema for this regional data element.

4.6 Relevant Past Drug History ICH 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.* This data element is captured as an additional <observation> using the regional terminology code C88065 to avoid conflict with ICH D.2.2 Age at Time of Reaction/Event and the value is captured as an HL7 PQ datatype with coded units of measure using UCUM.

4.6.1 Name of Drug as Reported ICH D.8.r.1

For vaccine reports, when the Medicinal Product Identifier (MPID) or Pharmaceutical Product Identifier (PhPID) is unknown, applicants may use the regional vaccine abbreviation as the US product trade name in the <kindOfProduct><name> data element. The VAERS vaccine name abbreviations are available at: http://www.cdc.gov/vaccines/about/terms/USVaccines.html. See **Appendix A** for an example of using this data element.

4.6.2 Medicinal Product Identifier (MPID)[11] ICH D.8.r.2

An FDA regional extension is needed for the ICH E2B (R3) Medicinal Product Identifier (MPID) to accommodate use of the 10 digit FDA NDC code. According to ISO IDMP definitions, the 10 digit NDC code is equivalent to the ISO IDMP Medicinal Product Package Identifier (PCID). However, since package identifiers are not supported in all ICH regions, the ISO IDMP MPID is used as the generic regional identifier for ICH reporting. FDA has determined that the two-segment NDC (labeler code + product code) is not sufficient for safety reporting and requires use of the 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)[12] Resources webpage at: http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm240580.htm. This website is updated daily and a comprehensive NDC report is available for download in comma delimited (CSV) file format or as a compressed zip file (.zip). Questions concerning these identifiers should be addressed to spl@fda.hhs.gov. The 10 digit NDC code is captured using the <kindOfProduct><code> data element, and the regional MPID Version Date/Number (ICH D.8.r.2b) is the date and time that the file was downloaded from the FDA website.

4.6.3 Pharmaceutical Product Identifier (PhPID)[13] ICH D.8.r.3

Applicants should use this data element only if the regional MPID is not unknown and the PhPID TermID is available. The PhPID should be entered into the <kindOfProduct><code> data element. The proposed ISO PhPID is a Universally Unique Identifier (UUID) or Globally Unique Identifier (GUID) format. UUID/GUID format consist of 32 hexadecimal digits with hyphen grouping 8-4-4-4-12. For more information about UUID and GUID formats, please refer to the Internet Engineering Task Force's RFC 4122[14] standard available at: http://www.ietf.org/rfc/rfc4122.txt. FDA will update this section when more information is available.

5 Information Concerning the Parent ICH D.10

[11] The ISO Medicinal Product Identifier (MPID) is defined as the unique identifier allocated to a Medicinal Product supplementary to any existing authorization number as ascribed by a Medicines Regulatory Agency in a jurisdiction. However, FDA NDC codes are generated using two or three segments. The two-segment NDC code, (e.g., labeler code + product code) is equivalent to the ISO MPID. The three-segment NDC code, (e.g., labeler code + product code + package type) is equivalent to the ISO IDMP Medicinal Product Package Identifier (PCID).

[12] Structured Product Labeling (SPL) is a document markup standard approved by Health Level Seven (HL7) and adopted by FDA as a mechanism for exchanging product and facility information

[13] ISO IMDP Pharmaceutical Product Identifier (PhPID) is defined as a unique identifier for a pharmaceutical product. This identifier is a generic identifier that is generated using an agreed upon algorithm.

[14]RFC 4122 is technically equivalent to the International Telecommunications Union – Telecommunication Standards Sector X.667 and International Standards Organization/International Electrotechnical Commission (ISO/IEC) standard 9834-8

5.1 Parent Contact Information ICH D.10.1

FDA extensions to ICH D.10 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. When the parent is the source of exposure, the parent's contact information (e.g., address and telephone number) should be provided in the relevant section (e.g., Primary Source(s) of Information or Patient Information) in the ICSR file. 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.

5.2 Parent Age at Time of Vaccination

The VAERS data element, *Parent Age at Time of Vaccination*, is captured using the <observation> data element and regional terminology code C103173 when known. The age value should be captured using the PQ data type and coded units of measure using UCUM.

5.3 FDA Race and Ethnicity Information for the Parent

The VAERS data element, *FDA Race and Ethnicity* information is extended within the ICH D.10 section to collect race and ethnicity information for the parent. The information is collected using the same <observation> data elements described in the patient section (see section **C.4.4: Patient Race and Ethnicity (Ancestry) Information** of this document.

5.4 Parent Relevant Past Drug History ICH D.10.8.r

FDA regional extensions and terminology used in this section for ICH D.10.8.r.1 (Name of Drug as Reported), D.10.8.r.2 (MPID) and D.10.8.r.3 (PhPID) are the same regional extensions described in section **C.4.6 Patient Relevant Past Drug History** of this document.

6 Reactions/Events ICH Section E.i

For VAERS 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. With regard 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 and associated guidance and their medical judgment. AEs which are treated or evaluated in an emergency room, physician's office, or clinic may or may not be considered medically important conditions. Senders should request clarification of VAERS reporting for ICH E.i.3.2f by submitting questions to the VAERS Program via email at: info@vaers.org.

FDA regional extensions to ICH E.i.3.2 Seriousness Criteria at Event Level support additional VAERS patient outcome options for: *Emergency room (ER)/emergency department (ED) visit, Doctor or other healthcare professional office/clinic visit, Hospitalization, Number of Days Hospitalized, VAERS AE Treatment Facility Information (Hospital Name, City and State) Prolongation of existing hospitalization* and *none of the above.*

The VAERS regional terminology codes for *Hospitalization*, *Number of Days Hospitalized*, *Prolongation of Hospitalization* and *AE Treatment Facility* are required when the Boolean value for the ICH E.i.3.2c Caused / Prolonged Hospitalisation data element is "true" in the XML file. The regional data elements should be completed in accordance with ICH guidance by using the allowable values of "true" or the HL7 null flavor value "NI" for the regional Boolean data elements. The FDA OID and value set is provided in Table 5. The VAERS data element, *none of the above*, is captured as the HL7 null flavor value OTH (other).

Table 5: VAERS Reaction/Event Outcome Terminology

NCI Object Identifier	NCI Concept Identifier	Description
2.16.840.1.113883.3.26.1.1	C53513	Emergency Room
	C16988	Physician Office
	C50414	Hospitalization Required
	C102450	Resulted in Prolongation of Hospitalization
	C102443	Number of Days Hospitalized

6.1 VAERS Number of Days Hospitalized

The VAERS data element, *Number of Days Hospitalized*, is captured as an associated outbound observation when *Hospitalization* is valued as a patient outcome option. The number of days is captured as an integer (INT) value.

6.2 VAERS AE Treatment Facility: Hospital Name, City and State

The VAERS AE Treatment facility information should be provided when known 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. US State information should be captured using free text or USPS two letter state abbreviations. If the information is unknown, the HL7 null flavor value NI should be used. Information about the AE Treatment Facility datatype and field length information is available in **Appendix B** of this document.

The VAERS option, *Physician Office* should be selected as the regional 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 VAERS option, *Emergency Room* should be selected for the regional AE Outcome value for events where the patient's adverse event was evaluated and/or treated at an emergency room or emergency department. The information about the VAERS AE treatment facility is a separate and distinct concept from the ICH E2B (R3) AE Outcome criteria for assessing reaction/event seriousness.

7 Drug(s) Information ICH Section G.k

7.1 Integration with ISO Identification of Medicinal Product (IDMP) Standards

ICH supports harmonization of medicinal product information and provided input to the ISO workgroup, Health Informatics and Pharmacy, and the ICH E2B (R3) IG through its Multidisciplinary Expert Workgroup 5 (M5). IDMP standards are designed to facilitate the exchange and practical use of medicinal product data by regulators, pharmaceutical industry and healthcare providers. ICH E2B (R3) references the use of a constrained set of M5 controlled terminologies in section G.K as optional data elements. Since the ICH M5 group is no longer active, FDA plans to support full adoption and integration of the ISO IDMP standards for ICSR reporting in the future and regional terminology is allowed for several data elements in this section. The suite of related ISO IDMP standards is listed below and information about these standards is available at the ISO TC 215 website: http://www.iso.org/iso/home/store/catalogue_tc/home/store/catalogue_tc/catalogue_tc_browse.htm?commid=54960&published=on&development=on

- Substance/Specified Substance Identifiers (ISO 11238:2012)
- Pharmaceutical Dose Forms, Routes of Administration, Units of Presentation and Packaging (ISO 11239:2012)
- Units of Measurement (ISO 11240:2012)
- Medicinal Product Identifiers (ISO 11615:2012)
- Pharmaceutical Product Identifiers (ISO 11616:2012)

7.2 FDA Regional Product Identification

The FDA regional extensions described in this section are the same regional extensions described in the Patient Past Drug History Section (see section **C.4.6.3: Relevant Past Drug History ICH D.8)**.

7.3 FDA Medicinal Product Identifiers (MPID) ICH G.k.2.1.1b

The FDA National Drug Code (NDC) should be used as the regional MPID when known. The regional MPID is equivalent to the ISO IDMP PCID. Information about obtaining a list of FDA NDCs can be found on the FDA Structured Product Labeling (SPL) Resources webpage at: http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm240580.htm. Foreign MPIDs are also allowed when available. 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.

7.4 Pharmaceutical Product Identifier (PhPID) ICH G.k.2.1.2b

FDA will update this section when more information is available. Refer to section **C.4.6.3 Pharmaceutical Product Identifier (PhPID) ICH D.8.r**. of this document for information about the PhPID format.

7.5 Medicinal Product Name as Reported by the Primary Source ICH G.k.2.2

For US licensed products, FDA validates medicinal product names against the available SPL file or the submitted label. When the product has an SPL file, ICSR senders should use the naming convention used in the previously submitted SPL file for ICH G.k.2.2. Do not send previously submitted SPL files as an ICSR attachment. For more information about ICSR attachments, please refer to Section **E. ICSR Attachments** of this document.

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

7.6 FDA Unique Ingredient Identifier (UNII) ICH 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 known. FDA UNII codes can be obtained from the FDA Substance Registration System website. SRS information is updated on a monthly basis and 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.

The FDA SRS website is updated monthly and FDA UNII codes are provided as tab delimited text files. Questions concerning these identifiers should be addressed to fda-srs@fda.hhs.gov. ICH guidance should be followed for the use of terms and identifiers for Substance/Specified Substance. If no medicinal product name is provided and only the active substance name is known (G.k.2.3r.1), 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.

7.7 Identification of the Country Where the Drug Was Obtained ICH G.k.2.4

For vaccine ICSRs, additional regional data elements about the location of the vaccination facility are needed to support national, state and local immunization programs. The value for ICH G.k.2.4 should be populated based upon the information provided for the regional data element, *VAERS Vaccination Facility*. ICH G.k.2.4 country information should be the same as the *VAERS Vaccination Facility* address <country> where the vaccine was administered.

7.7.1 VAERS Vaccination Facility Information

The VAERS regional data element, *Vaccination Facility Information* is required for US cases and should be provided when known or the HL7 null flavor code NI (No Information) should be used. 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 **Appendix B** of this technical specifications document for more information about how to capture this data element in the XML file.

7.7.2 US State and Foreign Province Names

When the immunization occurred within the US, the vaccination facility location <state> address data element should be populated using the US Postal Service two letter state abbreviations.

7.7.3 VAERS Vaccination Facility Type

The FDA regional data element, *VAERS Vaccination Facility Type* is 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 used provided in Table 6 below:

Table 6: VAERS Vaccination Facility Type

FDA Object Identifier	NCI Concept Identifier	Description
2.16.840.1.113883.3.26.1.1	C16988	Physician Office
	C16696	Hospital
	C51282	Clinic

	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 will be supporting using the appropriate HL7 null flavor values (OTH and UNK).

7.7.4 Military Facility Indicator

The VAERS data element, *Military Facility Indicator*, is used to further specify whether the VAERS 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.

7.8 VAERS Best Doctor/Healthcare Professional to Contact about the Adverse Event

The FDA regional data element, *Best Doctor/Healthcare Professional to Contact about the Adverse Event* is captured using <author> participation reference for the substance administration as the <assignedPerson>. The additional <prefix> name part data element is used to capture the provider's professional title information (e.g., DR, 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.

7.9 FDA Authorisation/Application Number ICH G.k.3.1

FDA requires the use of a prefix to determine the application type associated with suspect products. For licensed vaccines, include the appropriate acronym "BLA" "STN" or "PLA" followed by the primary six-digit number (e.g., STN123456).

7.10 Dosage Information ICH G.k.4.r

FDA regional extensions to ICH G.k.4.r are required to support use of coded dosage form terms, route of administration terms, VAERS Approach site and VAERS Dose Number in Series

7.10.1 FDA Pharmaceutical Dose Form TermID ICH G.k.4.r.9.2b

FDA will adopt the ISO IDMP Dosage Form terminology when it becomes available. In the interim, FDA supports the use of free text or regional dosage form terminology using the FDA SPL Dosage Form value set available at:
http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm162038.htm.

7.10.2 Route of Administration TermID ICH G.k.4.r.10.2b

FDA will adopt the ISO IDMP Route of Administration terminology when it becomes available. In the interim, FDA supports the use of free text or coded terms using the ICH E2B (R2) Route of Administration or FDA SPL Route of Administration value sets. The ICH Route of Administration OID is 2.16.840.1.113883.3.989.2.1.1.14. The three-digit ICH Route of Administration codes are found in Attachment 2 of the ICH Electronic Transmission of Individual Case Safety Reports Message Specification (ICH ICSR DTD Version 2.1). The ICH message specification is available for download from ICH ESTRI website at: http://www.ich.org/products/electronic-standards.html. The FDA SPL Route of Administration list is available from the SPL website at: http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm162034.htm.

7.10.3 VAERS Anatomical Approach Site

An additional FDA element is required to support the *VAERS Anatomical Approach Site* 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 7 below.

Table 7: FDA ICSR Vaccination on Body Site Terminology

FDA Object Identifier	NCI Concept Identifier	Description
2.16.840.1.113883.3.26.1.1	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

7.11 Additional Information on Drug ICH G.k.10.r: Specialized FDA Product Categories

FDA extensions are used in ICH G.k.10.r to support the identification of specialized FDA product categories such as combination products, compounded and repackaged products. For example, pharmacy compounding is a practice in which a licensed pharmacist combines, mixes, or alters ingredients in response to a prescription to create a medication tailored to the medical needs of an individual patient. Pharmacy compounding, if done properly, can serve an important public health need if a patient cannot be treated with an FDA-approved medication. The FDA

regional data element <characteristic.code> is used to support coding of specialized FDA product categories in the drug information section using the concept identifier C. FDA regional codes for combination product package types and codes for compounded products are listed in Table 8 below:

Table 8: FDA Specialized Product Categories

FDA Object Identifier	NCI Concept Identifier	Description
2.16.840.1.113883.3.26.1.1	C94031	Product Type Code
Allowable Values	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)
Compounded Product Types		
	C73626	Bulk ingredient
	C96793	Bulk Ingredient For Human Prescription Compounding
	C95602	Unapproved Drug Product Manufactured Exclusively for Private Label Distributor

7.11.1 VAERS Dose Number in Series

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. If an event occurred after a series of several vaccinations (e.g., 3 doses of hepatitis B vaccine), an additional regional <Organizer> section is used to capture prior immunizations as the regional data element: *VAERS Vaccines Given within 4 Weeks*.

8. VAERS Vaccines Given Within 4 Weeks

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.

8.1 Vaccine Type

The vaccine name or type can be provided using the regional vaccine abbreviation as the US product trade name in the <kindOfProduct><name> data element. The VAERS vaccine name abbreviations are available at: http://www.cdc.gov/vaccines/about/terms/USVaccines.html.

8.2 Medicinal Product Identifier and Version Number

The FDA National Drug Code (NDC) should be used as the regional MPID when known. The regional MPID is equivalent to the ISO IDMP PCID. Refer to section **IV.D.7.3 FDA Medicinal Product Identifiers (MPID) ICH G.k.2.1.1b** of this document for more information about the use of FDA NDC codes.

8.3 Date Given

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. 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.

8.4 Route of Administration

The vaccine route of administration should be provided in accordance with the information provided in section C.**7.10.2 G.k.4.r.10.2b Route of Administration TermID** of this document.

8.5 Vaccine Anatomical Approach Site

The vaccination site of administration should be provided in accordance with the information provided in section **C.7.10.3 Vaccine Anatomical Approach Site** of this document.

8.6 Dose Number in Series

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.

8.7 Lot Number

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.

8.8 Manufacturer Name

The vaccine *Manufacturer Name* data element is captured using the <playingOrganization> data element for the <asManufacturedProduct> information in the XML file. Refer to **Appendix A** of this technical Specifications Document for an example of how to populate this information in the XML file.

E. ICSR Attachments

ICSR attachments should not be compressed. In accordance with 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). FDA is providing additional regional guidance concerning the submission of ICSR attachments, including literature articles. Senders should not include the content of the document in the XML file if it is **not** provided as an ICSR attachment (see **IV.D. 1.3 Additional Available Documents Held by Sender ICH C.1.6** of this document for more information).

The FDA data element, *Attachment file name*, is used to help facilitate automated ICSR file attachment identification and processing in CBER's Electronic Document Room (EDR). This data element is supported using the <reference value> data element in the XML file. ICSR attachments should not be resubmitted with follow up reports if the content of the attachment has not changed or the document was previously sent with the initial ICSR. 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)
- rtf - Rich text format (.rtf.)
- Text format (.txt)
- Spreadsheet file format (.xls, .xlsx)
- Word processing document format (.doc, .docx, .wpd)

APPENDIX A: FDA ICSR INSTANCE EXAMPLE

Due to the length and evolving content of the XML file, the regional instance example is provided as a separate document on FDA's website at: http://www.fda.gov/forindustry/electronicsubmissionsgateway/ucm387293.htm.

APPENDIX B: eVAERS CONSOLIDATED SPREADSHEET AND BUSINESS RULES

The eVAERS Consolidated Spreadsheet and Business Rules spreadsheet provides technical information about VAERS database field lengths and datatypes. 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 FDA's website at: http://www.fda.gov/forindustry/electronicsubmissionsgateway/ucm387293.htm.

APPENDIX C: Reconciliation of VAERS-1 Form Data Elements

The VAERS-1 form has been updated (see CDC announcement in the Federal Register at: https://www.federalregister.gov/articles/2014/11/24/2014-27678/request-for-comment-on-draft-vaccines-adverse-event-reporting-system-vaers-20-form. The FDA Electronic Safety Reporting Rule (eSRR) referenced the VAERS-1 form

APPENDIX C: RECONCILIATION OF VAERS-1 AND VAERS-2 FORM DATA ELEMENTS

This Appendix provides information about how to reconcile legacy VAERS-1 form data elements in the ICSR file. The guidance reference is based upon the September 1998 guidance: *Guidance for Industry: How to Complete the Vaccine Adverse Event Reporting System Form (VAERS-1).* Questions concerning this Appendix should be sent to CBERICSRSUBMISSIONS@fda.hhs.gov.

VAERS-1 Form Data Element	VAERS-1 Guidance Description	VAERS-2 Form Data Element	eVAERS Recommendations
Vaccine administered by (Name)	Provide the name of the health care provider who administered the vaccination (not prescribing health care provider, unless it is the same person)	No longer captured as a separate data field	When known, provide the name of the Vaccine Administrator in ICH H.1: Case Narrative
Responsible Physician (Name) Facility Name, Address, Telephone	Name of prescribing or responsible physician in the health care setting where the vaccine was given	No longer captured as a separate data element	When known, provide the name and contact information for the prescribing physician in ICH H.1: Case Narrative
Form completed by and Relation to Patient Checkbox	Provide the name, mailing address and phone number of the initial reporter (the person who initially reported the adverse event to the manufacturer) who can be contacted to provide information on the event if follow up is necessary	Person Completing This Form (Box 13)	Use ICH C.2.r Primary Source(s) of Information and FDA regional and ICH controlled terminology codes to select the most appropriate value (e.g., VAERS *Vaccine Provider* should be mapped to ICH C.2.r.4 code 3: *Other health professional*)
State where administered (Box 1)	Provide two-letter postal abbreviation for state where vaccine was administered	Information About the Facility Where Vaccine was Given (Box 15)	Information should be captured in new FDA regional data element: *Vaccination Facility Address*
County where administered (Box 2)	Provide full name of county where the vaccine was administered, if known.	Item has been reconciled to the Patient Address	Data element is no longer used. Legacy data may be provided

		Information (Box 1)	in the case narrative when known
Date of Birth (Box 3)	Enter the patient's birth date, if known; otherwise enter the patient's age at the time of vaccination	Date of Birth (Box 2)	Use ICH D.2.1 Patient Birth Date
Patient Age at Vaccination (Box 4)	Provide patient's age at time of vaccination. Identify units as years, months or days.	Age at Vaccination (Box 6)	Use new regional data element: *Age at Time of Vaccination*
Sex (Box 5)	Check box for the patient's gender	Sex (Box 3)	Use ICH D.5: Patient Sex
Date form completed (Box 6)	Date the report is filled out	Today's Date (Box 7)	Use ICH C.1.2: Date of Creation
Describe adverse events(s) (symptoms, signs, time course) and treatment, if any (Box 7)	Describe the event in detail using the reporter's own words, including a description of what happened and a summary of all relevant clinical information (signs and/or symptoms; differential diagnosis for the event in question; clinical course; treatment; outcome, etc.).	Describe the adverse event(s), treatment, and outcome(s), if any: (symptoms, signs, time course, etc.) – (Box 18)	Use ICH H.1: Case Narrative
AE Outcome (Box 8)	AE outcome checkbox options used to convey case seriousness based upon the outcome of the patient event.	Result or outcome of adverse event(s): (Check all that apply) – (Box 21)	Use ICH E.i.3.2: Seriousness at Event Level. HL7 null flavor used for *None of the above.*
Patient recovered (Box 9)	Check status of patient at time form was completed	Has the patient recovered from the adverse event(s)? (Box 20)	Use ICH E.i.7: Outcome of Reaction/Event at the Time of Last Observation
Date of vaccination (Box 10)	Provide date of last vaccination before event	Date and time of vaccination (Box 4)	Use the appropriate data elements (e.g., start/end date) in ICH G.K: Drug Information Section
Adverse event onset (Box 11)	Provide date and time of onset of event symptoms following vaccination. If more than one adverse event	Date and time adverse event started (Box 5)	Use ICH E.i.4: Date of Start of Reaction/Event

	occurred, provide information for the most serious event.		
Relevant diagnostic tests/laboratory data (Box 12)	Provide all appropriate information, including relevant negative test and laboratory findings, in order to convey most completely how the medical work-up and assessment led to consideration of vaccine as a possible etiology for clinical status, as other differential diagnostic considerations were being eliminated.	Medical tests and laboratory results related to the adverse event(s): (include dates) – (Box 19)	Use the appropriate data elements (e.g., Test Name) in ICH F: Results of Tests and Procedures Relevant to the Investigation of the Patient Section
Vaccines Given (Box 13)	Enter all known vaccines administered on that date, regardless of presumption of causal relationship to event	Enter all vaccines given on the date listed in item 4: (Route is HOW vaccine was given, Body site is WHERE vaccine was given) – (Box 17)	Use the appropriate data elements in the ICH G.K: Drug Information Section
Vaccines Given Within 4 Weeks (Box 14)	Enter all known vaccines administered within 4 weeks of the date the primary suspect vaccines were given, regardless of presumption of causal relationship to event	Any other vaccines received within one month prior to the date listed in item 4 (Box 22)	Use the appropriate ICH G.K Drug Information data elements (e.g., product name) in the new FDA regional data element section (organizer) header: *Vaccines Given within Four Weeks*
Vaccinated at (Box 15)	Check box options used to describe the type of vaccination facility where the vaccine was given	Information About the Facility Where Vaccine was Given (Box 16) and Vaccinated at Military/DoD site (Box 28)	Use the new FDA regional terminology and data element: *Vaccination Facility Type*. Note that VAERS-2 Box 28 is captured as a separate observation code using a Boolean value

Vaccine purchased with (Box 16)	Check appropriate box based on how the facility or person who administered the vaccine purchased it, not to payment by the patient's health insurance.	Not supported	Data element is no longer used. Legacy reports may include this information in the case narrative (ICH H.1) when known
Other medications (Box 17)	List and provide therapy dates for any other medical products (drugs, biologics, and medical devices) that a patient was using at the time of the event. Include routine medications, prophylactic medications such as over-the-counter (OTC) antipyretics, and medications given before the onset of symptoms. Include tuberculin skin test if given on the date of vaccination. Do NOT include products used to treat the event, which should be reported in Box 7.	Prescriptions, over-the-counter medications, dietary supplements, or Street address: herbal remedies being taken at the time of vaccination (Box 9)	Use the appropriate ICH G.K Drug Information Section data elements and ICH G.k.1, Characterisation of the Drug Role, option code should be 2: *Concomitant*
Illness at time of vaccination (Box 18)	Provide information on any short-term illness, condition or symptom present at or about the time of vaccination (e.g., cold, fever, ear infection).	Other illnesses at the time of vaccination and up to one month prior (Box 11)	Use new FDA regional data element: *Illness at the Time of Vaccination*
Pre-existing physician-diagnosed allergies, birth defects, medical conditions (Box 19)	If available, provide information on other known physician-diagnosed medical conditions in the patient (e.g., asthma, seizure disorder, immunosuppression, etc.) and significant historical information (allergies, birth defects, etc.).	Allergies to medications, food, or other products (Box 10) and Chronic or long-standing health conditions (Box 12)	Use ICH D.7 Relevant Medical History and Concurrent Conditions
Have you reported this adverse event previously? (Box 20)	Indicate if the initial reporter has also notified the patient's	Not supported	Data element is not supported for eVAERS reporting

	physician or health department. Check “To manufacturer” if another manufacturer has been notified by initial reporter or by reporting manufacturer. Otherwise leave blank.		
Adverse event following prior vaccination (Box 21): Sibling Information	List any suspected adverse events the patient, or the patient's brothers or sisters, may have had to previous vaccinations, specifying the implicated vaccine, if possible. If more than one brother or sister, or if the patient has reacted to more than one prior vaccine, use additional pages to explain	Has the patient ever had an adverse event following any previous vaccine?: (If yes, describe adverse event, patient age at vaccination, vaccination dates, vaccine type, and brand name – (Box 23)	Sibling information is no longer supported on the VAERS-2 form. ICH D.8.r Relevant Past Drug History should be used only for the patient and legacy information about siblings can be provided in the case narrative (ICH H.1).
Birth weight (Box 22)	Provide the patient's birth weight (in pounds and ounces) for children 5 years of age or younger. Current weight, if relevant, should be noted in the narrative (Box 7).	Not supported	Data element is no longer supported on the VAERS-2 form. Follow ICH guidance to include information as a comment in ICH D.7 Relevant Medical History and Concurrent Conditions when known.
Number of brothers and sisters (Box 23)	Provide the number of patient's brothers and sisters, as of the date of vaccination, if the patient is 5 years of age or younger.	Not supported	Data element is no longer supported as a structured data element. Legacy sibling information can be provided in ICH H.1
Mfr/imm. proj. report number (Box 24)	Provide manufacturer’s name and unique identification number for this event. All follow-up reports should have the same number as the initial	Immuniz. proj. report no.: (Health Dept use only). (Box 26)	Immunization Project Report Number not used. Use ICH C.1.1 Sender’s (case) Safety Report Unique Identifier

	report		
Date received by mfr./imm. project (Box 25)	Provide the date when the manufacturer received adequate information to determine that the adverse event was reportable; namely that a patient, vaccine, adverse event, and reporter can be identified. For follow-up reports, use the date that the follow-up information was received.	Not supported	Use ICH C.1.4: Date Report Was First Received from Source
NEW REGIONAL DATA ELEMENT		Patient's race: (Check all that apply) – (Box 24)	Captured as new observation code – See Section D. 4.4 FDA Patient Race and Ethnicity (Ancestry) Information
NEW REGIONAL DATA ELEMENT		Patient's ethnicity (Box 25)	Captured as new observation code – See Section D. 4.4 FDA Patient Race and Ethnicity (Ancestry) Information
NEW REGIONAL DATA ELEMENT		Best doctor/healthcare professional to contact about the adverse event (Box 14)	Captured using the SUBADMIN author information. See Section D.7.8: VAERS Best Doctor/Healthcare Professional to Contact about the Adverse Event
NEW REGIONAL DATA ELEMENT		Status at time of vaccination (Box 27)	Captured as new regional observation code for U.S. Military/Department of Defense (DoD) Related Reports
ICH Data Elements		Is the report about vaccine(s) given to a pregnant woman? (Box 8)	Use D.7 Relevant Medical History and Concurrent Conditions and if known, including

			information in ICH D.6 Last Menstrual Period Date. If the report is for a child/foetus, then the mother's last menstrual period is captured in the data element D.10.3 and relevant medical history for the mother is captured using ICH D.10.7

APPENDIX D
DETAILED DOCUMENT REVISION HISTORY

Section	Description
Global Document Change	Substantial revisions as a result of pilot testing with industry September 2014 – March 2015. Appendix D contains the detailed changes by section. Replaced the term “attribute” with the term “data element.
Cover Page	Added new VAERS Guidance to Industry document reference, document revision number and date
Document Revision History	New page insert. After publication of the May 2015 version, subsequent updates will be listed in this section and Appendix D will be deleted.
Introduction	Streamlined language and corrected link for FAERS reporting
Background	Updated all ICSR reference document descriptions, hyperlinks and new document Appendix B reference added
Background	New paragraph added to alert readers that ICH E2B has issued a new Questions and Answers to describe changes to their E2B (R3) guideline.
Background	Removed FAERS reference and updated email address for VAERS reporting email address
FDA Regional Implementation of ICH E2B(R3)	Section reformatted to add new subsections for: Regional Terminology and Use of the Display Name Data element and removed FAERS reference.
FDA ESG Connection Options	Updated subsection to clarify FDA ESG connection options, file size limitations and removed reference to FAERS
FDA Small Business Support	Streamlined paragraph and updated eSubmitter link
Regional Controlled Terminology	Reorganized section to update reference links and included new definitions for the terms, “controlled terminology” and “value set”. New Table 1 added to provide regional code system object identifier (OID) information
FDA ESG Transaction	Updated text and references. Removed

Partners and Testing	FAERS reference
FDA ESG Routing Identifiers	Updated text to clarify use of the FDA ESG Routing ID
ICSR Acknowledgements	Renumbered section and updated links to FDA Guidance documents
Failed ICSR Submissions	Corrected Acknowledgment relationships and reference numbers
Type of Messages in Batch N.1.1	Updated subsection to update the numeric allowable value "1" based upon ICH E2B data type conformance criteria and updated description about the information contained in the batch and generic transmission wrapper. Updated the message interaction ID information
Batch Sender Identifier N.1.3	Updated subsection to clarify regional use of the Dun and Bradstreet organization identifiers and updated reference link
Message Receiver Identifier N.2.r.3	Section changed to reference the FDA ESG Routing ID for N.2.r.3
ICSR Terminology for Clinical Information and Units of Measurement	Updated section title and include reference links to the full and constrained UCUM value sets for medication dosing units. Clarified use of the case sensitive format for all coded units of measurement
Identification of the Individual Case Safety Report C.1.1 and C.1.8	Renumbered subsections to include a new section to clarify FDA support for non-standardized report ID formats based upon previous paper submissions for C.1.1 and C.1.8
Linking of Initial and Follow up ICSRs ICH using C.1.1 and C.1.8	Renumbered paragraph and insert new email address for VAERS Electronic Submissions Coordinator
ICH C.1.6 Additional Documents Held By Sender	Clarified use of optional and required data elements for documents not provided as ICSR attachments
Identification of Expedited and Non-Expedited ICSRs using ICH C.1.7	Renumbered paragraph
Primary Source(s) of Information C.2.r: Patient	Renumbered subsection and clarified reporting requirements for ICH C.2.r when the patient is the primary source reporter
Reporter Qualification ICH C.2.r.4	Clarified allowable ICH, regional and HL7 null flavor codes used to populate ICH C.2.r.4. The VAERS data element, Relation to Patient, is not supported as a separate data element for eVAERS reporting.

ICH C.2.r.4 Regional Terminology	Reformatted Table 1 which describes acceptable terms/codes
ICH Section D: Patient Information	Renumbered and updated subsection text in accordance with requirements specified under the National Childhood Vaccine Injury Act. Clarified support for additional name and address part data elements and removed FAERS reporting reference. Updated allowable values for US State abbreviations and added new paragraph for capturing US State County information and new reference to Appendix B
ICH D.2 Patient Age	Removed the additional FDA Patient Age observation from this section and will accept VAERS Age at Time of Vaccination or ICH Patient Age
Birth Weight	Data element no longer supported on updated VAERS form. Information should be captured as Relevant Medical History section in ICH D.3. Clarified acceptance of gram and kilogram as acceptable units of measurement.
VAERS Number of Brothers and Sisters (Number of Siblings)	Data element no longer support on updated VAERS form. Appendix C provides guidance that information should be provided in the case narrative
Patient Military Status	Paragraph moved from the Drug Information section and moved to the Patient Information section and renumbered
Relevant Medical History and Concurrent Conditions ICH D.7	Removed VAERS Illness at the Time of Vaccination from this section. Information is now captured as new regional data element outside the ICH organizer
ICH D.8 Past Drug History: VAERS Dose Number in Series	Data element name changed from Number of Previous Doses to align with updates to in the VAERS form
ICH D.8.r.2a Medicinal Product Identifier (MPID) Version Date/Number	Clarified regional the MPID Version Date/Number when FDA NDC is used
VAERS Illness at the Time of Vaccination	Clarified regional guidance concerning relationship with date/time information provided ICH G.k for the primary suspect product
ICH D.8.r.3 Pharmaceutical Product Identifier (PhPID)	Provided interim guidance concerning the datatype and format for the PhPID termID and technical reference information

ICH D.10 Parent Information	New subsection added to clarify that parent contact information for address, telephone number and email address should be captured in ICH D.1 for parent/child reports if the parent is the primary contact person
ICH D.10.2 Parent Age	New subsection added and removed VAERS Patient Age data element
Parent Race and Ethnicity Information	New subsection added and clarified information captured in this section should be consistent with the new regional data elements described in ICH D Patient Information section
D.10.8.r Parent Relevant Past Drug History	New subsection added and clarified information captured in this section should be consistent with the new regional data elements described in ICH D.8.r Patient Past Drug History section
ICH Section E.i: Reactions/Events	Clarified regional conformance for VAERS data elements: Hospitalization, Number of Hospitalization days, Prolongation of Hospitalization and AE Treatment Facility when ICH E.i.3.2c is valued as “true”. Provided email contact for questions related to ICH E.i.3.2f
VAERS AE Treatment Facility Information	Reordered text and added regional terminology reference for US State names/abbreviations and reference to Appendix B for datatype and field length information
ICH Section G.K: Drug(s) Information	Section has been renumbered and reorganized to group data elements related to FDA regional product identification
ICH G.k.2.1.1b: FDA Medicinal Product Identifiers (MPID)	Clarified the MPID Version Date/Number when FDA NDC is used.
G.k.2.1.2b Pharmaceutical Product Identifier (PhPID)	Added new paragraph as placeholder for more information about the PhPID when available.
ICH G.k.2.2: Medicinal Product Name as Reported by the Primary Source	Paragraph renumbered.
ICH G.k.2.3.r: FDA Unique Ingredient Identifier (UNII)	Changed reference to acceptance of ISO IDMP and FDA regional terminology
ICH G.k.2.3.4 Country where obtained	Paragraph moved and renumbered
Vaccination Facility	Paragraph and related sub-paragraphs

Information	moved and renumbered. Clarified use of the US Postal Service State abbreviations for US cases.
ICH G.k.3.1: FDA Authorisation/Application Number	Paragraph moved and renumbered
ICH G.k.4.r: Dosage Information	Section moved and renumbered.
ICH G.k.4.r.9.2b: FDA Pharmaceutical Dose Form TermID	Paragraph moved and renumbered. Clarified acceptance of ISO IDMP and regional terminology
G.k.4.r.10.2b Route of Administration TermID	New paragraph and clarified acceptance of allowable Route of Administration terminology and reference sources
VAERS Anatomical Approach Site	Paragraph moved and renumbered
VAERS Dose Number in Series	Paragraph moved and renumbered. The data element name has been changed to align with updates to the VAERS form
VAERS Vaccines Given Within 4 Weeks	Paragraph renumbered and new subparagraphs added to describe how data elements should be captured in the XML file.
FDA Specialized Product Categories	Paragraph and associated terminology table updated to reflect change in regional terminology concept identifier
E. ICSR Attachments	Paragraph renumbered and updated to include new data element to capture ICSR attachment filenames and tentative limit on ICSR attachment file size
New Appendix B: Consolidated Business Rules Spreadsheet	Appendix B provides a listing of all ICH and eVAERS data elements and includes information about datatypes, field length and validation rules for creating compliant files
New Appendix C: Reconciliation of VAERS-1 and VAERS-2 Form Data Elements	Appendix C provides information about how the VAERS-1 and VAERS-2 form data elements have been reconciled to the ICH E2B (R3) specification, as well as new regional data elements
New Appendix D: Detailed Revision History	Appendix D provides a detailed listing of all changes made the Regional Technical Specifications Document as a result of industry pilot testing. Subsequent releases of this document will summarize all changes in the new Document Revision

	History Section and Appendix D will be deleted.