FDA Regional Implementation Specifications for ICH E2B(R3) Implementation

Postmarket Submission of Individual Case Safety Reports for Drugs and Biologics, Excluding Vaccines

Technical Specifications Document

This document is incorporated by reference into the following guidance document:

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

For questions regarding this technical specifications document, contact the Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research, Food and Drug Administration, Suranjan De, Phone: (240) 402-0498; or Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 3128, Silver Spring, MD 20993-0002, 800-835-4709 or 240-402-8010.

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

June 2016

This page intentionally left blank.

Document Revision History

Date	Version	History of Changes (include section and page number)
2016-06-22	1.0	Initial Version

Table of Contents

List of Tables

List of Figures

FDA Regional Technical Specifications for ICH E2B(R3)

I. INTRODUCTION

This technical specifications document is to assist interested parties in electronically submitting individual case safety reports (ICSRs) (and ICSR attachments) to the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) in the Food and Drug Administration (FDA or Agency). This document describes FDA's technical approach for submitting ICSRs, for incorporating its regionally controlled terminology,[1] and for adding FDA Adverse Event Reporting System (FAERS) regional data elements that are not addressed in the International Conference on Harmonisation's (ICH) E2B (R3) Implementation Guideline (IG) for the following FDA-regulated products:

- Drug products marketed for human use with approved new drug applications (NDAs) and abbreviated new drug applications (ANDAs)
- Prescription drug products marketed for human use without an approved application
- Nonprescription (over-the-counter human drug products marketed without an approved application)
- Biological products marketed for human use with approved biologic license applications (BLAs).

This document does not apply to prophylactic vaccines; whole blood, or components of whole blood; and human cellular and tissue-based products regulated under section 361 of the Public Health Service Act or Investigational New Drug Safety Reports.[2]

ICSRs (and any ICSR attachments) should be prepared in accordance with the ICH E2B(R3) data elements, in extensible markup language (XML)[3] file format and submitted through FDA's "Electronic Submissions Gateway" (ESG). ICSRs should *not* be submitted to the electronic Common Technical Document (eCTD). Agency information about electronic submissions will be updated as necessary to reflect the evolving nature of the technology and the experiences of those using this technology.

---

[1] *Controlled terminology* is a finite set of values that represent only the allowed values for a data item.

[2] For vaccine-related ICSR submissions, please reference the technical specifications document entitled *FDA Regional Technical Specifications for ICH E2B(R3) Implementation: Postmarket Submission of Individual Case Safety Reports (ICSRs) for Vaccines*, which is available on the CBER ICSR Specifications Web page athttp://www.fda.gov/forindustry/electronicsubmissionsgateway/ucm387293.htm.

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

A. Background

The ICH E2B Expert Workgroup (E2B EWG) released the revised, *ICH Implementation Guide for the Electronic Transmission of ICSRs: E2B(R3) Data Elements and Message Specification* for pharmacovigilance reporting guideline. The revised guideline describes the harmonized core set of ICH E2B(R3) data elements, ICH business rules, and other technical specifications for creating ICH-compliant XML files for ICSR data exchange. FDA adopted that guideline and in February of 2014 published it as FDA Guidance for Industry *E2B(R3) Electronic Transmission of Individual Case Safety Reports Implementation Guide — Data Elements and Message Specification* (ICH E2B(R3) IG).[4]

Regional data elements are considered non-harmonized; however, the ICH XML file structure allows regions to use regionally controlled terminology and to add region-specific elements as specified in this document.

In addition to the regional specifications described in this document, FDA supports use of all the ICH E2B(R3) data elements and recommends that stakeholders refer to other relevant technical documents to help create compliant ICSR files, such as the following:

- The ICSR message specification identified as Health Level Seven (HL7) and the International Standards Organization (ISO) International Standard 27953-2:2011 entitled *Individual case safety reports (ICSRs) in pharmacovigilance -- Part 2: Human pharmaceutical reporting requirements for ICSR* (available for purchase) provides technical information about the HL7 Version 3 message specification, schemas, and data types used to support ICSR data exchange;

- The ICH E2B(R3) IG guidance for industry provides technical and business specifications for the harmonized, core set of ICH data elements;

- The FDA Adverse Event Reporting System (FAERS) Electronic Submissions Web site provides procedures and examples for accommodating FDA regional data elements, and ICH file validation rules to support automated XML file validation and a sample FDA instance file; and

- The guidance for industry *Appendix I (B) to the ICH E2B(R3) ICSRs Implementation Guide: Backwards and Forwards Compatibility* supplements the ICH E2B(R3) IG, and assists reporters and recipients in implementing systems with a special focus on the recommendations for conversion between the previous standard (ICH E2B(R2)) and this standard (ICH E2B(R3)).

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)-

[4] The guidance for industry is available on the FDA Drugs guidance Web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm274966.htm.

formatted submissions; these updates will be published on FDA Web sites. Stakeholders interested in submitting ICSRs to FAERS in ICH E2B(R3) format should contact the FAERS Electronic Submissions Coordinator (via email at FAERSESUB@fda.hhs.gov) for more information about specific program adoption, testing, and implementation timelines or refer to the FAERS Electronic Submissions Web site.

B. FDA Regional Implementation of ICH E2B(R3)

FDA recognizes the need to support both the current and previous versions of ICH E2B standards and will continue to provide support for ICH E2B(R2). Information about FAERS E2B(R3) migration planning and pilot testing will be made available on the FAERS Electronic Submissions Web site.

In this technical specifications document, FDA's regional specifications for receiving only ICH E2B(R3) electronic submissions, for incorporating regionally controlled terminology, and for adding region-specific data elements will be provided.

1. Technical Approach for Receiving Electronic Submissions

FDA regional specifications comply with ICH E2B(R3) conformance criteria. Use of the term *conformance* in this document refers to data element definitions, formats, and use (e.g., required or optional) as specified by the ISO/HL7 27953-2:2011 standard and in accordance with the content specifications described in the ICH E2B(R3) IG. Regional specifications for submitting ICSRs are defined in section II.A (Electronic ICSR Submissions Using the FDA ESG)

2. Technical Approach for Incorporating Regionally Controlled Terminology

ICH elements accept regionally controlled terminology without compromising ICH E2B(R3) conformance criteria. Regional implementation includes incorporating regionally controlled terminology drawn from the National Cancer Institute's Enterprise Vocabulary Service (EVS) code set (namespace) 2.16.840.1.113883.3.26.1.1.

FDA's regionally controlled terminology is described in section II.C.2 of this document ("Terminology"); specifications are provided in section II.C.5.b of this document (FDA Regionally Controlled Terminology for Section G.k Drug(s) Information).

3. Technical Approach forAdding FDA Regional Data Elements

FDA incorporates the collection of regional data to help improve overall ICSR data quality and support other FDA safety initiatives. The data are accommodated in the ICSR file using the XML schema attributes supported. FDA uses the XML observation attribute to provide details and the characteristic attribute to provide descriptions about the subject. FDA regional data collected are:

- FDA Race (<observation> about the patient or parent)
- FDA Ethnic Group (<observation> about the patient or parent)

Specifications for regional observation data FDA Race and FDA Ethnic Group are provided in section II.C.4.a (FDA Regional Data Elements) of this document.

II. FAERS FDA REGIONAL TECHNICAL SPECIFICATIONS

A. Electronic ICSR Submissions Using the FDA ESG

1. FDA ESG Connection Options

Connections to the FDA ESG are supported through a direct gateway-to-gateway or Web-based communications interface that uses Hyper Text Transfer Protocol Secure (HTTPS) for transmission according to Applicability Statement 2 (AS/2) standards. Information about FDA ESG connection options can be found in the FDA ESG User Guide.

The current exchange of ICSRs with FDA is a one-way inbound file transaction between the ICSR sender organization and the FDA ESG. The FDA ESG supports the receipt of electronic regulatory submission of files up to 100 GB in size. The attachment size should be limited to 15 MB with a case limit of 20 MB. ICSR attachments should not be individually compressed. Senders should follow FDA guidance for file compression in Appendix B: Creating .tar Files and Compressing Files for Submission.

2. FDA ESG Transaction Partners and Testing

a. ESG Transaction Partners

To submit files electronically to FDA, organizations must apply for a Transaction Partner account. Account requests should include the organization's digital certificate information and be submitted to the ESG Help Desk via email at esgprep@fda.hhs.gov. For more information about digital certificate specifications, refer to Appendix C: Digital Certificates. Upon approval by the FDA ESG Administrator, organizations can initiate communication testing with ESG.

b. ESG Testing

Senders will need to complete two levels of testing: (1) to establish a successful Transaction Partner account and (2) to confirm the senders' ability to generate FAERS guidance-compliant ICSR files for Adverse Event (AE) program review. To test connectivity, senders should submit all ICSR connectivity test submissions to the appropriate Center's "GW_TEST CONNECTION" account using the submission type "CONNECTION TEST," not to the Center's production account.

- For more information about ESG connectivity testing, email esgprep@fda.hhs.gov.
- For more information about FAERS testing, email FAERSESUB@fda.hhs.gov.

3. FDA ESG Header Information

When exchanging ICSRs with the FDA ESG, senders must use the following FAERS gateway header to insure that the submissions are routed to the targeted receiving system. The FAERS ESG header values are:

- For WebTrader Accounts use CDER AERS
- For AS/2 Accounts use FDA_AERS

4. ICSR Acknowledgments

FAERS implemented two acknowledgments (ACKs) described in Table 1. FDA Acknowledgements.

Table 1. FDA Acknowledgements

ACK#	Description	Use
ACK1	FDA Message Delivery Notification (MDN)	Notifies the sender that the submission was received in the ESG, successfully and is being processed. It also provides the official FDA receipt date but does not imply FDA acceptance of the submission. For more information about FDA receipt dates, refer to FDA's guidance for industry, *Providing Regulatory Submissions in Electronic Format—Receipt Dates*.
ACK2	FAERS Review Acceptance/Rejection	Notifies the sender that the FAERS system reviewed the submission and either accepted or rejected all or part of the submsssion. The notification provides codes indicating validation errors. Review Acceptance/Rejection means: 1. Acceptance: The ICSR file meets FAERS ICSR file validation specifications without the need for correction and resubmission. 2. Rejection: Failure to meet FAERS ICSR file validation may result in the need to correct and resubmit ICSR files. Note: FAERS ICSR file validation codes are consistent with the ICSR file validation codes provided in the of the European Medicines Agency's Implementation Guide.

a. Submission Tracking

For more information about FDA submissions tracking, refer to Chapter 4.8, "Tracking Submissions," on the ESG Web Interface Electronic Submissions Web page.

b. ESG Failure

If an ACK1 is not received within 24 hours, confirm system status through the ESG System Status Web page. This Web page provides ESG status information, such as operational status, downtime history, submission statistics, and links to other ESG-related topics. If the ESG Web page is non-operational, go to the ESG home page for information on whom to contact.

c. ICSR Submission Failure

1. If an ACK2 acknowledgement is not received within 24 hours of receiving the ACK1 ESG message delivery notice of acknowledgement, resubmit the original ICSR submission without changing the batch identifier.

2. If an FDA ACK2 response is received for an unsuccessful (failed) ICSR submission, please refer to the following instructions:

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

b. For ICSR submissions containing multiple ICSR files (batch submissions), and one or more ICSRs in the submission failed to process, do the following:

1) Separate the failed ICSRs from the successfully submitted ICSRs
2) Correct the failed ICSRs
3) 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 correct and resubmit the failed 15 ICSRs ONLY. The failed ICSRs must be submitted with a new unique batch identifier. The resubmission must not contain any of the successfully processed ICSRs.

B. Creating FDA ICSR Files

Refer to the FAERS Electronic Submissions Web site for XML schema examples and for more information about the following procedures for populating ICSR data elements.

1. ICSR Batch and Message Wrapper Information

The HL7 batch message wrapper supports individual and batch ICSR files 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. Because this information is provided in the batch wrapper, the Generic Message Transmission Wrapper is not used. For more information about HL7 Batch and Generic Message Transmission wrappers, refer to the Transmission Infrastructure topic in the ISO/HL7 27953-2:2011standard.

2. Type of Messages in Batch N.1.1

ICH E2B(R3) uses one ICSR message type, which is characterized by the HL7 message interaction IDPORR_IN049016UV. FDA does not support additional HL7 interaction identifiers or message types for Follow Up or Withdrawn ICSRs described in the ISO/HL7 27952-2 standard. FDA accepts only the value of "1" (**ichicsr**) for N.1.1-Type of Messages in Batch.

3. Batch Number N.1.2

Each electronic submission of ICSRs must have a stakeholder-unique batch identifier (filename or number). Organizations may choose their own format to maintain uniqueness. For more information about the use of the ICSR batch number in ICSR acknowledgements, refer to Section 4.0 of the E2B(R3) Electronic Transmission of ICSR IG , entitled "The ICSR Acknowledgment Transaction," and to section II.A.4 (ICSR Acknowledgments) of this document.

4. 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 Identifier1.3.6.1.4.1.519.1. The DUNS number for Business Entity Identifiers is used to validate business entities in various FDA information systems.

- For more information about Business Entity Identifier initiative, refer to the FDA D&B Verification Web page.

- For more information about how to obtain a DUNS number, refer to the FDA Business Entity Identifiers Web page.

5. Message Receiver Identifier N.2.r.3

FDA uses two different message receiver identifiers for test and production submissions. These identifiers are:

- For Test ICSR Submissions: ZZFDATST
- For Production ICSR Submissions: ZZFDA

Refer to section II.A (Electronic ICSR Submissions Using the FDA ESG) of this document for more information about FDA ESG connection options and testing specifications.

C. FDA ICSR Content

1. 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 specifications not addressed in the ICH E2B(R3) IG; these exceptions, though, are noted in the relevant section headers of this technical specifications document.

2. Terminology

FDA supports the recommendations of the ICH E2B(R3) concerning use of the terminology found in the Medical Dictionary for Regulatory Activities (MedDRA)[5] 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). Stakeholders should refer to the ICH E2B(R3) IG for data elements that specify the use of MedDRA coding.

FDA supports the use of constrained Unified Codes for Units of Measurement (UCUM) for coding units of measure (e.g., medication dosing units). FDA regional terminology supports the controlled terminology of the U.S. National Cancer Institute (NCI), the EVS, and the FDA internal Substance Registration System (SRS) (among others). ICH elements that use FDA controlled terminologies are noted and defined in the relevant sections of this document.

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

3. Section C: Identification of the Case Safety Report

a. C.1.7 Data Element - Does this Case Fulfill the Local Criteria for an Expedited Report?

FDA concurs with ICH E2B(R3) conformance criteria for the C.1.7 data element—entitled *Does this Case Fulfill the Local Criteria for an Expedited Report?* to specify if the case fulfills regional specifications for expedited reporting. FDA *does not* support use of the HL7 nullFlavor NI for this data element in initial submissions. Initial submissions with nullFlavor NI will be rejected. Subsequent submissions for ICSRs already received by FDA will default to the initially submitted value.

For FDA reporting, if C.1.7 is populated with a "false" value, the ICSR is considered a non-expedited report. Refer to the FAERS Electronic Submissions Web site for procedures and examples for populating C.1.7.

b. Linking Initial and Follow-up ICSRs

If the initial ICSR was submitted on paper but its follow-up ICSR will be submitted electronically, include the C.1.1 Sender's (case) Safety Report Unique Identifier from the initial report in both C.1.1 and in C.1.8.1 Worldwide Unique Case Identification in the follow-up electronic submission.

Note that the Sender's (case) Safety Report Unique Identifier is also referred to as the *Manufacturer Control Number*[6] (MCN) listed in Box G9 of FDA Form 3500A.

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 a 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.*

Refer to the FAERS Electronic Submissions Web site for XML schema examples of correctly populating the ICH C.1.1 data element.

c. Correcting an Incorrect Safety Report Identifier

In the event that an incorrect safety report ID has been used in a follow-up report, contact the FAERS Electronic Submissions Coordinator at FAERSESUB@fda.hhs.gov.

4. Section D: Patient Characteristics

a. FDA Regional Data Elements

If patient race and ethnic group observations are available, use the codes listed in Table 2. FDA Race Codes and in Table 3. FDA Ethnic Group Codes. If patient race or ethnic group information is unknown or not available, use the HL7 null flavor NI (No Information) code (HL7

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

nullFlavor NI) for these elements. Validation information and example XML coding is available on the FAERS Electronic Submissions Web site.

1) FDA Race

Senders may submit multiple observation codes for patient race from Table 2.

Table 2. FDA Race Codes (C17049)

Factor	Description
FDA Object Identifier	2.16.840.1.113883.3.26.1.1
Regional Identifier	D.1.FDA.1
Name	FDA Race Information
User Guidance	
Conformance	Optional
FDA UUID	NA
Data Type	6 AN (ANNNNN)
Value Allowed	**NCI Concept Identifier** — **Race** C16352 — African American C41259 — American Indian or Alaska Native C41260 — Asian C41219 — Native Hawaiian or Other Pacific Islander C41261 — White
Business Rule(s)	Multiple patient race classification codes can be used. If the patient information is not available or unknown, use the HL7 nullFlavor NI.

2) FDA Ethnic Group

Senders should submit only one observation code for each patient ethnic group from Table 3.

Table 3. FDA Ethnic Group Codes (C16564)

Factor	Description
FDA Object Identifier	2.16.840.1.113883.3.26.1.1
Regional Identifier	D.1.FDA.2
Name	FDA Ethnic Group
User Guidance	
Conformance	Optional
FDA UUID	C16564
Data Type	6 AN (ANNNNN)
Value Allowed	**NCI Concept Identifier** — **Ethnicity** C17459 — Hispanic or Latino

Factor	Description
	C41222 Not Hispanic or Latino
Business Rule(s)	Only one (1) ethnic group code should be used. If the patient ethnicity information is not available or unknown, use the HL7 null flavor NI for these data elements.

b. D.1 Patient Information

FDA concurs with the ICH E2B(R3) guidance stating that at least one of the available data elements in ICH Section D should be populated to help fulfill reporting criteria for an identifiable patient. If the patient is not the primary source reporter and other available data elements (e.g., age, date of birth, or sex) are unknown, then the HL7 null flavor codes NI or ASKU (Asked But Unknown) can be used. When the patient information is not provided due to regional privacy restrictions (e.g., foreign reports), FDA supports the use of the HL7 null flavor code MSK (Masked).

5. Section G.k: Drug(s) Information

a. Integration with ISO Identification of Medicinal Product (IDMP) Standards

ICH supports harmonization of medicinal product information and provides input to the ISO workgroups Health Informatics, and the Pharmacy and Medicine Business, and the E2B(R3) Electronic Transmission of ICSR IG through its Multidisciplinary Expert Workgroup 5 (M5).[7] IDMP standards are designed to facilitate the exchange and practical use of medicinal product data by regulators, pharmaceutical industry workers, 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.

FDA plans to support full adoption and integration of the ISO IDMP standards for ICSR reporting and supports the use of regionally controlled terminology for data elements in this section. The suite of related ISO IDMP standards is summarized below, and information about these standards is available on the ISO/TC 215 Web site.

b. FDA Regionally Controlled Terminology for Section G.k Drug(s) Information

FDA regionally controlled terminologies are defined in Section G.k: Drug(s) Information to support use of FDA regional product identifiers and FDA specialized product categories:

- Medicinal Product Identifier (MPID) (ISO 11615:2012)
- Medicinal Product Name as Reported by the Primary Source
- Substance/Specified Substance TermID (ISO 11238:2012)
- Authorisation/Application Number

[7] The maintenance and use of ICH M5-controlled terminology was integrated into the E2B Implementation Working Group work plan per decisions undertaken by the ICH Steering Committee during a June 2013 meeting in Brussels.

- Pharmaceutical Dosage Form TermID (ISO 11239:2012)
- Additional Information on Drug (FDA Specialized Product Category)

1) Medicinal Product Identifiers G.k.2.1.1b

The FDA National Drug Code (NDC), when known, should be used as the regional MPID. If the NDC or MPID is unknown, please refer to the ICH E2B(R3) IG. Information about obtaining a list of the NDCs can be found on the NDC Structured Product Labeling Data Elements ("NDSE") Web page.

2) Medicinal Product Name as Reported by the Primary Source G.k.2.2

FDA validates medicinal product names for products licensed in the United States against the available Structured Product Labeling (SPL)[8] XML file or the label that was submitted with the ICSR as an attachment. When the product has an SPL file, use the same naming convention in the ICSR as the name appears in the SPL file. When submitting a product label as an attachment to an ICSR, use the name as it appears on the submitted product label.

If the Medicinal Product Name is not provided but the active substance name is known, provide the active substance as it appears in the FDA Substance Registration System (SRS) Unique Ingredient Identifiers (UNII) list using the free text element G.k.2.3.r.1 Substance/Specified Substance Name.

If the Medicinal Product Name as Reported by the Primary Source is a foreign product trade name, provide the active substance name as it appears in the FDA SRS UNII list using the free text element G.k.2.3.r.1 Substance/Specified Substance Name. See Figure 1. Medicinal Product Name as Reported by the Primary Source. Additionally, provide the foreign product trade name in G.k.2.2.

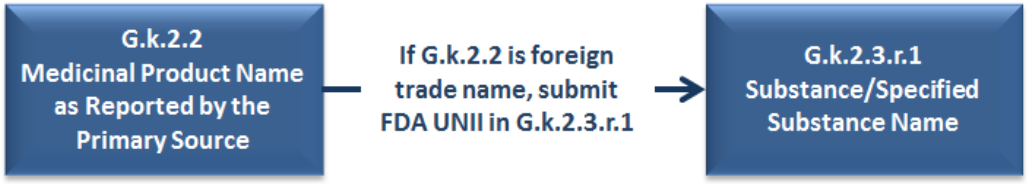

Figure 1. Medicinal Product Name as Reported by the Primary Source

[8] SPL is a document markup standard approved by HL7 and adopted by FDA as a mechanism for exchanging product and facility information.

3) Substance/Specified Substance TermID G.k.2.3.r.2b

If the Substance Name TermID (G.k.2.3.r.2b) is not available, the FDA SRS UNII list should be used to populate element Substance/Specified Substance Name (G.k.2.3.r.1). See Figure 2. Substance/Specified Substance TermID.

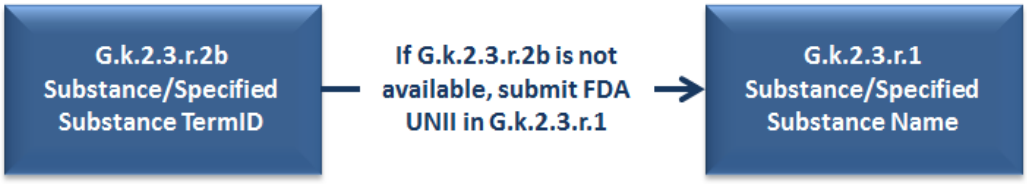

Figure 2. Substance/Specified Substance TermID

FDA recommends that applicants proactively validate substance information with primary source reporters before preparing the ICSR submission. FDA UNII codes are updated monthly and may be obtained from the FDA SRS UNII list.

4) Authorisation/Application Number G.k.3.1

FDA requires the use of a prefix to determine the application type associated with suspect products. For example, for human drug products, include the acronym "NDA" or "ANDA" immediately followed by the application number with no spaces; for example, NDA012345, ANDA012345. Table 4. FDA Application Number Formats describes format specifications for FDA application numbers and exceptions such as non-application prescriptions, non-approved applications, and compounded products.

Table 4. FDA Application Number Formats

Product Type	FDA Application Type	Recommended Format
Human drug products	NDA/ANDA	NDA123456 or ANDA012345
Biologics License Application	BLA	BLA123456
Prescription drug products marketed without an approved application	Rx No Application	000000
Non-prescription drug product marketed without an approved application	Non-Rx No Application	999999
Compounded products marketed	Compounded Products	COMP99

Procedures and examples for capturing FDA application numbers in the XML file are provided on the FAERS Electronic Submissions Web site.

5) Pharmaceutical Dose Form TermID G.k.4.r.9.2b

FDA plans to adopt use of ISO IDMP dosage form terms and IDs when available. Where IDMP codes are not available, populate G.k.4.r.9.1 Pharmaceutical Dose Form (free text) with a regionally controlled terminology value from the FDA SPL regional "Dosage Form" Web page. See Figure 3. Pharmaceutical Dose Form TermID.

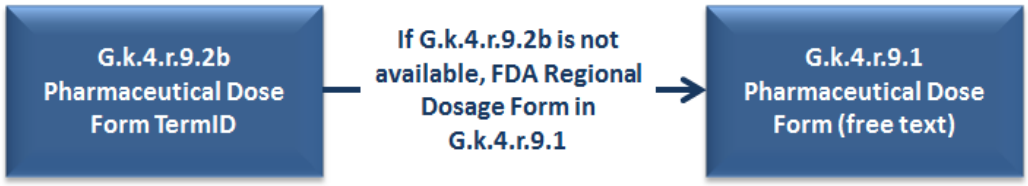

Figure 3. Pharmaceutical Dose Form TermID

Procedures and examples for populating FDA Pharmaceutical Dose Form TermIDs are provided on the FAERS Electronic Submissions Web site.

6) Additional Information on Drug G.k.10.r

FDA regionally controlled terminology for FDA Specialized Product Categories is used to provide characteristics associated with product information**.** These codes comprise the combination product types and the compound products listed in Table 5. FDA Specialized Product Categories.

Table 5. FDA Specialized Product Categories

FDA Object Identifier: 2.16.840.1.113883.3.26.1.1	
NCI Concept Identifier	**Description**
Combination Product	
C102834	Type 1: Convenience Kit or 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 Labelling
C102841	Type 8: Possible Combination Based on Cross Labelling of Separate Products (Temporary Type)
C102842	Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)
Compounding Product	
C73626	Bulk ingredient
C96793	Bulk Ingredient For Human Prescription Compounding
C95602	Unapproved Drug Product Manufactured Exclusively for Private Label Distributor

See Figure 4. Snippet for FDA Product Information Characteristic Code for an example of XML code using FDA regionally controlled terminology as a characteristic for product information.

```
<consumable typeCode="CSM">
 <instanceOfKind classCode="INST">
  <kindOfProduct classCode="MMAT" determinerCode="KIND">
   <asManufacturedProduct classCode="MANU">
    <subjectOf typeCode="SBJ">
     <characteristic classCode="OBS" moodCode="EVN">
      <code code="C5469" displayName="combination product"codeSystem="2.16.840.1.113883.3.26.1.1" />
      <value xsi:type="CV" code="C73626" displayName="Bulk ingredient"codeSystem="2.16.840.1.113883.3.26.1.1"/>
     </characteristic>
    </subjectOf>
```

Figure 4. Snippet for FDA Product Information Characteristic Code

Procedures and other examples for capturing FDA Specialized Product Categories are provided on the FAERS Electronic Submissions Web site.

D. ICSR Attachments

ICSR attachments can be sent as embedded files using base 64 encoding; see E2B(R3) Electronic Transmission of ICSR IG Section 3.5 Document Attachments for further information. FDA supports the following data types:

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

As mentioned previously, ICSR attachments should not be individually compressed. For FDA's file compression specifications, refer to section II.A.1 ("FDA ESG Connection Options") of this document.