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ICH E2B(R3) Clinical Safety Data Management: Data Elements for Transmission of Individual Case Safety Reports

Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs)

Module II of III

June 2025

International Council for Harmonisation of Technical Requirements
for Pharmaceuticals for Human Use

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Legal Notice

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ICH E2B Training Module II

Target audience:	Regulatory authorities, pharmaceutical companies, clinical trial sponsors, IT system vendors and other interested parties with a background in IT, regulatory and/or safety reporting.
Learning outcomes:	At the end of this Module you should be able to: • Understand the main principles and concepts in ICH E2B reporting. • Have a high-level understanding of the data elements and differences between ICH E2B(R2) and ICH E2B(R3). • Understand where to obtain supporting information.
Further information:	• ICH E2B training modules I and III. • ICH E2B(R3) Implementation Guide Package.
Note:	This set of ICH E2B training modules is progressive, i.e., high-level information is presented in earlier slides and more technical and detailed information is presented in subsequent modules.

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Outline

1. Introduction to ICH E2B(R3)
2. ICH E2B(R3) Documentation
3. Summary of ICH E2B(R3) Guideline
4. ICH ICSR Acknowledgement Message
5. Summary

ICH E2B(R3)

- **First published in 2013, supersedes ICH E2B(R2)**
- **Message standard is based on an HL7 ICSR model.**

Please ensure that, when using the ISO/HL7 standard for Individual Case Safety Reports (ICSR), the following version is used: "*ISO/HL7 27953-2:2011 Health informatics -- Individual case safety reports (ICSRs) in pharmacovigilance -- Part 2: Human pharmaceutical reporting requirements for ICSR*".

Do not use other versions of the standard since they might include changes that are not relevant for the submission of ICSRs in the regulated biopharmaceutical domain.

Source: ICH E2B(R3) Website: https://www.ich.org/page/e2br3-individual-case-safety-report-icsr-specification-and-related-files

ICH E2B(R2) -> ICH E2B(R3) Change Summary

- **Greater use of standardised terminologies - Code lists.**
- **Data structure** (Repeatable Sections; Numbering of data elements; Other changes)
- **New features** (In-line attachment, amendments)
- **Date/Time format changes**
- **New and reclassified data elements** (Field length)
- **Use of Null Flavors**

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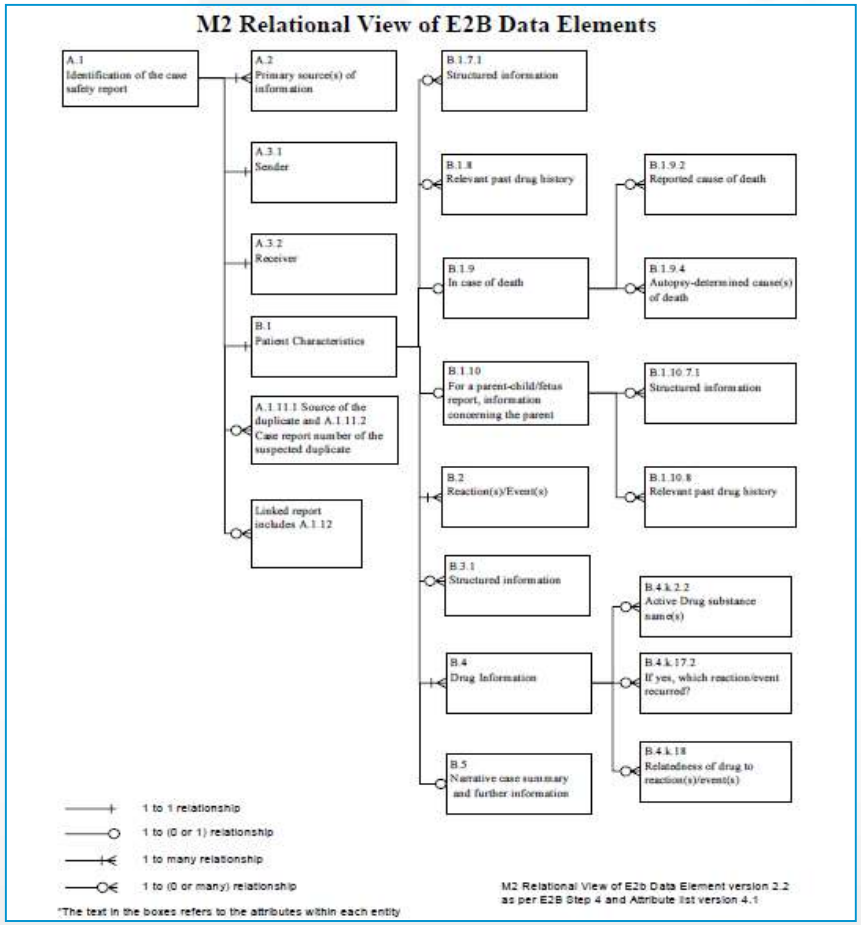
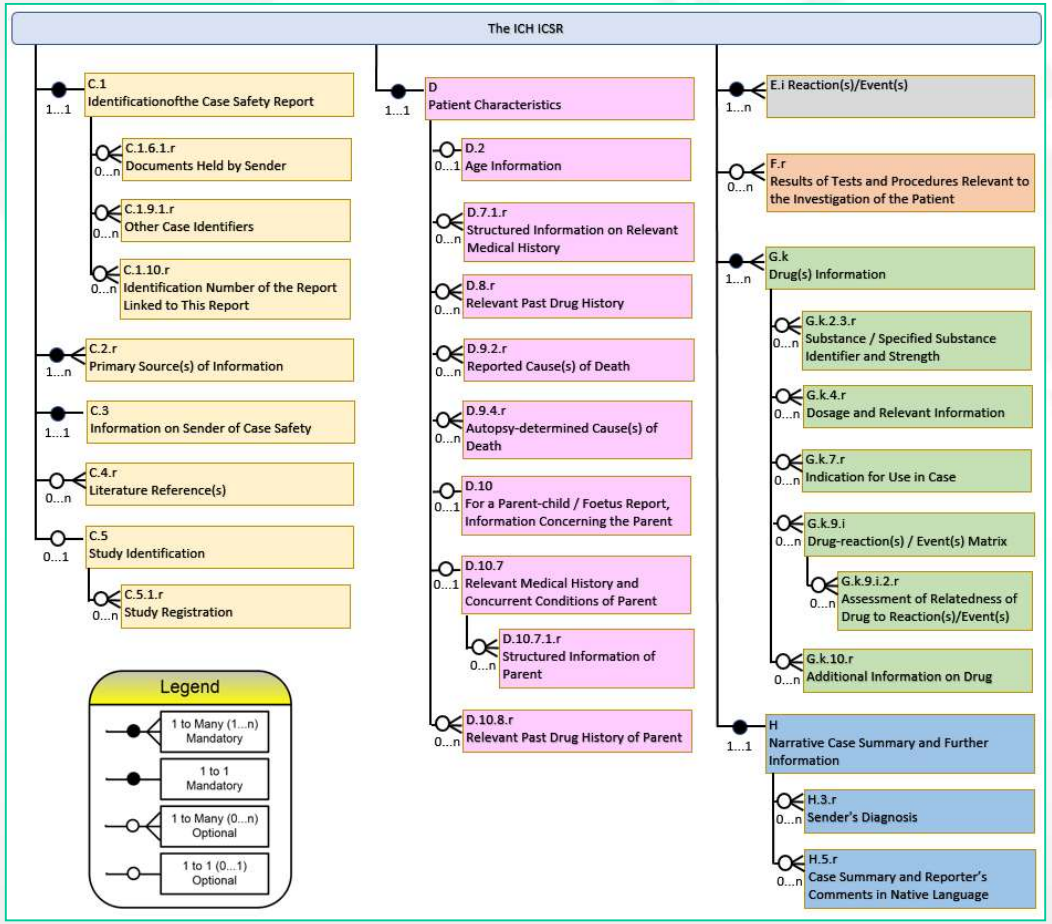
Introduction to ICH E2B(R3)

Get Familiar With Changed Structure

ICH E2B(R2)



ICH E2B(R3)



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Introduction to ICH E2B(R3)

Different Message Formats

ICH E2B(R2)

```
<safetyreport>
  <safetyreportversion>0</safetyreportversion>
  <safetyreportid>GB-EMA-2010060622</safetyreportid>
  <primarysourcecountry>GB</primarysourcecountry>
  <transmissiondateformat>102</transmissiondateformat>
  <transmissiondate>20100629</transmissiondate>
  <reporttype>1</reporttype>
  <serious>1</serious>
  <seriousnessdeath>2</seriousnessdeath>
  <seriousnesslifethreatening>2</seriousnesslifethreatening>
  <seriousnesshospitalization>1</seriousnesshospitalization>
  <seriousnessdisabling>2</seriousnessdisabling>
  <seriousnesscongenitalanomali>2</seriousnesscongenitalanomali>
  <seriousnessother>2</seriousnessother>
  <receivedateformat>102</receivedateformat>
  <receivedate>20100628</receivedate>
  <receiptdateformat>102</receiptdateformat>
  <receiptdate>20100629</receiptdate>
  <additionaldocument>2</additionaldocument>
  <fulfillexpeditecriteria>1</fulfillexpeditecriteria>
  <authoritynumb/>
  <companynumb>GB-122994774-2010060622</companynumb>
  <medicallyconfirm>1</medicallyconfirm>
```

ICH E2B(R3)

```
- <PORR_IN049016UV>
      <!--N.2.r.1: Message Identifier-->
    <id root="2.16.840.1.113883.3.989.2.1.3.1" extension="GB-EMA-
      1905JPN003641JAA"/>
      <!--N.2.r.4: Date of Message Creation-->
    <creationTime value="20200408093927"/>
    <interactionId root="2.16.840.1.113883.1.6" extension="PORR_IN049016UV"/>
    <processingCode code="P"/>
    <processingModeCode code="T"/>
    <acceptAckCode code="AL"/>
      <!--N.2.r.3: Message Receiver Identifier-->
  - <receiver typeCode="RCV">
    - <device determinerCode="INSTANCE" classCode="DEV">
        <id root="2.16.840.1.113883.3.989.2.1.3.12" extension="EMA"/>
      </device>
    </receiver>
      <!--N.2.r.2: Message Sender Identifier-->
  - <sender typeCode="SND">
    - <device determinerCode="INSTANCE" classCode="DEV">
        <id root="2.16.840.1.113883.3.989.2.1.3.11" extension="ABC"/>
      </device>
    </sender>
  - <controlActProcess classCode="CACT" moodCode="EVN">
      <code code="PORR_TE049016UV" codeSystem="2.16.840.1.113883.1.18"/>
        <!--C.1.2: Date of Creation-->
      <effectiveTime value="20200408093927"/>
    - <subject typeCode="SUBJ">
      - <investigationEvent classCode="INVSTG" moodCode="EVN">
          <!--C.1.1: Sender's (case) Safety Report Unique Identifier -->
        <id root="2.16.840.1.113883.3.989.2.1.3.1" extension="GB-EMA-
          1905JPN003641JAA"/>
          <!--C.1.8.1: Worldwide Unique Case Identification Number -->
        <id root="2.16.840.1.113883.3.989.2.1.3.2" extension="GB-EMA-
          M2019-14223"/>
```

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ICH E2B(R3) Documentation

- **The ICH E2B(R3) Implementation Guide and associated documents:**
  - ICH E2B(R3) Implementation Guide package.
  - Questions and Answers.
  - Information paper regarding ISO Identification of Medicinal Products (IDMP) use in ICH E2B(R3) messages.
  - Information Paper for Object Identifiers (OIDs) and Universally Unique Identifier (UUIDs).

- **In addition to ICH requirements for ICH E2B(R3) messages, there may be regional requirements in specific regulatory jurisdictions. To ensure compliance, consult the regional regulators for additional information.**

Note to implementers: The ICH E2B(R3) Implementation Guide and associated documents refer to *ISO/HL7 27953-2:2011 Health informatics -- Individual case safety reports (ICSRs) in pharmacovigilance -- Part 2: Human pharmaceutical reporting requirements for ICSR* and other ICH guidance. These documents were carefully assembled to complement each other and other versions should not be used.

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- **ICH M2 Recommendation**
  - The ICH M2 EWG has provided expert consultation and advice to the ICH E2B EWG/IWG regarding technical standards for the electronic exchange of E2B messages.
  - This E2B(R3) Implementation Guide reflects recommendations from the ICH M2 EWG that are based on various open international standards that allow for the international transmission of ICSRs.
  - The ICH M2 recommendations have been endorsed by the ICH Steering Committee/ICH Management Committee and the ICH Assembly.
  - For additional information, see https://ich.org/page/m2-recommendations-technical-references (ICH M2 Recommendations & Technical References).

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ICH E2B(R3) Documentation

- **ICH E2B(R3) Implementation Guide package**
  - Guide for implementing the standard adopted by the ICH for electronic transmission of ICSRs according to the ICH E2B(R3) message standard.
  - Focuses on medicinal products and therapeutic biologics for human use.
  - Intended to support the implementation of software and tools for creating, editing, sending and receiving electronic ICSR messages.
  - Intended audience includes system developers, IT professionals, system implementers and system users who need to understand the technical requirements for constructing and using valid electronic messages to transmit ICSRs.

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ICH E2B(R3) Documentation

- **ICH E2B(R3) Implementation Guide (IG) package**

0_Summary of document history

1_ICH_ICSR_Implementation_Guide

3_ICH_ICSR_BFC

4_ICH_ICSR_Schema_Files

5_Reference_Instances

6_Example_Instances

7_E2B Bilingual Code Lists

8_Technical_Information

9_EU BFC_conversion

10_User_Guide_Dose_Forms_and_Routes_of_Administration

11_ICH E2B(R3) Core Data Elements and Business Rules

ICH E2B(R3) Documentation

0_Summary of document history

- This table summarises which documents in this package have been updated after ICH *Step 4.*
- More detailed change histories for each document are provided as separate tables.

1_ICH_ICSR_Implementation_Guide

- This document is a guide for implementing the ICH E2B(R3) requirements for the electronic transmission of ICSRs.
- The ICH ICSR IG is intended to support the implementation of software tools for creating, editing, sending, and receiving electronic ICSR messages.
- It provides instruction on how stakeholders intend to use the ISO/HL7 ICSR standard to construct messages for exchanging pharmacovigilance information between and among themselves in ICH regions and in other countries that adopt ICH guidelines.

Source: ICH E2B(R3) Website: https://www.ich.org/page/e2br3-individual-case-safety-report-icsr-specification-and-related-files

ICH E2B(R3) Documentation

3_ICH_ICSR_BFC

- Describes the relationship between elements from ICH E2B(R2) and ICH E2B(R3) for Backwards and Forwards Compatibility (BFC).
- Intended to assist reporters and recipients in implementing systems with special focus on the rules for conversion back and forth between ICH E2B(R2) and ICH E2B(R3).
- Includes mappings of the elements against one another, with explanations of differences, and guidance on how to convert between the two message structures, including compatibility issues.

4_ICH_ICSR_Schema_Files

- Includes a full set of XML schema files that contain rules, elements, and attributes stemming from the HL7 v3 messaging standard.
- These are the technical files required by the IT tools which actually construct, export, read or validate the messages.
- Descriptions of these schemas are found in the ICH ICSR Implementation Guide Appendix I (A) and Appendix I (C).

Source: ICH E2B(R3) Website: https://www.ich.org/page/e2br3-individual-case-safety-report-icsr-specification-and-related-files

ICH E2B(R3) Documentation

5_Reference_Instances

- Includes a reference file that illustrates the coding of an ICSR according to the constraints encoded in the schema files and in compliance with the IG.
- Reference Instances use the ICH E2B(R3) data element numbers in the XML rather than real coded data.
- Allows an implementer to identify how and where the ICH E2B(R3) elements would appear in an actual transmittable ICSR.
- Example file provides a similar illustration of an ICH E2B(R3) ICSR Acknowledgement Message.

6_Example_Instances

- Includes example files that illustrate the coding of an ICSR according to the constraints defined in the schema files and in compliance with the IG.
- Example Instances use real values generated from simulated typical use cases to create an ICH E2B(R3) message.

Source: ICH E2B(R3) Website: https://www.ich.org/page/e2br3-individual-case-safety-report-icsr-specification-and-related-files

ICH E2B(R3) Documentation

7_E2B Bilingual Code Lists

- An OID is a construct used to identify an object globally.
- OID values have been assigned for each required code list or namespace.
- Many elements within the ICH E2B(R3) message have specific codes to reference defined values.
- Separating the code lists from the IG makes it easier for code lists to be adapted without altering the technical message standard itself.
- Technical systems can be more readily maintained if the code lists are provided in a clearly identified, traceable manner.

8_Technical_Information

- Describes supplemental technical information to prepare a valid ICH ICSR message or an ICSR acknowledgement message.
- Provides information on ICH/HL7 data types, XPath references for each ICH E2B(R3) element and also XML “snippets” that illustrate variation in how data elements may be described in the XML.
- Intended for technical software implementers.

Source: ICH E2B(R3) Website: https://www.ich.org/page/e2br3-individual-case-safety-report-icsr-specification-and-related-files

ICH E2B(R3) Documentation

9_EU BFC_conversion

- Includes a tool for conversion of ICH E2B(R2) messages to ICH E2B(R3) messages, and vice versa, in compliance with the conversion rules described in the BFC document (Appendix I (B)).
- Stylesheet that illustrates how an ICSR message can be converted from one version to another while preserving the data contained in the message.
- Provided to assist users and regions should this be mandated by their regional requirements.
- Implementers should refer to the ICH IG Package and Q&A to make any update(s) to the stylesheet.

10_User_Guide_Dose_Forms_and_Routes_of_Administration

- Should be used in conjunction with the ICH E2B(R3) IG and associated documents for electronic exchange of ICSRs.
- Applies only to the terms maintained by the European Directorate for the Quality of Medicines & HealthCare that relate to Pharmaceutical Dose Forms and Routes of Administration in ICH E2B(R3) format messages.

Source: ICH E2B(R3) Website: https://www.ich.org/page/e2br3-individual-case-safety-report-icsr-specification-and-related-files

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ICH E2B(R3) Documentation

11_ICH E2B(R3) Core Data Elements and Business Rules

- Provides a common template that summarises the core ICH E2B(R3) data elements, business rules and any associated questions and answers.
- Data elements are from the IG and details of the data element are documented in the IG.
- The purpose of this document is to use it as a tool to implement a common template across all regions and implementers.
- Regions can download this common template, add their regional data elements and publish them regionally.
- It is recommended that this format of the common template is maintained by regions for global consistency.

Source: ICH E2B(R3) Website: https://www.ich.org/page/e2br3-individual-case-safety-report-icsr-specification-and-related-files

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ICH E2B(R3) Documentation

- **Question and Answers (Q&A)**
  - Provides most up-to-date clarifications and interpretations of the ICH E2B(R3) IG package. It is intended to supplement the ICH ICSR Implementation Guide.
  - Facilitates the implementation of the electronic transmission of ICSRs in the ICH regions.
  - Section numbers of the Q&A document correspond to the section numbers of the ICH E2B(R3) IG.

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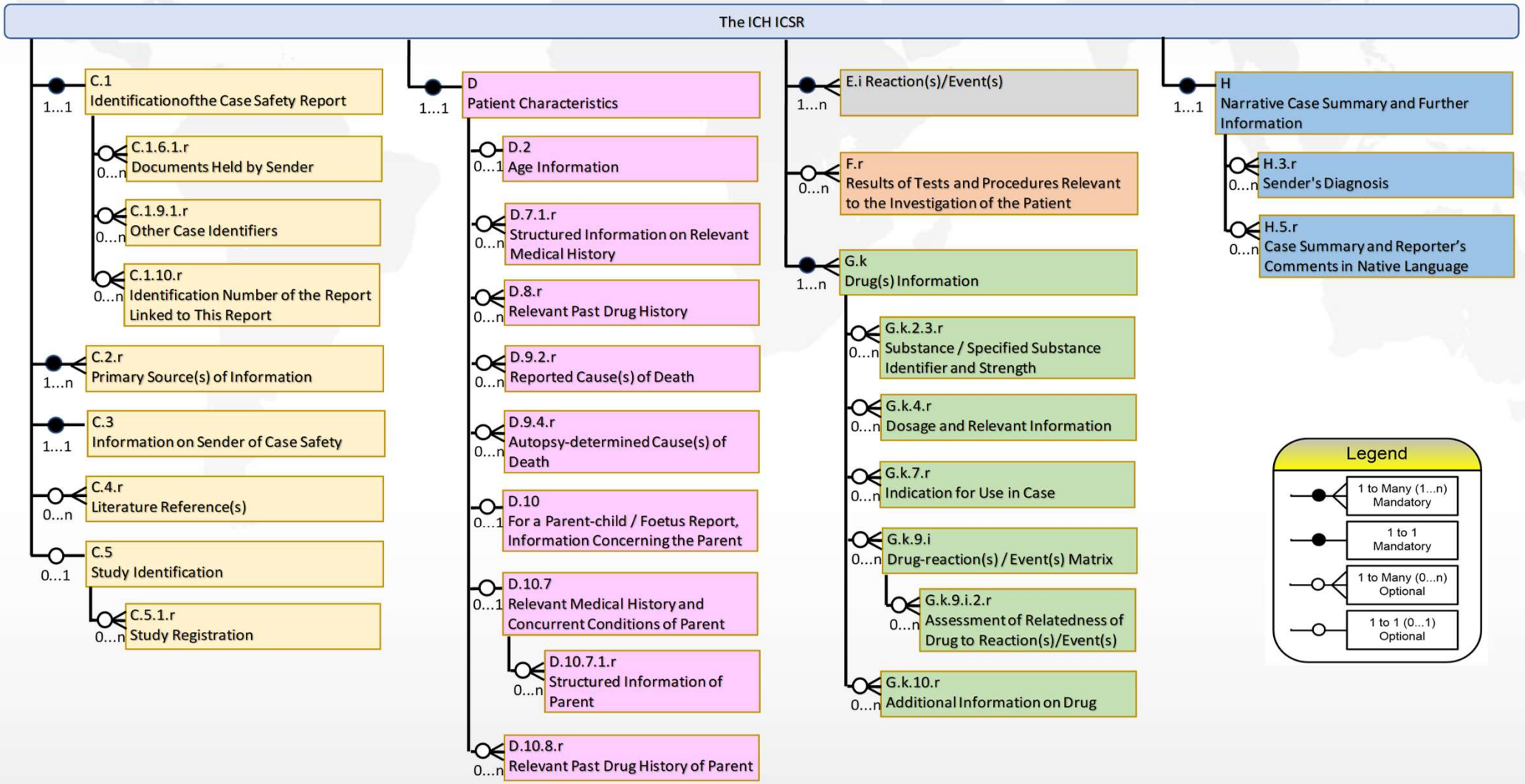
ICH E2B(R3) ICSR Structure



Reference: ICH ICSR Implementation Guide

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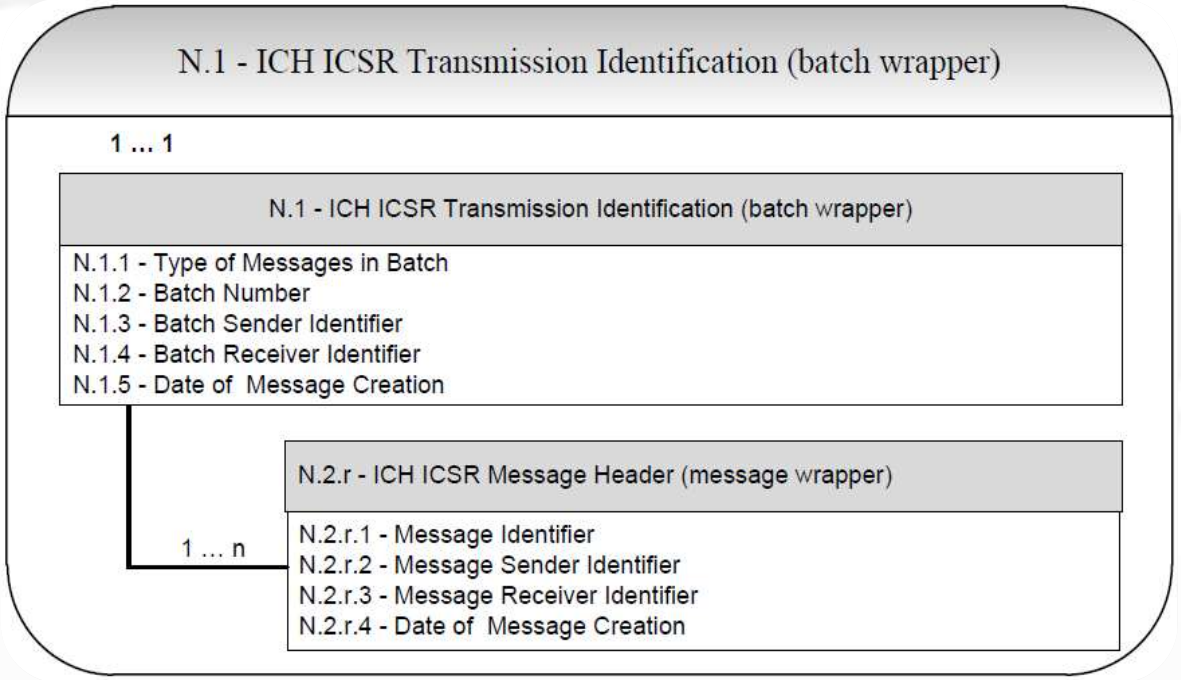
ICH ICSR Transmission Identification (Batch Wrapper)

- The 'wrapper' information is intended for routing purposes only (e.g. 'from' → 'to').
- Not usually stored or archived.
- *Electronic Data Interchange* (EDI) trading partnership agreement is established to define the Message number, Sender ID, Receiver ID, and Message date conventions.



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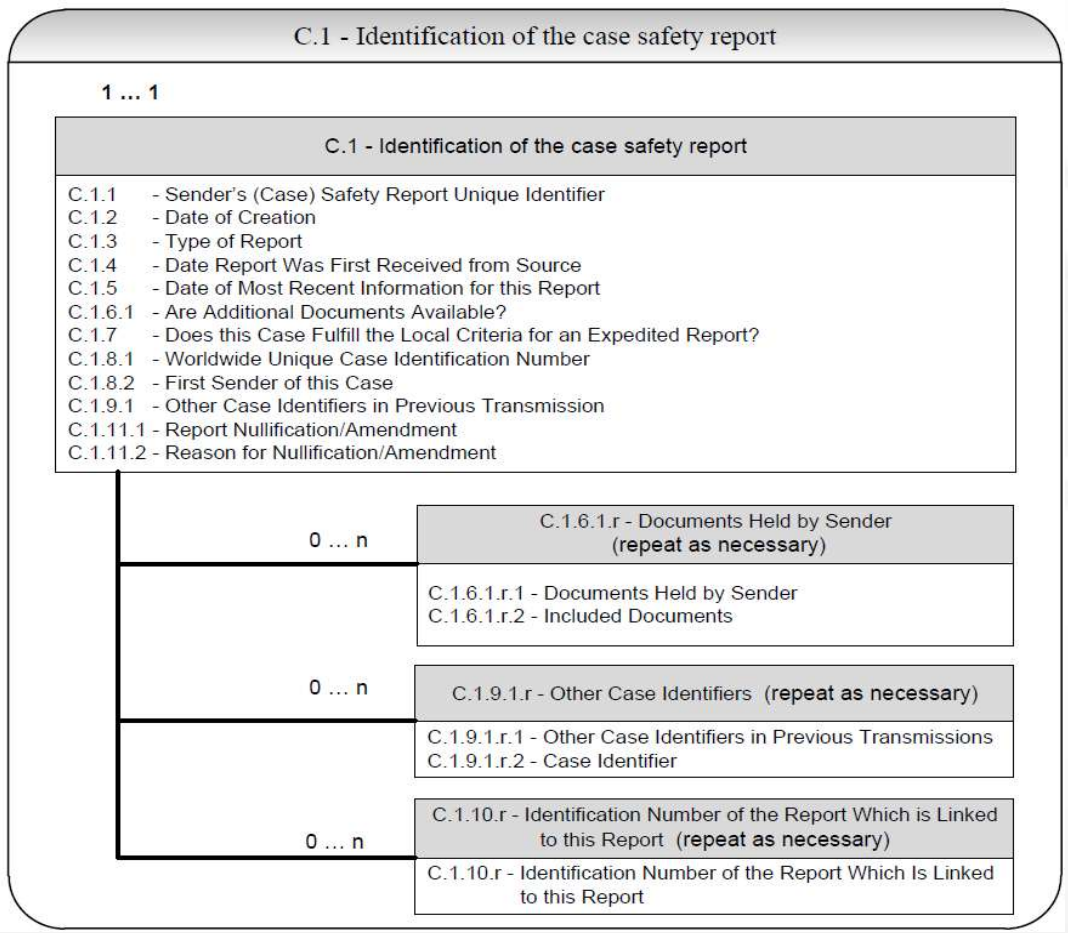
ICH E2B(R3) ICSR Structure

Identification of the Case Safety Report

- An ICH ICSR message file contains one and only one ICSR.
- ICH ICSR batch file contains one or more ICH ICSR messages.
- There must be one and only one ‘subject’ element within ‘controlActProcess’ in the ICSR message file.



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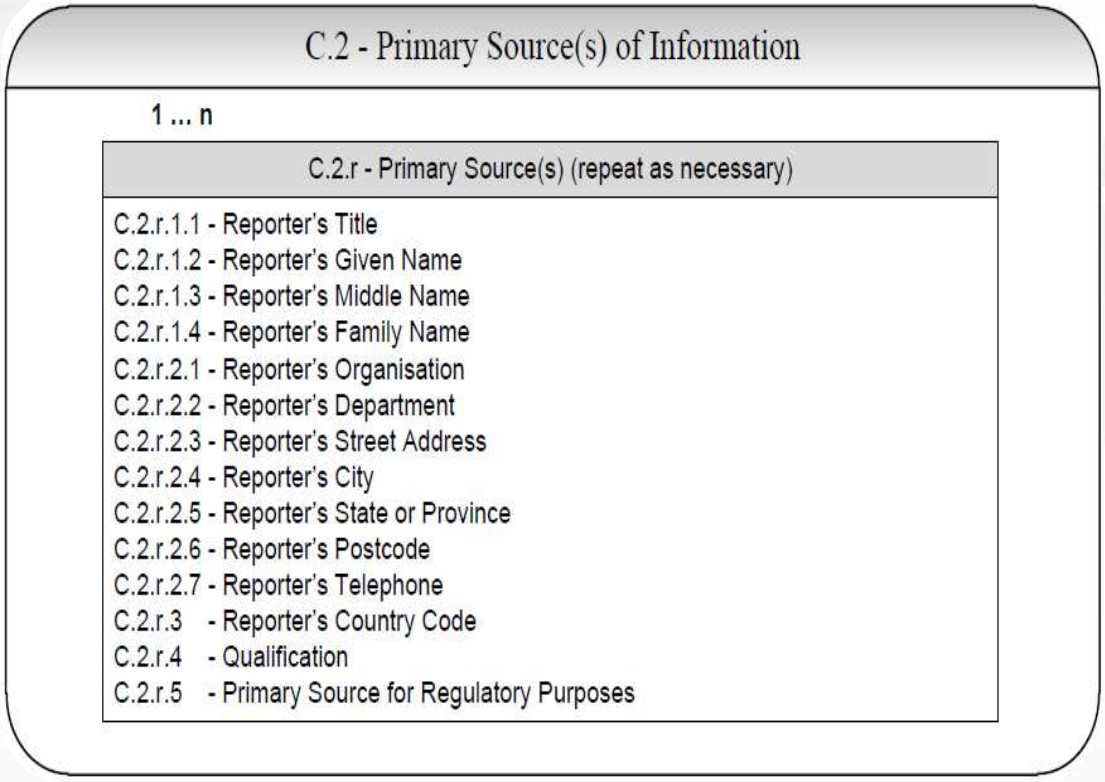
ICH E2B(R3) ICSR Structure

Primary Source(s) of Information

- A minimum of one reporter needs to be provided for each valid ICSR.
- The primary source of the information is the person who provides the facts about the ICSR.
- In case of multiple sources, the 'Primary Source for Regulatory Purposes' (C.2.r.5) is the person who first reported the facts to the sender.
- The primary source should be distinguished from senders and re-transmitters; the latter is captured in Section C.3.



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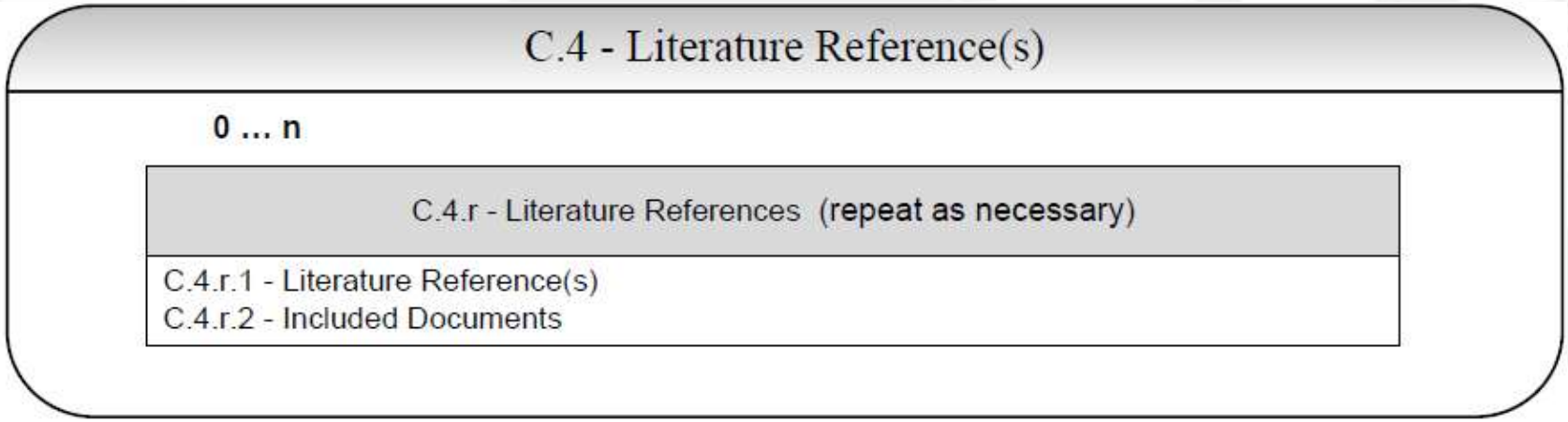
Literature Reference(s)



- The standard format for literature citations, as well as formats for special situations, should be provided in the style specified by the Vancouver Convention, known as 'Vancouver style', which has been developed by the *International Committee of Medical Journal Editors:*
  - International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med 1997; 336:309-15

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ICH E2B(R3) ICSR Structure

Information on Sender of Case Safety Report

C.3 - Information on Sender of Case Safety Report

1 ... 1

C.3 - Information on Sender of Case Safety ReportSender
C.3.1 - Sender Type
C.3.2 - Sender's Organisation
C.3.3.1 - Sender's Department
C.3.3.2 - Sender's Title
C.3.3.3 - Sender's Given Name
C.3.3.4 - Sender's Middle Name
C.3.3.5 - Sender's Family Name
C.3.4.1 - Sender's Street Address
C.3.4.2 - Sender's City
C.3.4.3 - Sender's State or Province
C.3.4.4 - Sender's Postcode
C.3.4.5 - Sender's Country Code
C.3.4.6 - Sender's Telephone
C.3.4.7 - Sender's Fax
C.3.4.8 - Sender's E-mail Address

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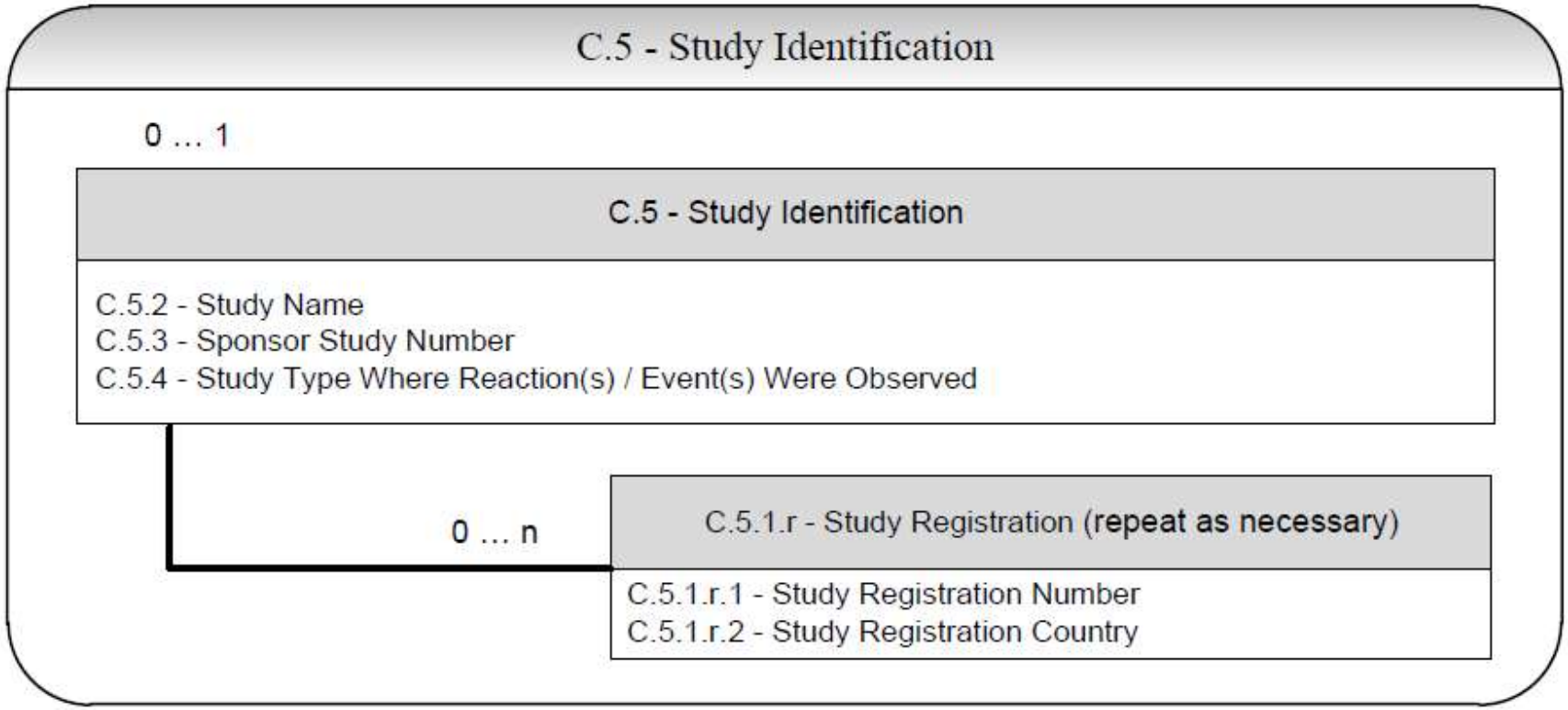
ICH E2B(R3) ICSR Structure

Study Identification



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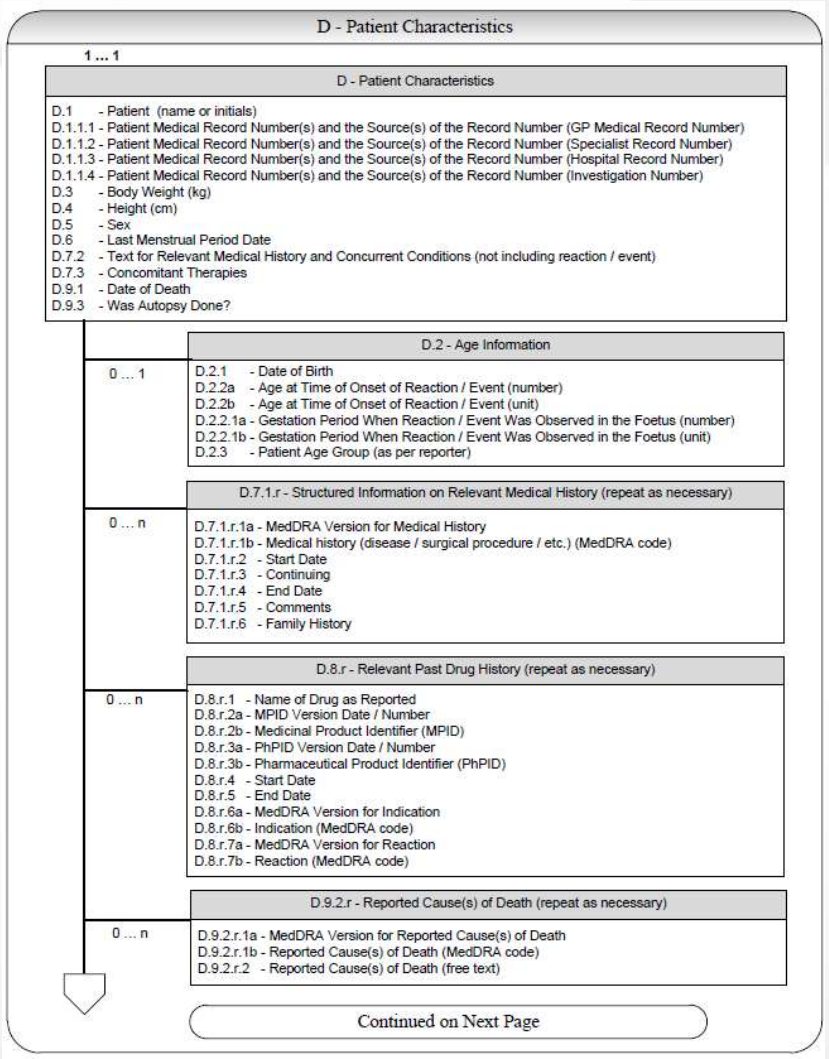
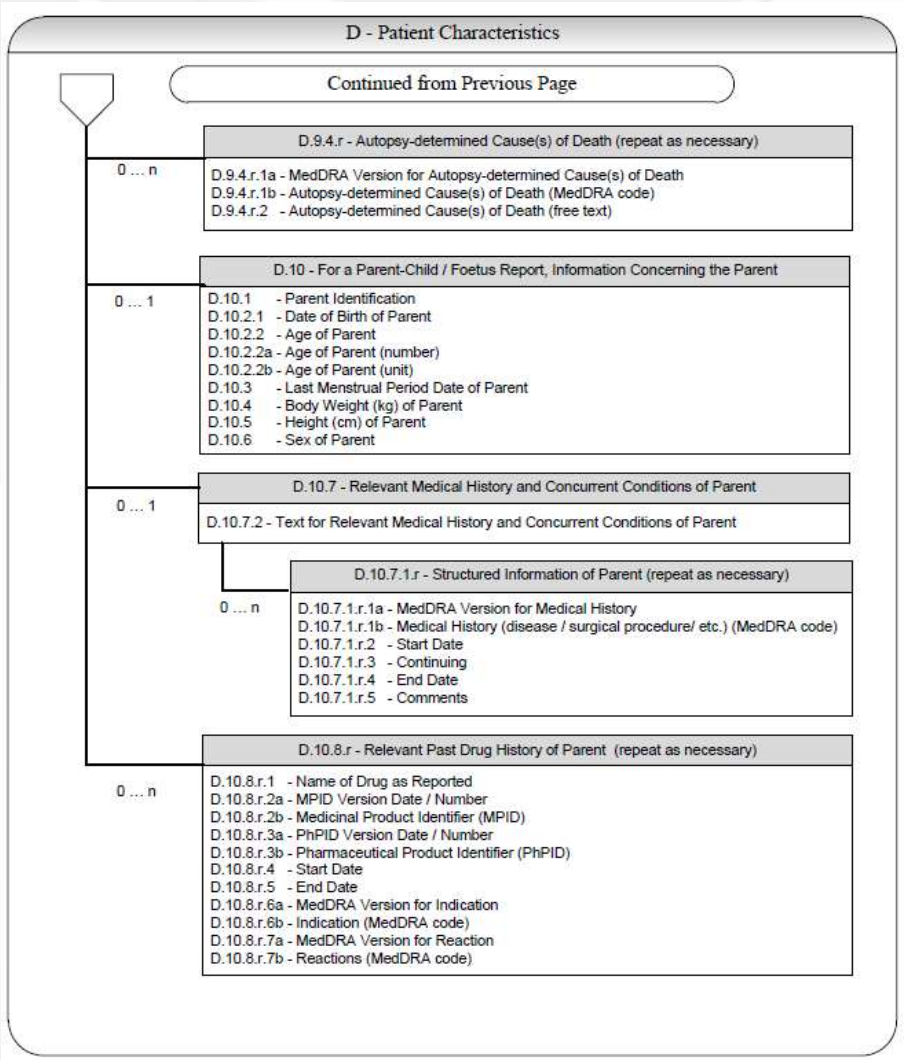
ICH E2B(R3) ICSR Structure

Patient Characteristics





- Describes the singular subject who experienced one or several adverse events/reactions.

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Reaction(s)/Event(s)

- A minimum of one reaction/event needs to be provided for each valid ICSR.
- The designation of ‘i’ in this section indicates that each item is repeatable and that it corresponds to the same ‘i’ in all subsections.

E - Reaction(s)/Event(s)
1 … n
E.i - Reaction(s)/Event(s) (repeat as necessary)
E.i.1.1a - Reaction / Event as Reported by the Primary Source in Native Language
E.i.1.1b - Reaction / Event as Reported by the Primary Source Language
E.i.1.2 - Reaction / Event as Reported by the Primary Source for Translation
E.i.2.1a - MedDRA Version for Reaction / Event
E.i.2.1b - Reaction / Event (MedDRA code)
E.i.3.1 - Term Highlighted by the Reporter
E.i.3.2 - Seriousness Criteria at Event Level
E.i.3.2a - Results in Death
E.i.3.2b - Life Threatening
E.i.3.2c - Caused / Prolonged Hospitalisation
E.i.3.2d - Disabling / Incapacitating
E.i.3.2e - Congenital Anomaly / Birth Defect
E.i.3.2f - Other Medically Important Condition
E.i.4 - Date of Start of Reaction / Event
E.i.5 - Date of End of Reaction / Event
E.i.6a - Duration of Reaction / Event
E.i.6b - Duration of Reaction / Event (duration unit)
E.i.7 - Outcome of Reaction / Event at the Time of Last Observation
E.i.8 - Medical Confirmation by Healthcare Professional
E.i.9 - Identification of the Country Where the Reaction / Event Occurred

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ICH E2B(R3) ICSR Structure

Results of Tests and Procedures Relevant to the Investigation of the Patient

F - Results of Tests and Procedures Relevant to the Investigation of the Patient	
0 ... n	
F.r - Results of Tests and Procedures Relevant to the Investigation of the Patient (repeat as necessary)	
F.r.1	- Test Date
F.r.2.1	- Test Name (free text)
F.r.2.2a	- MedDRA Version for Test Name
F.r.2.2b	- Test Name (MedDRA code)
F.r.3.1	- Test Result (code)
F.r.3.2	- Test Result (value/qualifier)
F.r.3.3	- Test Result (unit)
F.r.3.4	- Result Unstructured Data (free text)
F.r.4	- Normal Low Value
F.r.5	- Normal High Value
F.r.6	- Comments (free text)
F.r.7	- More Information Available

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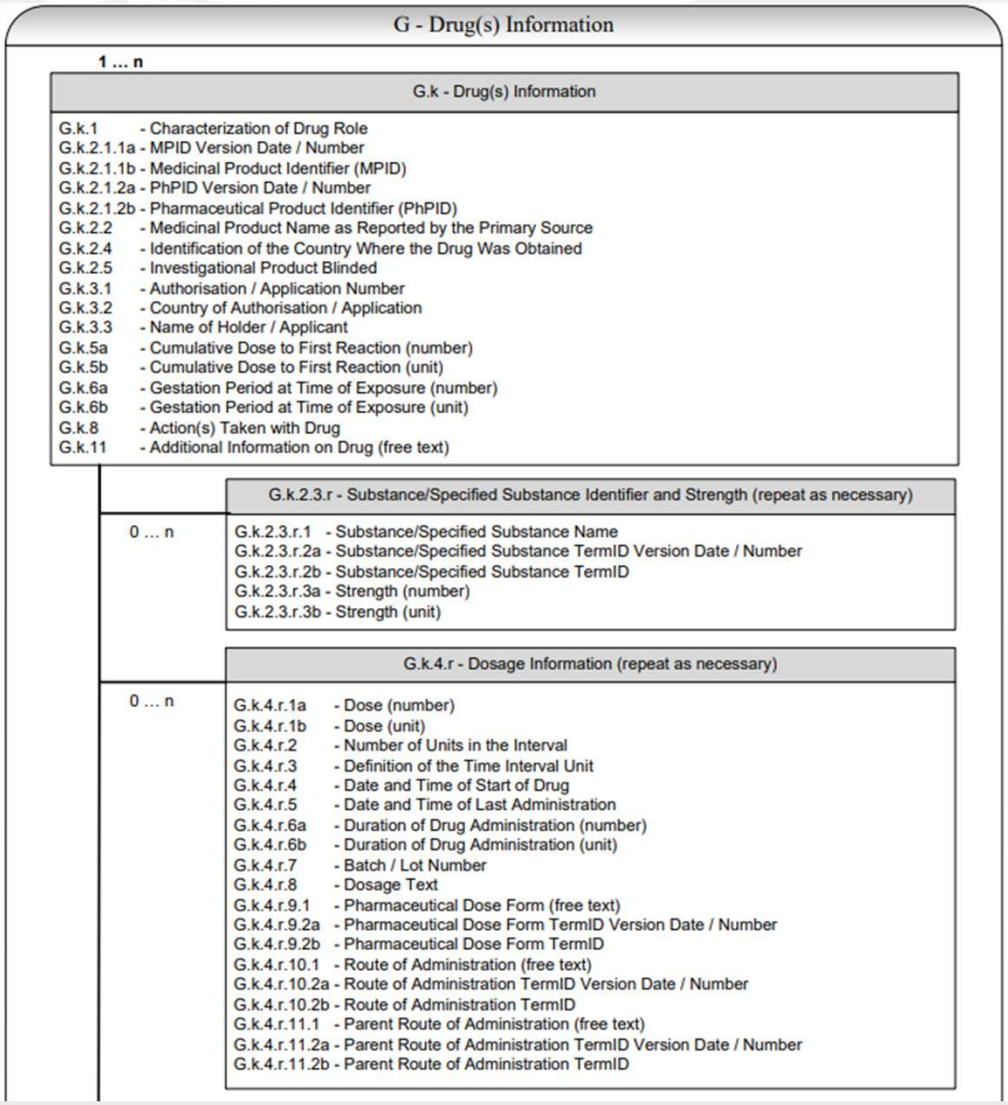
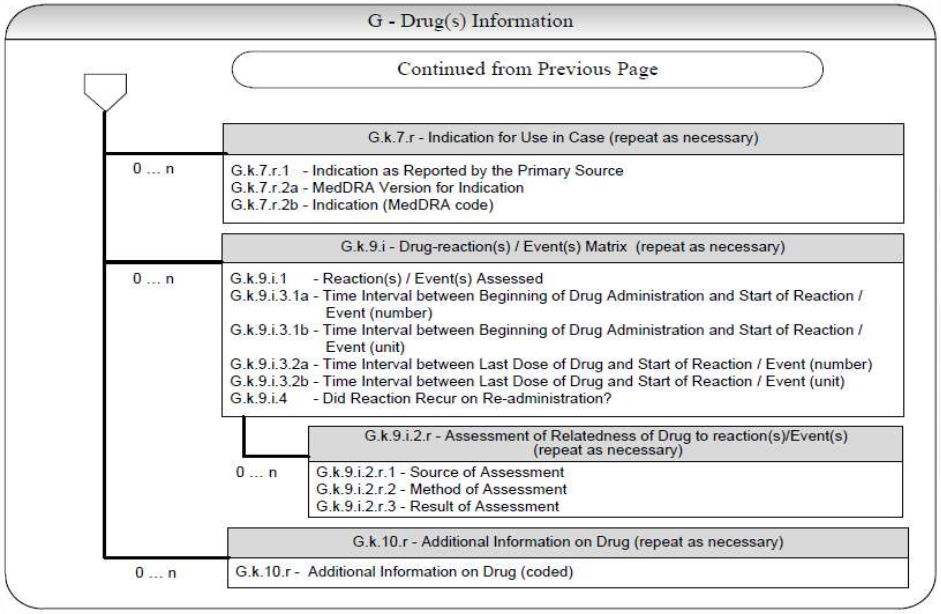
ICH E2B(R3) ICSR Structure

Drug(s) Information





- Covers both suspect and concomitant medications (including biologics) including drugs interaction.
- A minimum of one suspect medication needs to be provided for each valid ICSR.
- Medications used to treat the reaction/event should not be included here.

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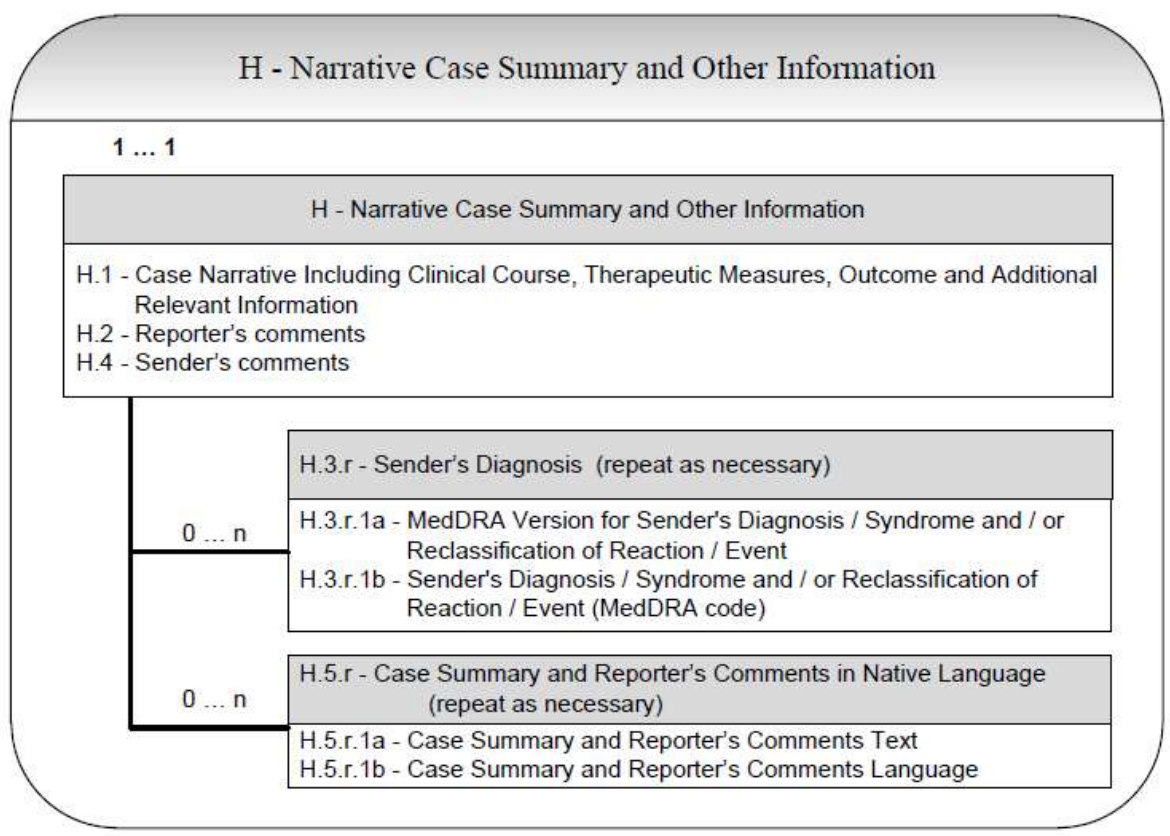
Narrative Case Summary and Further Information

- Sections H.3 and H.5 are repeatable.
- Allow for sufficient space to describe and comment on the reaction/event and to accommodate for the use of different languages.



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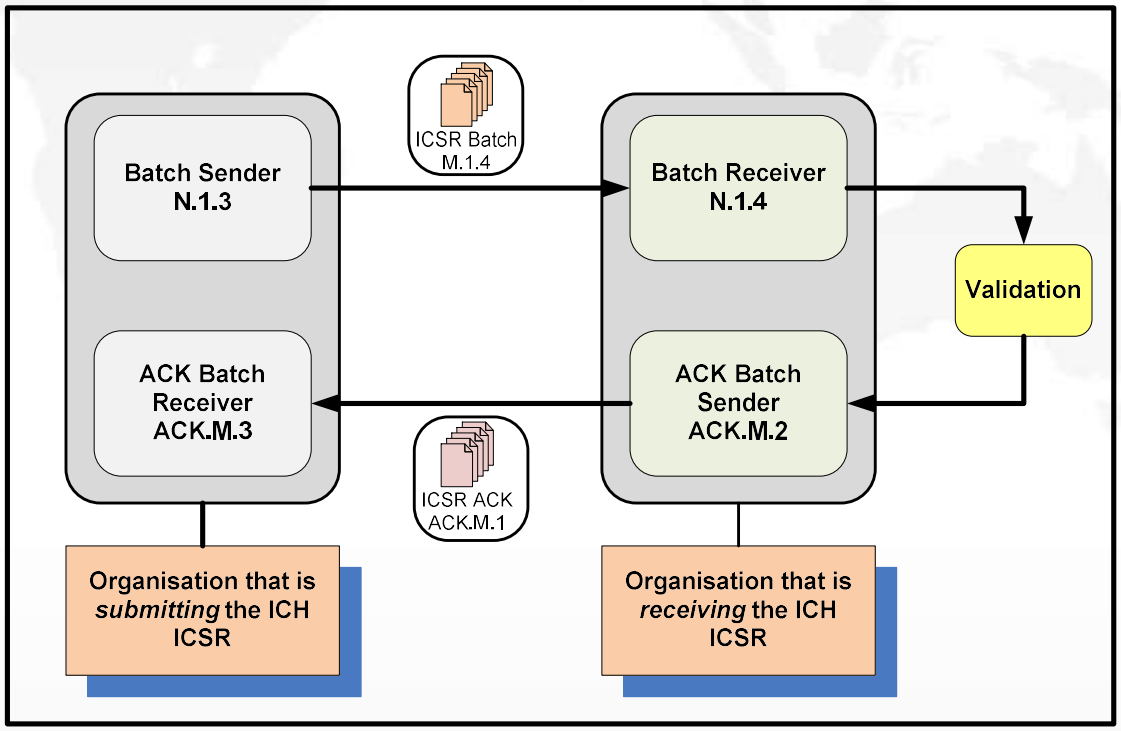
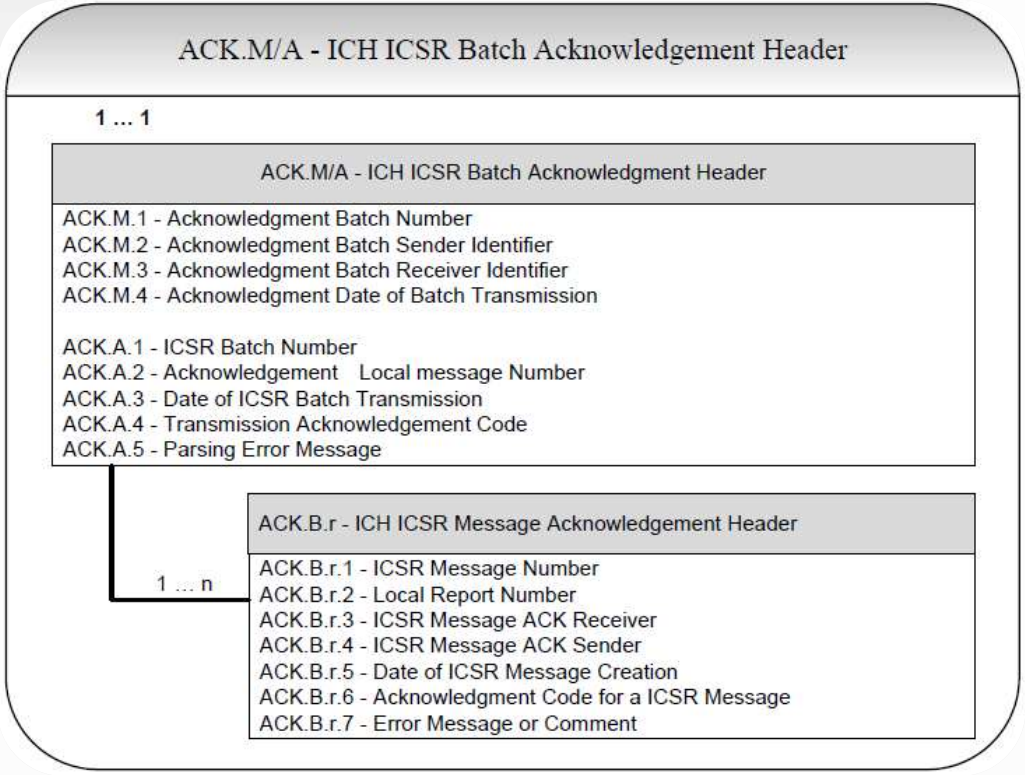
ICH ICSR Acknowledgement Message

- An acknowledgement message will be sent after receipt of every ICH ICSR.
- The acknowledgement message includes:
  - A standard header.
  - An acknowledgement for the message.
  - A repeating "details" section that provides information about the processing of the original ICSR message(s), e.g., successful parsing or problems that prevented parsing/accepting the message.



ICH ICSR Acknowledgement Message

- Acknowledgement header contains core transactional information related to the receipt of the batch transmission.
- Data elements beginning with ACK.M contain technical information required for acknowledgement message.
- Data elements beginning with ACK.A contain technical information relating to batch received.
- Data elements beginning with ACK.B contain information relating to each ICSR message within the received batch.



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Outline

1. Introduction to ICH E2B(R3)
2. ICH E2B(R3) Documentation
3. Summary of ICH E2B(R3) Guideline
4. ICH ICSR Acknowledgement Message
5. Summary

ICH harmonisation for better health

Summary

In this training module the following topics have been covered:

- Main principles and concepts in ICH E2B reporting.
- High-level differences between ICH E2B(R2) and ICH E2B(R3).
- Background ICH E2B(R3) documentation.

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Contact

- **For any questions please contact the ICH Secretariat:**

admin@ich.org