EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Implementing ISO ICSR/ICH E2B(R3): Key changes for pharmacovigilance

Training Module PhV-M2a

The impact of the new ISO/ICH E2B(R3) ICSR standard on adverse reaction reporting and the new business rules in EudraVigilance

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An agency of the European Union

Version 1.0

Overview Module PhV-M2a

- Introduction to this training module
- What is the origin of the ISO ICSR and ICH E2B(R3) standard?
- What are the legal basis and benefits for the use of the new ICSR standard?
- What are the key changes for the operation of pharmacovigilance?
- How can I get supporting information?

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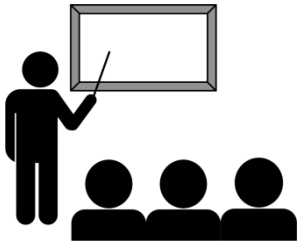
Introduction: Context PhV-M2a

- Target audience for this training module:
  - National Competent Authorities (NCAs) in the European Economic Area (EEA)
  - Marketing authorisation holders (MAHs)
  - Sponsors of clinical trials (Sponsors)
  - Research institutions/Academia
  - Other interested parties



Introduction: Learning Objectives

- At the end of module PhV-M2a you should be able to:
  - Refer to the origin of the development of the ISO ICSR standard and the ICH E2B(R3) Implementation Guide (IG)
  - Describe the legal basis and the benefits for the use of the ISO ICSR/ICH E2B(R3) guideline
  - Recognise the impact on pharmacovigilance with the move from the ICH E2B(R2)guideline /M2 format to the E2B(R3) guideline/ISO ICSR standard
  - Describe changes to the business rules as outlined in the EU ICSR IG
  - Understand where to obtain supporting information

Overview Module PhV-M2a

- Introduction to this training module
- **What is the origin of the ISO ICSR and ICH E2B(R3) standard?**
- What are the legal basis and benefits for the use of the new ICSR standard?
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- How I can I get supporting information?

Session overview: What is the origin of the ISO ICSR and ICH E2B(R3) IG?

In this session you will obtain an understanding of:

- The origin of the development of the ISO ICSR standard and the ICH E2B(R3) Implementation Guide (IG) that form the basis for the electronic exchange of Individual Case Safety Reports (ICSRs) as part of the enhanced functionalities of EudraVigilance

Development of new ISO ICSR/ICH E2B(R3) standard (1)

2001
E2B(R2)
editorial changes

Nov 2005
E2B(R2)
mandatory in EU

2006
ICH Steering Committee decision to work with SDOs

Dec 2011
Final ISO/HL7 standard published

ICH Step 4
Nov 2012
E2B(R3)

Last Release
July 2013

2004
ICH initiates work on E2B(R3)

2005
E2B(R3)
V3.96 Guideline
ICH Step 3 public consultation

June 2009
ICH Awareness publication

Sept 2011 – March 2012
ICH Step 3 public consultation

EU ICSR Implementation Guide
4 Dec 2014

Development of new ISO ICSR/ICH E2B(R3) standard (2)

- International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) adopted and published the guideline "Data Elements For Transmission Of Individual Case Safety Reports" in 1997 followed by minor revisions in 2000 (E2B(R1)) and February 2001 (E2B(R2))
- The electronic message for the ICH E2B(R2) ICSR is defined in the ICH ICSR M2 Version 2.3 Specification Document of February 2001
- Since then, the implementation of the electronic submission of ICSRs based on these guidelines has become widespread in the ICH regions – electronic reporting of ICSRs became mandatory in the EEA in November 2005

Development of new ISO ICSR/ICH E2B(R3) standard (3)

- A revision of the E2B(R2) guideline was initiated by ICH in 2004
- A revised guideline, E2B(R3), was released for public consultation in May 2005
- A key decision was taken by the ICH Steering Committee in 2006:
  - Technical specifications should be created in collaboration with Standards Development Organisations (SDOs) to enable wider inter-operability across the regulatory and healthcare communities
  - To work with the Joint Initiative on SDO Global Health Informatics Standardization:
    - International Organisation for Standards (ISO)
    - Health Level 7 (HL7)
    - European Committee for Standardization (CEN)
    - Clinical Data Interchange Consortium(CDISC)
    - International Health Terminology Standards Development Organisation (IHTSDO)
    - GS1

New ISO ICSR standard and the ICH E2B(R3) guideline (4)

- The draft ICH E2B(R3) guideline including the comments received during the May 2005 consultation, was provided to the SDOs to form the **ICH business requirements** for the development of the ISO ICSR standard
- The **created standard** is based upon an HL7 ICSR model that is capable of supporting message exchange for a wide range of product types (e.g. human medicinal products, veterinary products, medical devices etc.):
  - ISO/HL7 27953-1: 2011 Health informatics -- Individual case safety reports (ICSRs) in pharmacovigilance -- Part 1: The framework for adverse event reporting
  - *ISO/HL7 27953-2: 2011 Health informatics -- Individual case safety reports (ICSRs) in pharmacovigilance -- Part 2:* ***Human pharmaceutical*** *reporting requirements for ICSR*

Development of new ISO ICSR/ICH E2B(R3) standard (5)

- The **ISO ISCR standard** is complemented by guidance on how to apply the standard for the purpose of pharmacovigilance for human medicines:
  - The "**ICH E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports"** *(referred to as ICH E2B(R3) Implementation Guide (IG))*
    - Adopted in November 2012 with a minor revision published in July 2013
    - Provides the core set of requirements for the ICH content (data elements) of safety and acknowledgement (ACK) messages
  - The "**EU Individual Case Safety Report (ICSR) Implementation Guide"** *(referred to as EU ICSR IG)*
    - Adopted in December 2014
    - Complements the ICH E2B(R3) IG and defines EU specific requirements e.g. additional data elements, EU specific CVs, business rules

Session summary: What is the origin of the ISO ICSR and ICH E2B(R3) IG?

In this session you learned:

- About the ICH decision to work with SDOs on the development of technical specifications for the electronic transmission of ICSRs
- How the ISO ICSR standard is complemented by the ICH E2B(R3) Implementation Guide and the EU ICSR Implementation Guide for the use in the EEA

Overview Module PhV-M2a

- Introduction to this training module
- What is the origin of the ISO ICSR and ICH E2B(R3) standard?
- **What are the legal basis and benefits for the use of the new ICSR standard?**
- What are the key changes for the operation of pharmacovigilance?
- How I can I get supporting information?

Session overview: What are the legal basis and benefits for the use of the ICSR standard?

In this session you will learn to describe:

- The legal basis for the use of the ISO ICSR standard in the EEA
- The expected benefits of the use of the ISO ICSR standard

Legal basis for the use of the ICSR standard (1)

- Commission Implementing Regulation (EU) 520/2012, chapter IV, defines the use of terminology, formats and standards for the purpose of pharmacovigilance
  - Medical Dictionary for Regulatory Activities (MedDRA) (ICH M1)
  - Lists of Standard Terms published by the European Pharmacopoeia Commission
  - ICH E2B(R2) 'Maintenance of the ICH guideline on clinical safety data management: data elements for transmission of Individual Case Safety Reports'
  - ICH M2 standard 'Electronic Transmission of Individual Case Safety Reports Message Specification'
  - EN ISO 27953-2:2011 Health Informatics, Individual case safety reports (ICSRs) in pharmacovigilance — Part 2: Human pharmaceutical reporting requirements for ICSR (ISO 27953-2:2011)

Legal basis for the use of the ICSR standard (2)

- Use of terminology, formats and standards (continued) – *these standards will be implemented once the associated terminologies are available*
  - ISO 11615:2012, Health Informatics, Identification of Medicinal Products (IDMP) standard, 'Data elements and structures for unique identification and exchange of regulated medicinal product information'
  - ISO 11616:2012, Health Informatics, Identification of Medicinal Products (IDMP) standard 'Data elements and structures for unique identification and exchange of regulated pharmaceutical product information'
  - ISO 11238:2012, Health Informatics, Identification of Medicinal Products (IDMP) standard, 'Data elements and structures for unique identification and exchange of regulated information on substances'

Legal basis for the use of the ICSR standard (3)

- Use of terminology, formats and standards (continued) – *these standards will be implemented once the associated terminologies are available*
  - ISO 11239:2012, Health Informatics, Identification of Medicinal Products (IDMP) standard, 'Data elements and structures for unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation and routes of administration'
  - ISO 11240:2012, Health Informatics, Identification of Medicinal Products (IDMP) standard, 'Data elements and structures for unique identification and exchange of units of measurement'

Expected benefits for the use of the ICSR standard (4)

- Improved ICSR format (~ 10 years of operational experience)
- Better granularity based on additional data elements
- Alignment with new ISO Identification of Medicinal Products (IDMP) standards
- Improved quality of reports
- Interoperability with healthcare systems e.g. electronic health records
- Acceptance beyond ICH regions improving harmonisation of data formats

Session summary: What are the legal basis and benefits for the use of the ICSR standard?

In this session you learned to describe:

- What forms the legal basis for the use of the ISO ICSR standard in the EEA
- The expected benefits of the use of the ISO ICSR standard

Overview Module PhV-M2a

- Introduction to this training module
- What is the origin of the ISO ICSR and ICH E2B(R3) standard?
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- **What are the key changes for the operation of pharmacovigilance?**
- How I can I get supporting information?

Session overview: What are the key changes for the operation of pharmacovigilance?

In this session you will learn:

- To recognise the key changes that will occur with the use of the ICH E2B(R3)/ISO ICSR standard in comparison with the ICH E2B(R2)guideline /M2 format
- To define the areas where adaptation to your pharmacovigilance system and business processes will be required
- To discuss each ICSR section and modifications that have been introduced as part of the ICH ICSR IG
- To describe the main changes as regards the business rules to be applied for the electronic transmission of ICSRs as set out in the EU ICSR IG

Session overview: What are the key changes for the operation of pharmacovigilance?

NOTE 1: training module PhV-G2 will describe the main changes that will be introduced as part of revision 2 of the guideline on Good Pharmacovigilance Practices, Module VI, which will provide guidance on how to use the ICH E2B(R3) format for adverse reaction reporting in the EU

NOTE 2: training module IT-M1 will describe the aspects to be taken into account by IT developers for the ISO ICSR standards implementation

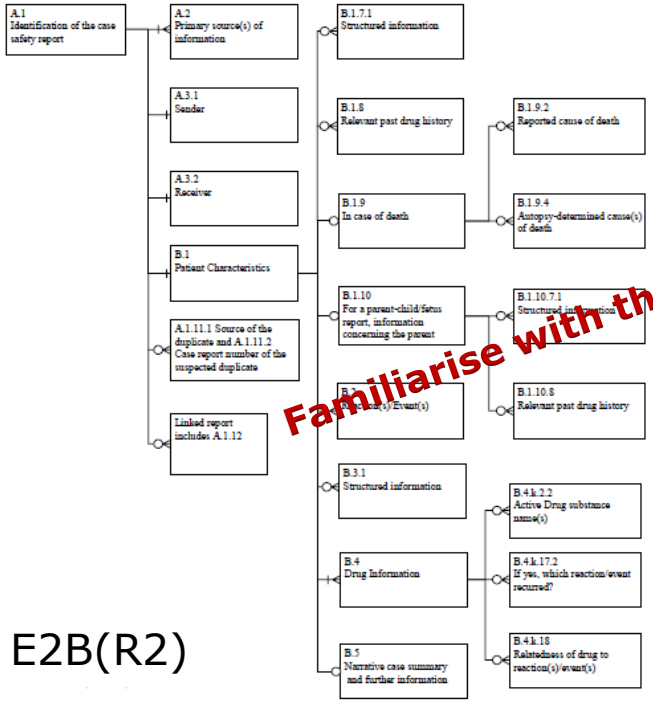
Changes that come with the E2B(R3) ICSR

In ICH E2B(R3) the following is changing compared to E2B(R2):

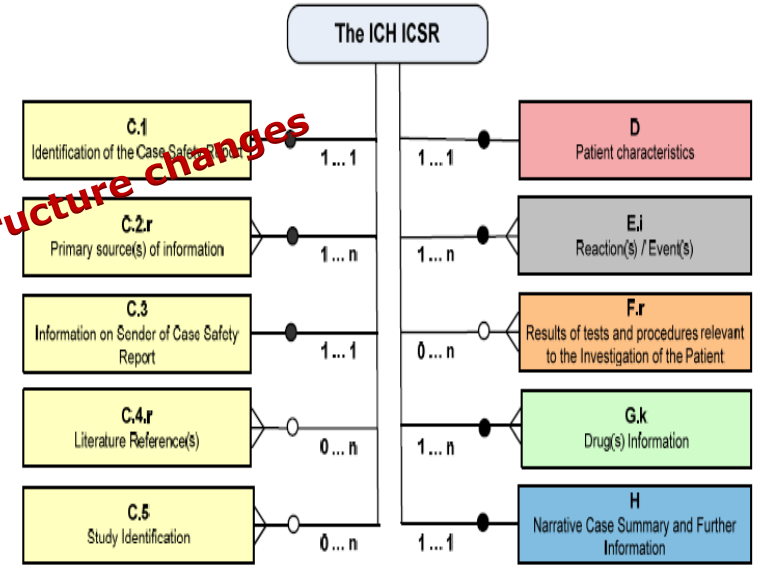
- Data structure
- Numbering of data elements
- New data elements have been added
- Data elements have been removed
- Sections have become repeatable
- Field length amendments
- Improved user guidance
- Use of Object Identifiers and NullFlavors
- Code lists

NOTE: Carefully review the ICH and EU ICSR IGs to familiarise yourself in detail with these changes

Changes to the ICSR data structure



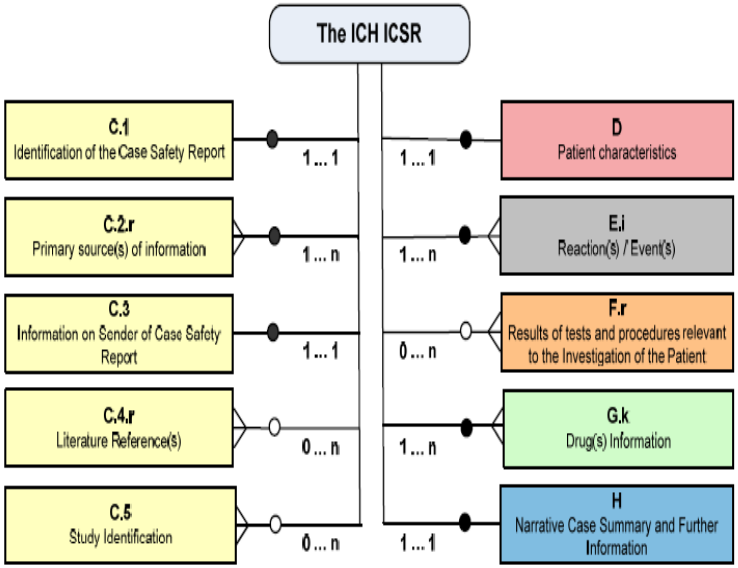
Familiarise with the data structure changes



ICH E2B(R2)

ICH E2B(R3)

The ICH E2B(R3) ICSR IG

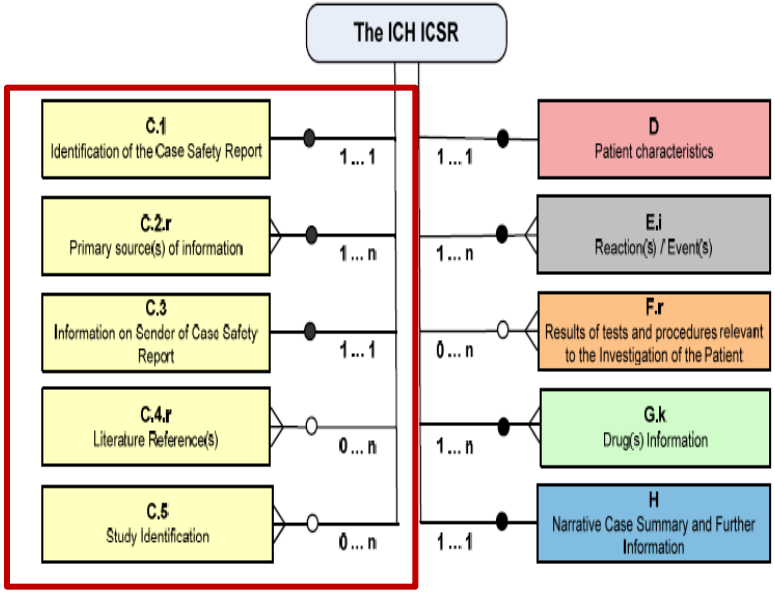


ICH E2B(R3)

- We are now going to discuss each of the 10 ICH E2B(R3) ICSR Sections
- We will focus on the main changes that will impact on the way how we collect, report and analyse information on suspected adverse reactions related to medicines

For details always refer to the ICH ICSR IG

The ICH E2B(R3) ICSR – Sections C1-C.5

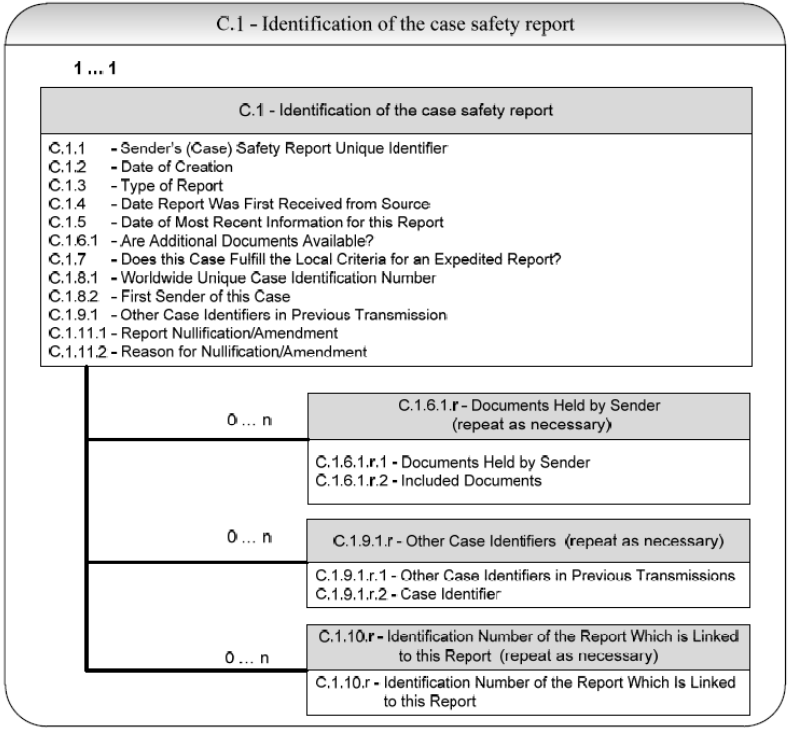


ICH E2B(R3)

C.1 Identification of Case Safety Report

ICH E2B(**R3**)
C.1. Identification of the case safety report

ICH E2B(**R2**)
A.1. Identification of the case safety report



C.1 Identification of Case Safety Report

E2B(R3)	Summary
C.1.2	"Date of Creation" is replacing the safety report version number and provides a timestamp with date and time to the second 'CCYYMMDDhhmmss[+/-ZZzz]'
C1.10.r 	"Identification Number of the Report Which is Linked to this Report" The reason for the linkage between ICSRs should be provided in H.4 "Senders Comments"

C.1 Identification of Case Safety Report

E2B(R3)	Summary
C.1.8.1	"Worldwide Unique Case Identification Number" C.1.8.1 should always be populated and should never change
C.1.8.2  	"First Sender of this Case" This data element is used to identify the type of sender that created and transmitted the original electronic ICSR There are two values permitted: "Regulator" or "Other" *This is replacing A.1.10.1 and A.1.10.2 in E2B(R2)* C.1.8.2 should always be populated and should never change

C.1 Identification of Case Safety Report

E2B(R3)	Summary
C.1.6.1.r.	"Documents held by the Sender" (repeatable)
C.1.6.1.r.1	Description of the documents held by the sender relevant to this ICSR (clinical record, hospital record, autopsy report, ECG strips, chest X-ray, photographs)
C.1.6.1.r.2 	"Included Documents" (attachments) allows to include the actual content if the sender chooses to send the document Media Type: Application/PDF, image/jpeg, application DICOM, text/plain

C.1 Identification of Case Safety Report

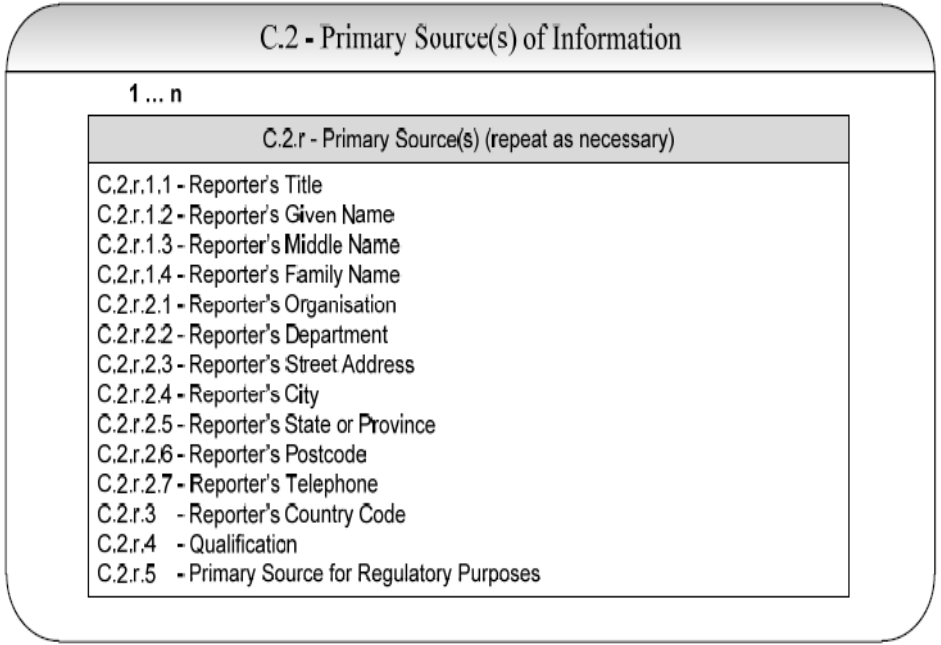
E2B(R3)	Summary
C.1.11	Report Nullification/Amendment
C1.11.1 	"Report Nullification/Amendment" Used to indicate that a previously transmitted ICSR needs to be amended without the receipt of new significant information (e.g. some items have been corrected) Value = "Amendment"
C1.11.2 	"Reason for Nullification/Amendment" Used to specify the reason for the amendment C.1.5 "Date of most recent information for this report" must remain unchanged for a nullification or amendment report if no new information on the case has been received from a primary source

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

(repeat as necessary)

ICH E2B(**R3**)
C.2.r Primary Source(s) of information

ICH E2B(**R2**)
A.2. Primary Source(s) of information



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

E2B(R3)	Summary
C.2.r 	"Primary Source(s) of Information" Depending on local legal data privacy requirements, it is possible to *mask* some of the elements to identify the reporter (see also slide 89)
C.2.r.2.7	"Reporter's Telephone" Captures the reporter's phone number

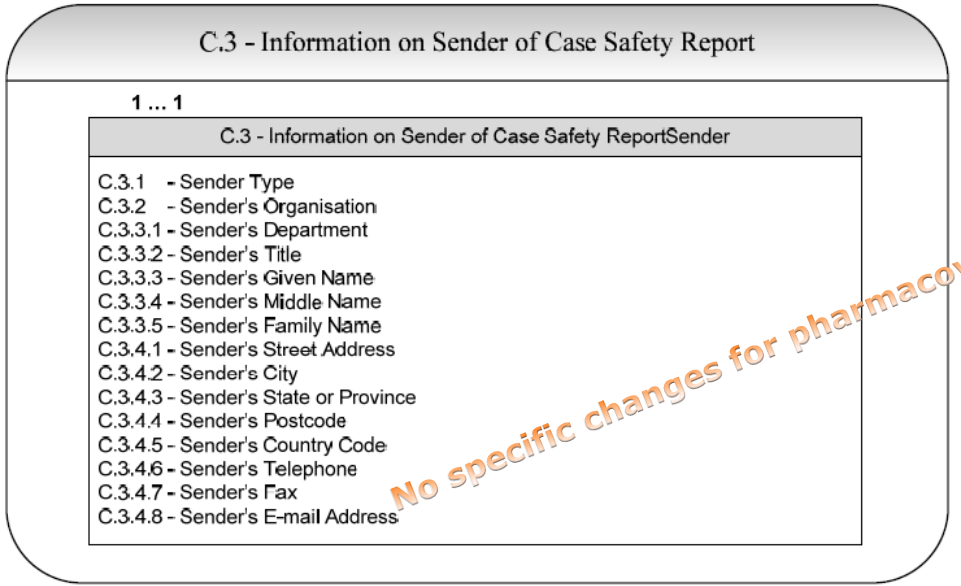
C.2.r Primary Source(s) of Information

E2B(R3)	Summary
C.2.r.5 	"Primary Source(s) for Regulatory Purposes" •This data element identifies, which primary source to use for regulatory purposes and in case of multiple resources, it identifies the source of the World Wide Case Unique Identification number •This source should identify where the case occurred •It is required that one C.2 "Primary Source of Information" is flagged for regulatory purposes •Value = Primary (can only be used once for one C.2 block)

C.3 Information on Sender of Case Safety Report

ICH E2B(**R3**)
C.3 Information on Sender

ICH E2B(**R2**)
A.3. Information on Sender

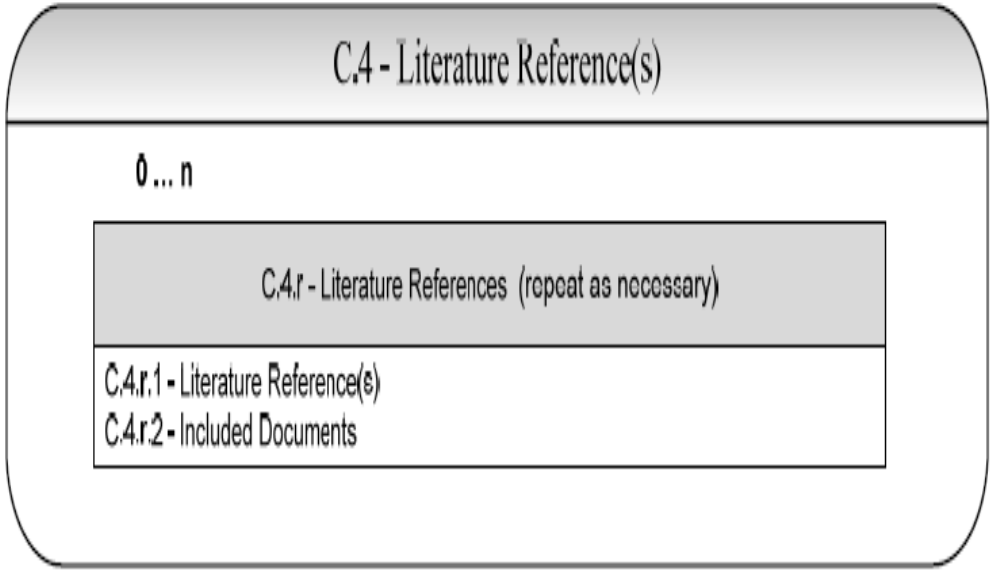


C.4.r Literature Reference(s)

(repeat as necessary)

ICH E2B(**R3**)
C.4 Literature Reference(s)

ICH E2B(**R2**)
A.2.2. Literature reference



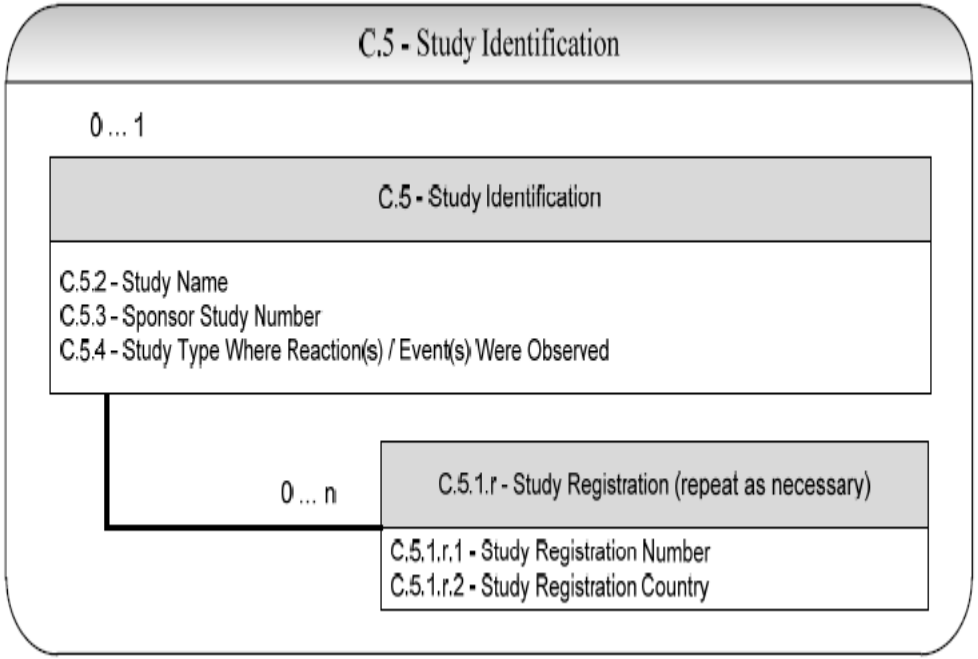
C.4.r Literature Reference(s)

E2B(R3)	Summary
C.4.r.1	"Literature References" •Used for literature articles that describe individual cases with literature references to be provided in Vancouver Style
C.4.r.2 	"Included Documents" (attachments) •This data element contains the actual content referenced in C.4.r.1, when the sender chooses to send a copy of the literature article Media Type: Application/PDF, image/jpeg, application DICOM, text/plain

C.5 Study Identification

ICH E2B(**R3**)
C.5 Study Identification

ICH E2B(**R2**)
A.2.3. Study Identification



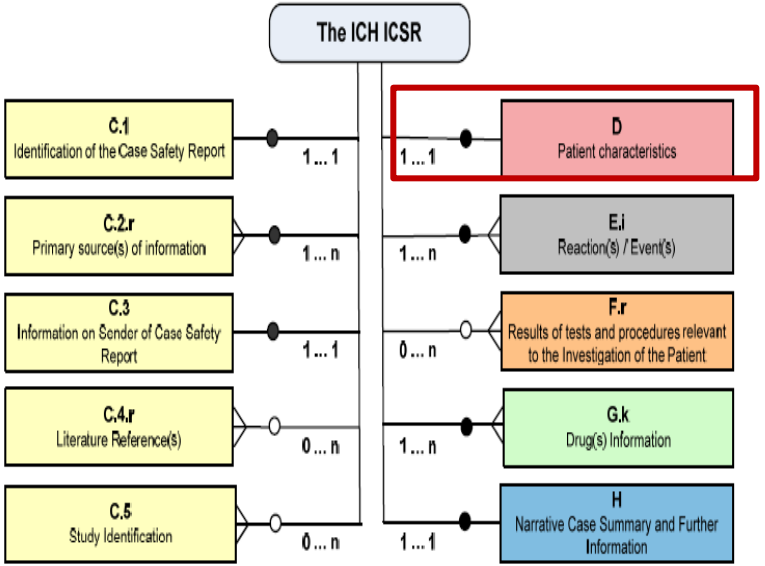
C.5 Study Identification (1)

E2B(R3)	Summary
C.5.2	"Study Name" As registered in jurisdiction where the ICSR is reported
C.5.3	"Sponsor Study Number" To be completed only if the sender is the study sponsor or has been informed of the study number by the sponsor
C.5.4	"Study Type Where Reaction(s)/Event(s) Were Observed" To be provided if C.1.3 is "Report from study" Value allowed: "Clinical trials", "Individual patient use" (e.g. 'compassionate use' or 'named patient basis'), "Other studies" (e.g. pharmacoepidemiology, pharmacoeconomics, intensive monitoring)

C.5 Study Identification (2)

E2B(R3)	Summary
C.5.1.	 "Study Registration" (repeat as necessary)
C.5.1.r.1	"Study Registration Number" - to be populated with the study registration number as assigned in the reporting region e.g. EudraCT number
C.5.1.r.2	"Study Registration Country" •Country code for the country that assigned the Study Registration Number presented in C.5.r.1 •Value = ISO Country Code and EU

The ICH E2B(R3) ICSR – Section D

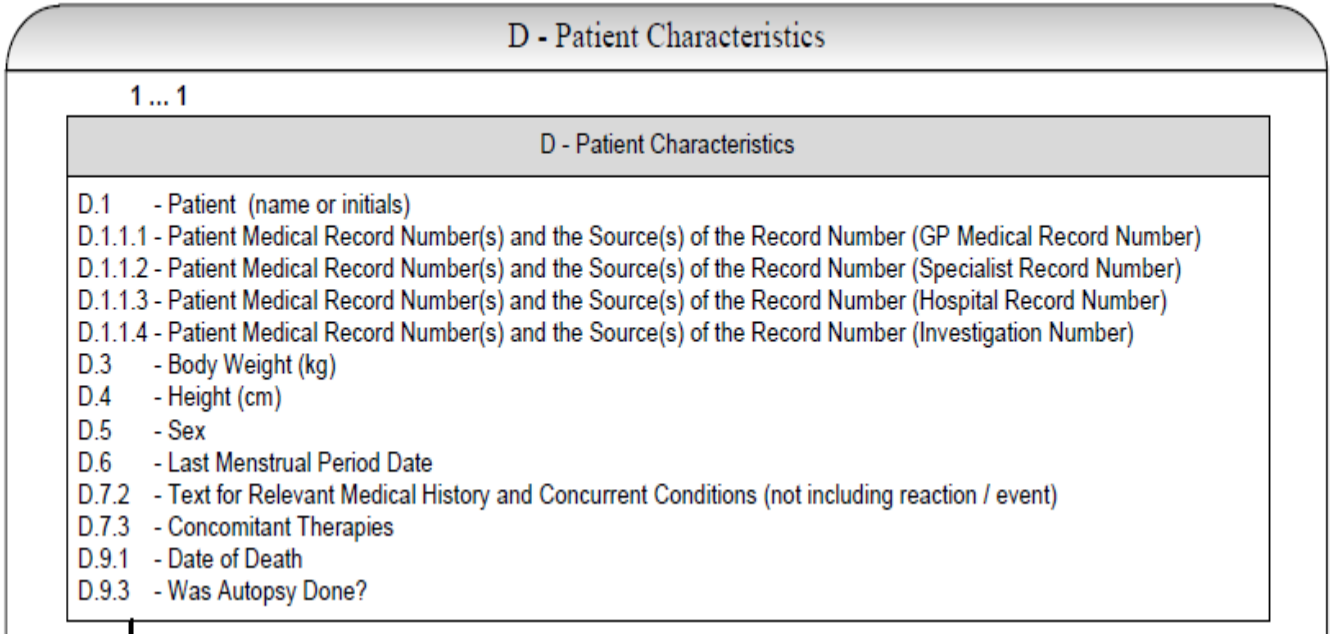


ICH E2B(R3)

D Patient Characteristics

ICH E2B(**R3**)
D Patient Characteristics

ICH E2B(**R2**)
B.1 Patient Characteristics



D - Patient Characteristics

1 ... 1

D - Patient Characteristics
D.1 - Patient (name or initials)
D.1.1.1 - Patient Medical Record Number(s) and the Source(s) of the Record Number (GP Medical Record Number)
D.1.1.2 - Patient Medical Record Number(s) and the Source(s) of the Record Number (Specialist Record Number)
D.1.1.3 - Patient Medical Record Number(s) and the Source(s) of the Record Number (Hospital Record Number)
D.1.1.4 - Patient Medical Record Number(s) and the Source(s) of the Record Number (Investigation Number)
D.3 - Body Weight (kg)
D.4 - Height (cm)
D.5 - Sex
D.6 - Last Menstrual Period Date
D.7.2 - Text for Relevant Medical History and Concurrent Conditions (not including reaction / event)
D.7.3 - Concomitant Therapies
D.9.1 - Date of Death
D.9.3 - Was Autopsy Done?

D Patient Characteristics

E2B(R3)	Summary
D.1.1.1	"Patient Medical Record Number and Source(s) of the Record Number" (GP) •New way to represent medical record number together with the source (E2B(R2) B.1.1.1a)
D.1.1.2	"Patient Medical Record Number and Source(s) of the Record Number" (Specialist) •New way to represent medical record number together with the source (E2B(R2) B.1.1.1b)

D Patient Characteristics

E2B(R3)	Summary
D.1.1.3	"Patient Medical Record Number and Source(s) of the Record Number" (Hospital) •New way to represent medical record number together with the source (E2B(R2) B.1.1.1c)
D.1.1.4	"Patient Medical Record Number and Source(s) of the Record Number" (Investigation) •New way to represent medical record number together with the source (E2B(R2) B.1.1.1d)

D Patient Characteristics

E2B(R3)	Summary
D.2.3 	"Patient Age Group (as per reporter)" •A new age group has been added: Value = "Foetus"
D.7.3 	"Concomitant Therapies" This data element indicates at the time of the reaction that there were concomitant therapies such radiotherapy, drug class, dietary supplements or other products not otherwise describable in Section G: Value = True Details should be provided in narrative section H.1

D Patient Characteristics (continued)

ICH E2B(**R3**)
D Patient
Characteristics

ICH E2B(**R2**)
B.1 Patient
Characteristics

D.9.1 - Date of Death
D.9.3 - Was Autopsy Done?

	D.2 - Age Information
0 ... 1	D.2.1 - Date of Birth D.2.2a - Age at Time of Onset of Reaction / Event (number) D.2.2b - Age at Time of Onset of Reaction / Event (unit) D.2.2.1a - Gestation Period When Reaction / Event Was Observed in the Foetus (number) D.2.2.1b - Gestation Period When Reaction / Event Was Observed in the Foetus (unit) D.2.3 - Patient Age Group (as per reporter)

	D.7.1.r - Structured Information on Relevant Medical History (repeat as necessary)
0 ... n	D.7.1.r.1a - MedDRA Version for Medical History D.7.1.r.1b - Medical history (disease / surgical procedure / etc.) (MedDRA code) D.7.1.r.2 - Start Date D.7.1.r.3 - Continuing D.7.1.r.4 - End Date D.7.1.r.5 - Comments D.7.1.r.6 - Family History

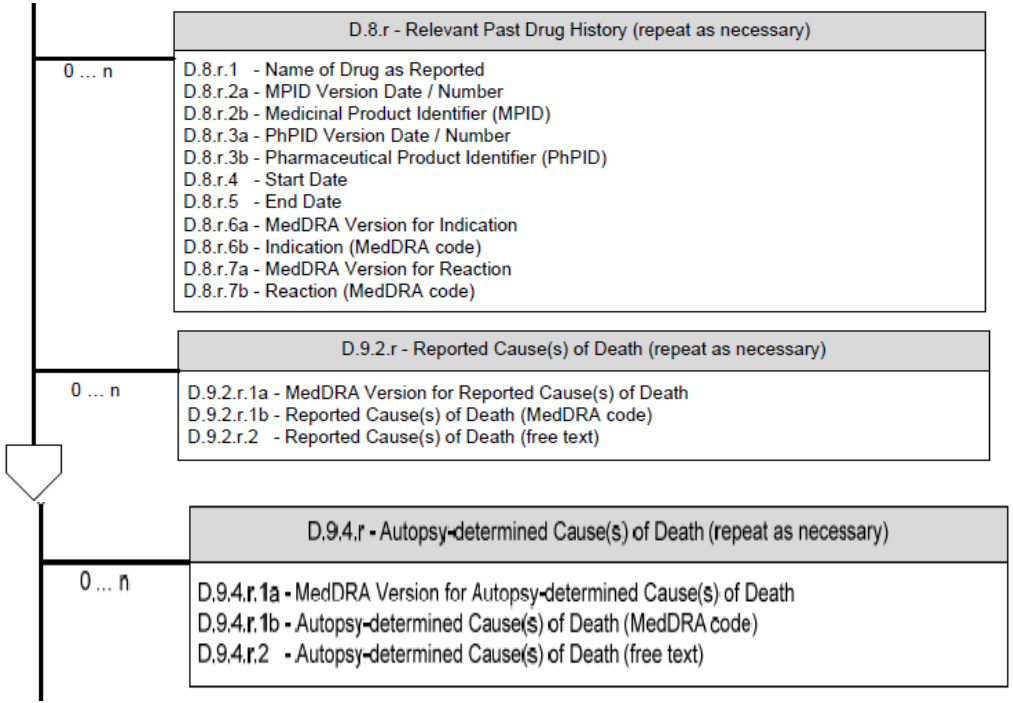
D Patient Characteristics

E2B(R3)	Summary
D.7.1.r	**"Structured Information on Relevant Medical History" (repeat as necessary)**
D.7.1.r.6 	"Family History" •Use this data element when the medical information provided for D.7.1.r is reported also to be present in another family member (e.g. hereditary diseases): Value = True •This data element is not used when the same medical concept is already provided in D.10.7 "Relevant Medical History and Concurrent Conditions of Parent" •Detailed information should be provided in narrative section H.1.

D Patient Characteristics (continued)

ICH E2B(**R3**)
D Patient Characteristics

ICH E2B(**R2**)
B.1 Patient Characteristics



D Patient Characteristics

E2B(R3)	Summary
D.8r.2a	"MPID Version Date/Number" (repeat as necessary) •This data element provides the version number for D.8.r.2b
D.8.r.2b	"Medicinal Product Identifier" (MPID) •This data element is used to capture the most specific identifier for the medicinal product NOTE: This will become applicable when the ISO IDMP related identifiers become available Meanwhile capture the information in D.8.r.1 "Name of Drug as Reported"

D Patient Characteristics

E2B(R3)	Summary
D.8r.3a	"PhPID Version Date/Number" (repeat as necessary) •This data element provides the version number for D.8.r.3b
D.8.r.3b 	"Pharmaceutical Product Product Identifier" (PhPID) •This data element is used to capture the most specific identifier for the pharmaceutical product NOTE: This will become applicable when the ISO IDMP related identifiers become available Meanwhile capture the information in D.8.r.1 "Name of Drug as Reported"

D Patient Characteristics

E2B(R3)	Summary
D.9.2.r	"Reported Cause(s) of Death" (repeat as necessary)
D.9.2.r.1a D.9.2.r.1b	- "MedDRA Version for Reported Cause(s) of Death" - "Reported Cause(s) of Death (MedDRA code)"
D.9.2.r.2	"Reported Cause of Death" (free text) •This data element captures the original reporter's words and or short phrases used to describe the cause of death

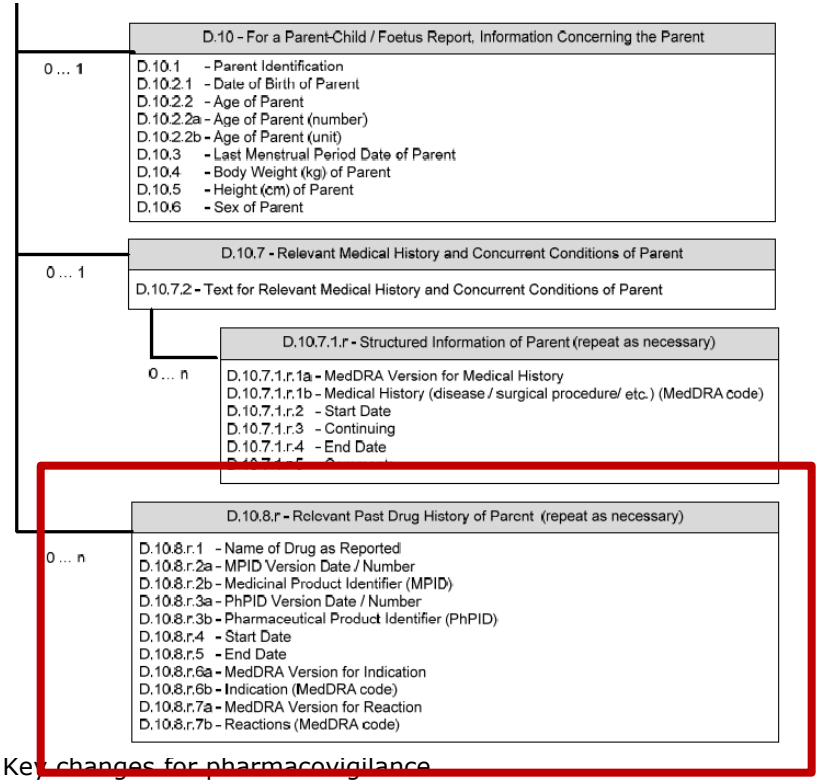
D Patient Characteristics

E2B(R3)	Summary
D.9.4.r.	"Autopsy determined Cause(s) of Death" (repeat as necessary)
D.9.4.r.1a D.9.4.r.1b	• MedDRA Version for Autopsy-determined Cause(s) of Death • Autopsy-determined Cause(s) of Death (MedDRA code)
D.9.4.r.2	"Autopsy determined Cause(s) of Death" (free text) •This data element captures the original reporter's words and or short phrases used to describe the autopsy determined cause of death.

D Patient Characteristics (continued)

ICH E2B(**R3**)
D Patient
Characteristics

ICH E2B(**R2**)
B.1 Patient
Characteristics



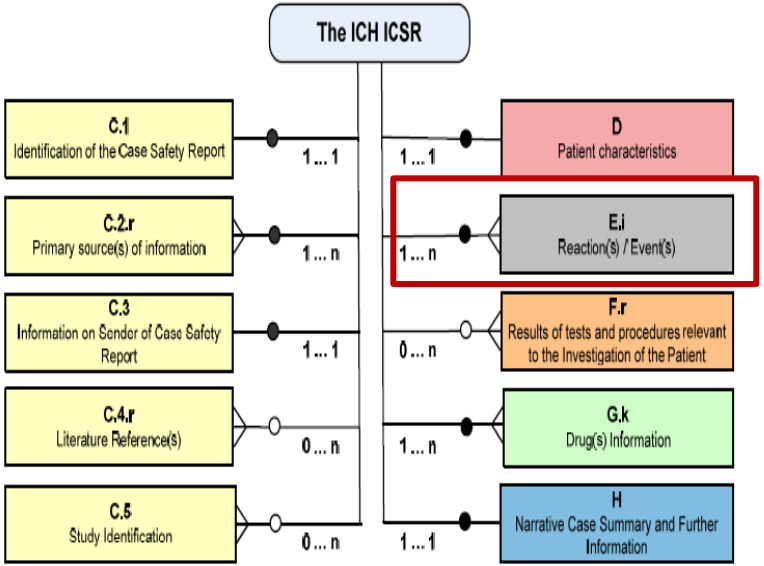
D Patient Characteristics

E2B(R3)	Summary
D.10.8r.2a	"MPID Version Date/Number" (repeat as necessary) •This data element provides the version number for D.10.8.r.2b
D.10.8.r.2b 	"Medicinal Product Identifier" (MPID) •This data element is used to capture the most specific identifier for the medicinal product NOTE: This will become applicable with the ISO IDMP related identifiers become available Meanwhile capture the information in D.10.8.r.1 "Name of Drug as Reported"

D Patient Characteristics

E2B(R3)	Summary
D.10.8r.3a	"PhPID Version Date/Number" (repeat as necessary) •This data element provides the version number for D.10.8.r.3b
D.10.8.r.3b 	"Pharmaceutical Product Product Identifier" (PhPID) •This data element is used to capture the most specific identifier for the pharmaceutical product NOTE: This will become applicable when the ISO IDMP related identifiers become available Meanwhile capture the information in D.10.8.r.1 "Name of Drug as Reported"

The ICH E2B(R3) ICSR – Section E



ICH E2B(R3)

E.i Reaction(s)/Event(s)

(Repeat as necessary)

ICH E2B(**R3**)
E.i Reaction(s)/ Event(s)

ICH E2B(**R2**)
B.2 Reaction(s)/ Event(s)

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

E.i Reaction(s)/Event(s)

E2B(R3)	Summary
E.i.3.2 	"Seriousness Criteria at Event Level" NOTE: The seriousness criteria are provided at reaction/event level and no longer at case level as specified in ICH E2B(R2) •More than one seriousness criteria can be chosen •If the reaction is non-serious, the seriousness criteria data elements E.i.3.2.a up to E.i.3.2.f should be left blank •In cases of foetal demise such as miscarriage, (where the ICSR should be prepared only for the parent being the patient), the seriousness criterion is '*Other medically important condition*'. •Depending if the parent (being the patient) experienced complications, the seriousness criterion could also include 'life-threatening' and/or 'hospitalisation'.

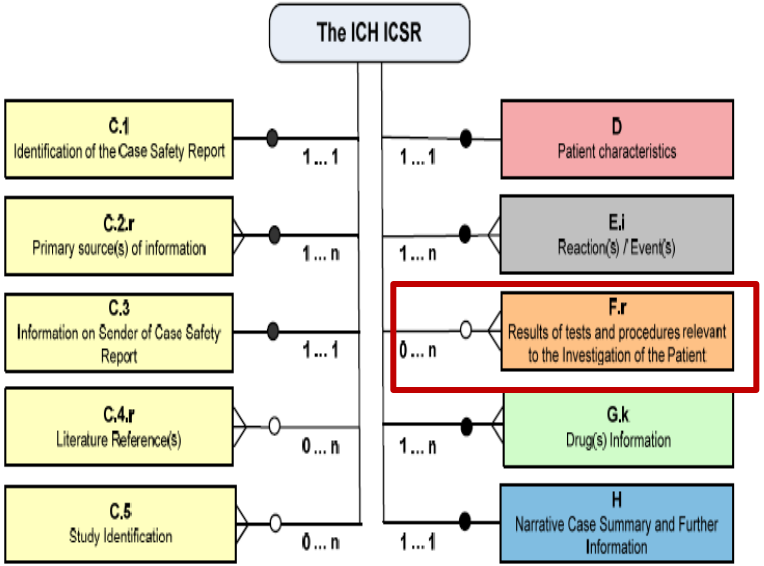
E.i Reaction(s)/Event(s)

E2B(R3)	Summary
E.i.8 	"Medical Confirmation by Healthcare Professional" NOTE: medical confirmation is now captured at reaction level In E2B(R2) medical confirmation was captured at case level (A.1.14) If an event is reported by a non healthcare professional (e.g. lawyers, consumers), this data element indicates whether the *occurrence* of the event was subsequently confirmed by a healthcare professional

E.i Reaction(s)/Event(s)

E2B(R3)	Summary
E.i.9 	"Identification of the Country Where the Reaction/Event Occurred" NOTE: the country where the reaction occurred is now captured at reaction level (see examples in the ICH ICSR IG) In E2B(R2) the occurrence country is captured at case level (A.1.2)

The ICH E2B(R3) ICSR – Section F



ICH E2B(R3)

F Results of Tests and Procedures

(Repeat as necessary)

ICH E2B(**R3**)
F Results of Tests & Procedures

ICH E2B(**R2**)
B.3 Results of Tests & Procedures

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

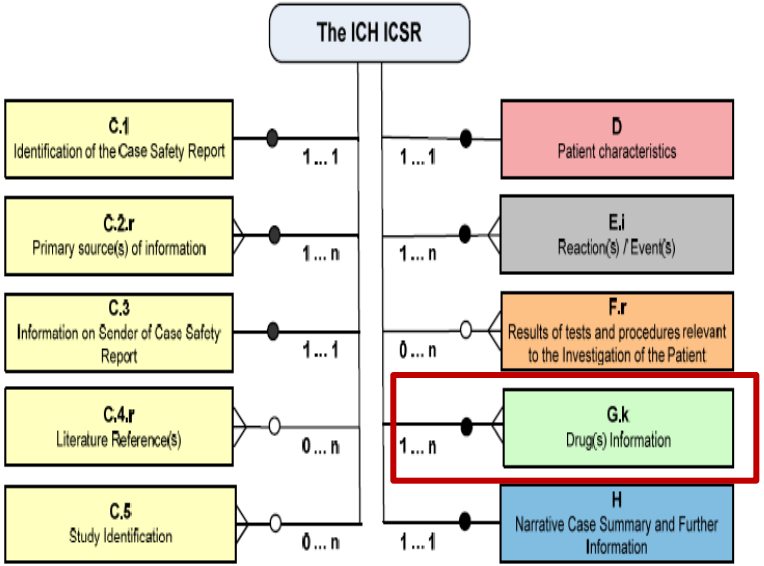
F Results of Tests and Procedures

E2B(R3)	Summary
F.r.2.2b	"Test Name" (MedDRA code) • A dedicated data element to code the test name in MedDRA is now available
F.r.3.1 	Test Result (code) • This is a new data element to provide a descriptive code for the test result. • Values allowed are: – Positive – Negative – Borderline – Inconclusive

F Results of Tests and Procedures

E2B(R3)	Summary
F.r.3.4	"Result Unstructured Data" (free text) •This data element can be used when 'results' and 'units' cannot be split often because a UCUM code is not available for the test unit e.g. for the test 'protein excretion' the result could be recorded here as 125 mg/24 hours
F.r.6	"Comments" (free text) •This data element captures any relevant comments made by the reporter about the test results
F.r.7	"More Information Available" •This allows to indicate if more info is held by the sender about the test results – Values: True or False

The ICH E2B(R3) ICSR – Section G



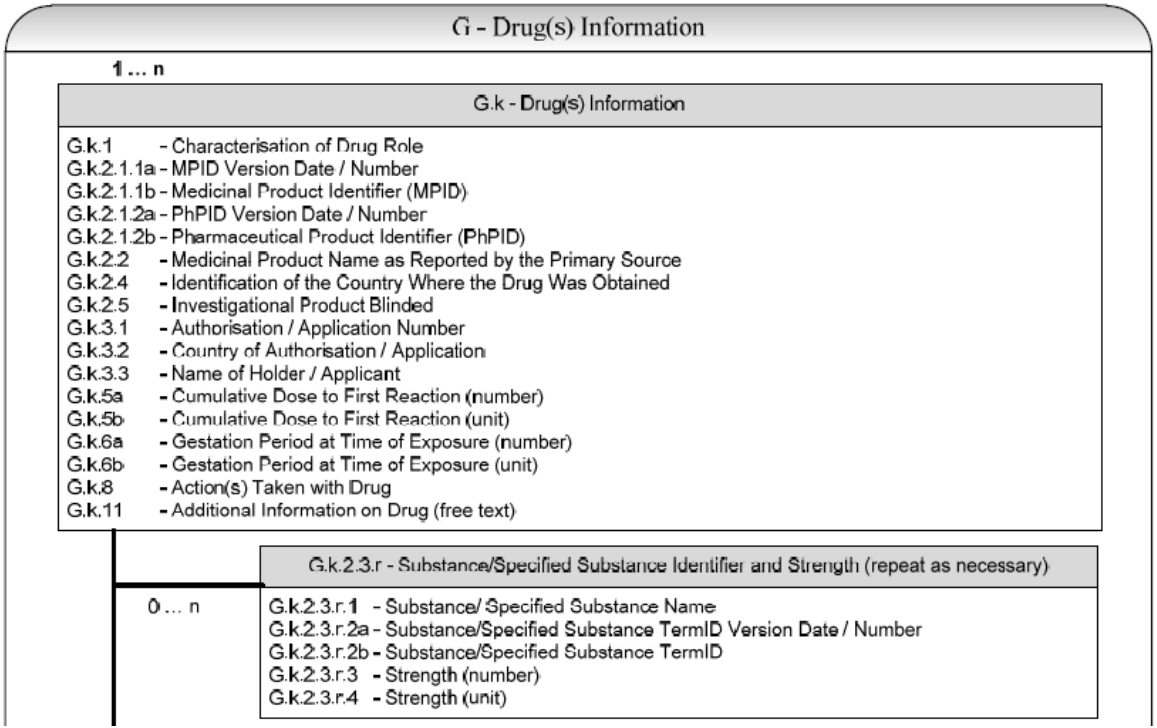
ICH E2B(R3)

G Drug(s) Information

(Repeat as necessary)

ICH E2B(**R3**)
G Drugs
Information

ICH E2B(**R2**)
B.4 Drug(s)
Information



G Drug(s) Information

E2B(R3)	Summary
G.k.1 	"Characterization of Drug Role" •This data element should describe the characterisiation of the drug role as provided by the primary reporter, or, if this information is missing, by the sender •All spontaneous reports should have at least **one** suspect drug •For suspected interactions, 'interacting' should be selected for all suspected interacting drugs •The type of interaction should be captured using the appropriate MedDRA LLT in Section E.i, e.g. drug interaction, food interaction, alcohol interaction etc

G Drug(s) Information

E2B(R3)	Summary
G.k.1 	"Characterization of Drug Role" •There is a new value: '*Drug not administered*' to be used for: i) Clinical trials where an adverse event occurred after the informed consent was signed but prior to the administration of the study drug (such as during the screening period or washout procedure); the adverse event should in general be reported as per the trial procedure. In that case only sections G.k.1, Gk.2 and G.k.8 are to be completed for section G ii) Medication error if the patient did not actually receive the prescribed drug (MedDRA LLT code to be captured in Section E.i) •The information on the suspect cause of the event should be provided in the narrative H.1 •Comments can be provided by the reporter in H.2 and by the sender in H.4

G Drug(s) Information

E2B(R3)	Summary
G.k.2	"Drug Identification" •*Medicinal product names or active ingredient names* should be provided in G.k.2.2 *as they were reported by the primary source* •To standardise the identification of medicinal products, the ISO IDMP standard identifiers have been incorporated in the ICSR standard •The most precise structured information should be provided when identifying medicinal products and redundant information does not have to be repeated •The identifiers resulting of the ISO IDMP standards should be used once available •**Until this time,** *G.k.2.2 "Medicinal Product as Reported by the Primary source"* **should be used**

G Drug(s) Information

E2B(R3)	Summary
G.k.2 	"Drug Identification" •In case of *investigational drugs*, provide as much information as known in G.k.2.2 and G.k.2.3.r.1 even if only an abstract code might be known •If more than one substance name is specified for a drug product, each of them should be included in this section by repeating the item G.k.2.3 as necessary

G Drug(s) Information

E2B(R3)	Summary
G.k.2.1	"Medicinal Product Unique Identifier/Pharmaceutical Product Unique Identifier" This section provides the necessary data elements for the relevant ISO IDMP identifiers as follows: •G.k.2.1.1a MPID Version Date / Number •G.k.2.1.1b Medicinal Product Identifier (MPID) •G.k.2.1.2a PhPID Version Date/Number •G.k.2.1.2b Pharmaceutical Product Identifier (PhPID) They should be used once they are available

G Drug(s) Information

E2B(R3)	Summary
G.k.2.2.EU.9.r.1 	"Device Component name" •For suspected adverse reactions relating to advanced therapies or involving medicinal products that have device component(s) •In the EU this data element can be used to specify the name of the device where applicable as text •Not allowed if G.k.2.1.1 is provided
G.k.2.2.EU.9.r.2	"Device Component TermID version Date/Number" •This data element captures the version date/number of the Device component TermID. If Device component TermID is known the TermID version must also be provided •Required if G.k.2.2.EU.9.r.3 is provided

G Drug(s) Information

E2B(R3)	Summary
G.k.2.2.EU.9.r.3	"Device Component TermID" •The Device component TermID should be provided if known •Required if G.k.2.2.EU.9.r.2 is provided
G.k.2.2.EU.9.r.4	"Device Batch Lot number" •The batch lot number if applicable to a unique device.

G Drug(s) Information

E2B(R3)	Summary
G.k.2.2.EU.1	"Name Part" •Medication Name Parts are a means of specifying the name of a product as separated components •This allows for input name strings to be automatically matched to possible medicinal products, rather than through manual recoding activities •The product name parts should be used if the MPID cannot be selected and if the medicinal product has been reported as a brand/invented name

G Drug(s) Information – "Name part"

Concept Code	Concept Name	Description	Example
CON	container name	container if present in the medicinal product name	*Totalflu suspension for injection in pre-filled syringe Influenza vaccine (surface antigen, inactivated, prepared in cell culture) (2009/2010 season)* **pre-filled syringe**
DEV	device name	name for device if present in the medicinal product name	*Fastaction InjectPen 100 IU/ml Solution for injection:* **InjectPen**
FRM	Form name	pharmaceutical form/ if present in the medicinal product name	*For Discopan 50 mg soft capsules:* ***Soft Capsules*** *For Totalflu suspension for injection in pre-filled syringe Influenza vaccine (surface antigen, inactivated, prepared in cell culture) (2009/2010 season):* **suspension for injection**

G Drug(s) Information – "Name part"

Concept Code	Concept Name	Description	Example
INV	invented name	product name without the trademark or the name of the marketing authorization holder or any other descriptor reflected in the product name and, if appropriate, whether it is intended e.g. for babies, children or adults	**Discopan** **Totalflu** **Fuldimil**
SCI	scientific name	product common or scientific name without the trademark or the name of the marketing authorization holder or any other descriptor reflected in the product name.	Discopan: **N/A** Totalflu: **Influenza vaccine (surface antigen, inactivated, prepared in cell culture) (2009/2010 season)** For Fuldimil: **N/A**

G Drug(s) Information – "Name part"

Concept Code	Concept Name	Description	Example
STR	strength name	strength if present in the medicinal product name	*Discopan 50 mg soft capsules:* **50mg** *Fuldimil 25mg-Filmtabletten:* **25 mg** *Totalflu suspension for injection in pre-filled syringe Influenza vaccine (surface antigen, inactivated, prepared in cell culture) (2009/2010 season):* `
TMK	trademark name	trademark/company element if present in the medicinal product name	*Insulin Human Syncopharm Comb 15:* **Syncopharm**
USE	intended use name	intended use if present in the medicinal product name without trademark or name of MAH or any other descriptor reflected in the product name	*Multivax PAEDIATRIC:* **Paediatric** *Multivax ADULT*: **Adult**

G Drug(s) Information

E2B(R3)	Summary
G.k.2.2.3.r	"Substance / Specified Substance Identifier and Strength" (repeat as necessary) • This section provides the necessary data elements for the relevant ISO IDMP identifiers as follows (to be used once available): – G.k.2.3.r.1 Substance / Specified Substance Name – G.k.2.3.r.2a Substance/Specified Substance TermID Version Date/Number – G.k.2.3.r.2b Substance/Specified Substance TermID • Strength has been added within the Substance section – G.k.2.3.r.3a Strength (number) – G.k.2.3.r.3b Strength (unit)

G Drug(s) Information

E2B(R3)	Summary
G.k.2.5 	"Investigational Product Blinded" •Is applicable only to ICSRs from clinical trials •Whilst according to ICH E2A case safety reports with blinded therapy should not be reported, there may be instances where it is important to exchange a blinded case; proceed as follows: – Until the investigational product is un-blinded, the status 'blinded' should be indicated: Value 'TRUE' – Section G.k.2 Drug Identification should be populated with the characteristics of the investigational product – If more than one investigational product is potentially suspect, each suspect product should be represented in separate G.k blocks – If appropriate, after unblinding, 'placebo' should be reported in G.k.2.3.r as a suspect drug

G Drug(s) Information (continued)

(Repeat as necessary)

ICH E2B(**R3**)
G Drugs
Information

ICH E2B(**R2**)
B.4 Drug(s)
Information

	G.k.4.r - Dosage Information (repeat as necessary)
0 ... n	G.k.4.r.1a - Dose (number) G.k.4.r.1b - Dose (unit) G.k.4.r.2 - Number of Units in the Interval G.k.4.r.3 - Definition of the Time Interval Unit 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.6a - Duration of Drug Administration (number) G.k.4.r.6b - Duration of Drug Administration (unit) G.k.4.r.7 - Batch / Lot Number G.k.4.r.8 - Dosage Text G.k.4.r.9.1 - Pharmaceutical Dose Form (free text) G.k.4.r.9.2a - Pharmaceutical Dose Form TermID Version Date / Number G.k.4.r.9.2b - Pharmaceutical Dose Form TermID G.k.4.r.10.1 - Route of Administration (free text) G.k.4.r.10.2a - Route of Administration TermID Version Date / Number G.k.4.r.10.2b - Route of Administration TermID G.k.4.r.11.1 - Parent Route of Administration (free text) G.k.4.r.11.2a - Parent Route of Administration TermID Version Date / Number G.k.4.r.11.2b - Parent Route of Administration TermID

G Drug(s) Information (continued)

E2B(R3)	Summary
G.k.4.r 	"Dosage and Relevant Information" (repeat as necessary) •Data elements G.k.4.r.1 through G.k.4.r.3 should be used to provide dosage information •The way to provide dosage information is changing

Field	R2 value	R3 value
G.k.4.r.1a	10	10
G.k.4.r.1b	mg	mg
B.4.k.5.3	3	*element removed*
G.k.4.r.2	1	8
G.k.4.r.3	day	hours

See Appendix I (G) of the ICH ICSR IG for further information

G Drug(s) Information (continued)

E2B(R3)	Summary
G.k.4.r.7 	"Batch/Lot Number" •Several batch numbers can now be repeated within the drug section •Expiration date and other related information should be reflected in G.k.11 'Additional Information on Drug' (free text) •Batch/lot number for biologics – value is mandatory and should be completed with the value or an appropriate nullflavor

G Drug(s) Information (continued)

E2B(R3)	Summary
G.k.4.r.9 	"Pharmaceutical Dose Form" •This section provides the data elements for the relevant ISO IDMP identifiers as follows (to be used once available): – G.k.4.r.9.2a Pharmaceutical Dose Form TermID Version Date/Number – G.k.4.r.9.2bPharmaceutical Dose Form TermID •If the Pharmaceutical Dose Form TermID is not available, free text in G.k.4.r.9.1 should be used

G Drug(s) Information (continued)

E2B(R3)	Summary
G.k.4.r.10. 	"Routes of Administration" •This section provides the data elements for the relevant ISO IDMP identifiers as follows (to be used once available): – G.k.4.r.10.2a Route of Administration TermID Version Date / Number – G.k.4.r.10.2b Route of Administration TermID •Until ISO IDMP identifiers are available, use the existing code list attached in Appendix I of the ICH ICSR IG •For a parent-child/foetus report, this data element indicates the route of administration for the child/foetus (patient); this is usually an indirect exposure, such as transmammary, but can include more usual routes of administration for other drugs given to the child •Parent route of administration should be provided in G.k.4.r.11.

G Drug(s) Information (continued)

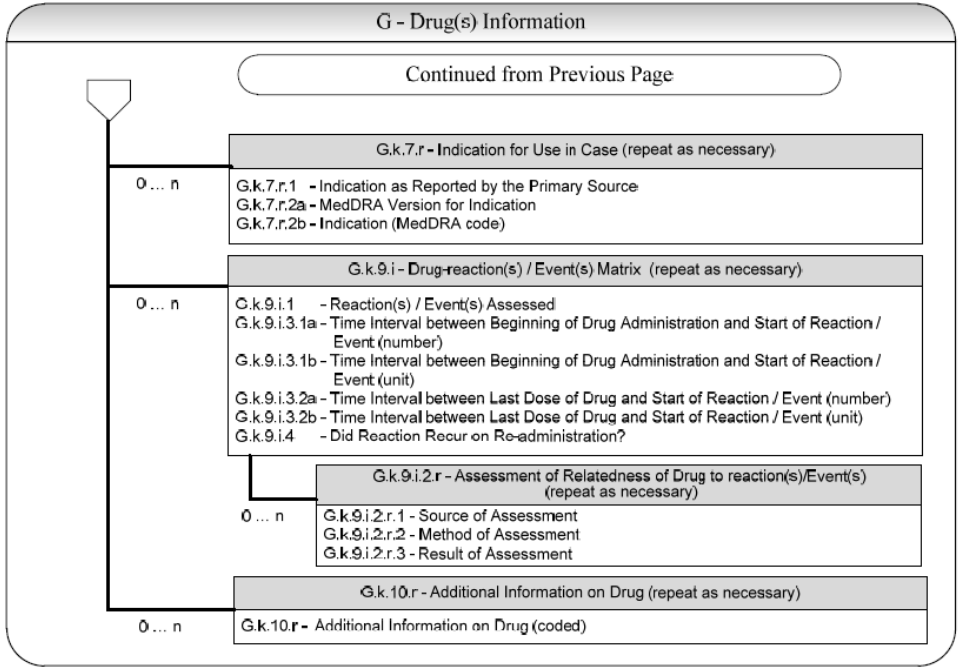
E2B(R3)	Summary
G.k.4.r.11	"Parent Route of Administration" (in case of a parent child/foetus report) •The same principles apply as for G.k.4.r.10

G Drug(s) Information (continued)

(Repeat as necessary)

ICH E2B(**R3**)
G Drugs
Information

ICH E2B(**R2**)
B.4 Drug(s)
Information



G Drug(s) Information (continued)

E2B(R3)	Summary
G.k.7.r 	"Indication for Use in Case" (repeat as necessary) •Indication for use can now be repeated within the drug section without the need to repeat the entire drug section •The following data elements are available to capture the indication as reported as well as the MedDRA version and the MedDRA code – G.k.7.r.1 Indication as Reported by the Primary Source (free text) – G.k.7.r.2a MedDRA Version for Indication – G.k.7.r.2b Indication (MedDRA code)

G Drug(s) Information (continued)

E2B(R3)	Summary
G.k.9.i	"G.k.9.i Drug-reaction(s)/Event(s) Matrix" (repeat as necessary) •This section provides the means to transmit the degree of suspected relatedness of the drug (k) with a suspect role to each reaction(s)/event(s) (i) in Section E •The repeating items (r) are used to provide the assessment of relatedness by different sources or methods of assessment

G.k.9.i.1	G.k.9.i.2.r.1	G.k.9.i.2.r.2	G.k.9.i.2.r.3
technical reference to event 1 in E.i	Reporter	global introspection	related
	Company	algorithm	possibly related
	Company	Bardi	0.76
technical reference to event 2 in E.i	Reporter	global introspection	not related
	Company	algorithm	possibly related
	Company	Bardi	0.48
technical reference to event 3 in E.i	Company	algorithm	unlikely related
	Company	Bardi	0.22

See ICH ICSR IG Page 133-137)

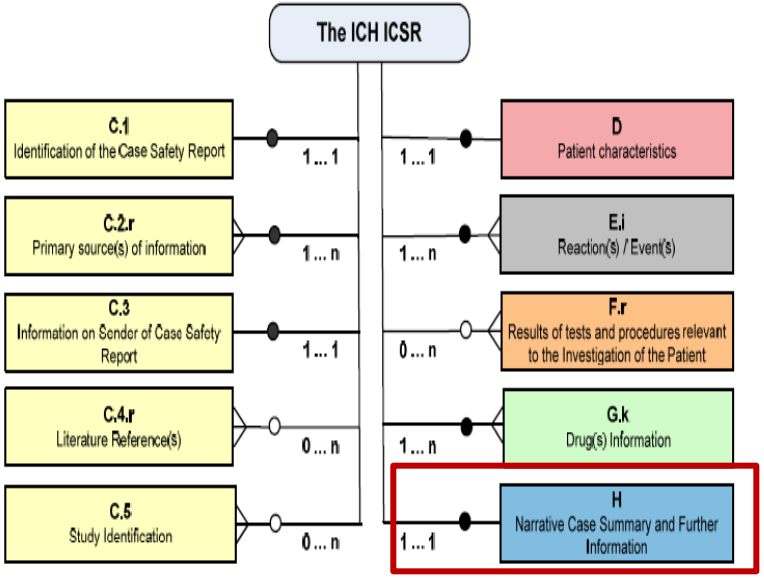
G Drug(s) Information (continued)

E2B(R3)	Summary
G.k.9.i.4 	"Did Reaction Recur on Re-administration?" (repeat as necessary) • This data element has been further structured • It indicates ***if the patient was rechallenged or not with the drug*** and the known outcome – 1=yes – yes (rechallenge was done, reaction recurred) – 2=yes – no (rechallenge was done, reaction did not recur) – 3=yes – unk (rechallenge was done, outcome unknown) – 4=no – n/a (no rechallenge was done, recurrence is not applicable) • ***The data element should not be coded if it was not reported whether or not a rechallenge was done***

G Drug(s) Information (continued)

E2B(R3)	Summary
G.k.10.r 	"Additional information on Drug (coded)" (repeat as necessary) •This data element captures additional information on the drug pertinent to the case •Values allowed are: –Counterfeit –Overdose –Drug taken by the father –Drug taken beyond expiry date –Batch and lot tested and found within specifications –Batch and lot tested and found not within specifications –Medication error –Misuse –Abuse –Occupational exposure –Off label use

The ICH E2B(R3) ICSR – Section H

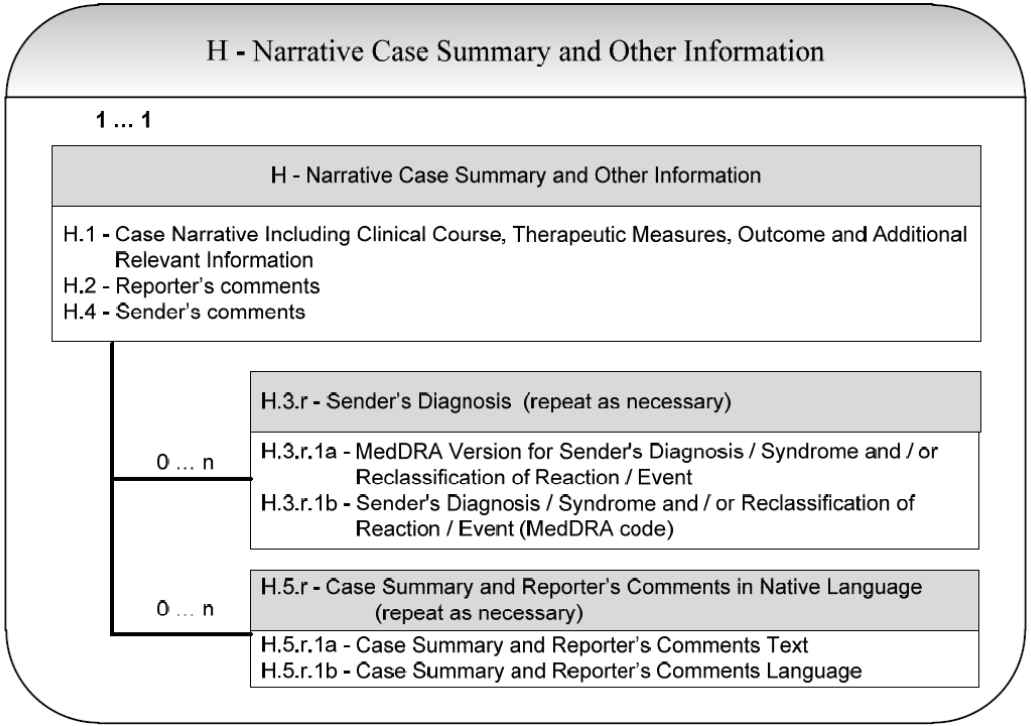


ICH E2B(R3)

H Narrative Case Summary and further Information

ICH E2B(**R3**)
H Narrative
Case Summary

ICH E2B(**R2**)
B.5 Narrative
Case Summary



H Narrative Case Summary

E2B(R3)	Summary
H.1 	"Case Narrative Including Clinical Course, Therapeutic Measures, Outcome and Additional Relevant Information" •The field length of the case narrative have been extended substantially from 20000 AN to 100000AN •A narrative must be provided for cases related to serious adverse reactions
H.5.r	"Case Summary and Reporter's Comments in Native Language" (repeat as necessary) •This section provides information on the clinical course of the case, therapeutic measures, outcome and other relevant information, as well as the reporter's comments on the case in a language different from that used in Sections H.1, H.2, and H.4 •H.5.r.1a and H.5.r.1b are used in combination to transmit the sender's and receiver's comments in a language other than English, as required in some countries and regions

Object Identifiers

E2B(R3)	Summary
	• E2B(R3) uses Object Identifiers (OIDs) to identify code systems for the ICSR message exchange • OIDs are presented in a form that consists only of numbers and dots (e.g., "2.16.840.1.113883.3.1”) • The list of OIDs is presented in the ICH E2B(R3) IG with EU specific OIDs reflected in the EU ICSR IG

Object Identifiers

E2B(R3)	Summary
	A summary of all OIDs is provided in the ICH ISCR IG: • Table 1: E2B (R3) data elements and IDMP OIDs • Table 2: E2B (R3) data elements and MedDRA OIDs • Table3: E2B (R3) data elements and ICH ICSR message Codes OIDs • Table4: E2B (R3) data elements and ICH ICSR message Codes OIDs (ICH constrained UCUM codes) • Table5: E2B (R3) data elements and ICSR message Namespace OIDs • Table6: E2B (R3) data elements and Ack message Namespace OIDs • Table7: ICSR / Ack common technical OIDs

MedDRA version

E2B(R3)	Summary
	• Only one MedDRA version is allowed per ICSR

nullFlavors

E2B(R3)	Summary
 	• ICH ICSR uses nullFlavors from the HL7 Messaging Standard to categorise exceptions • The ICH ICSR IG indicates, where nullFlavors should be used and which types are allowed to be used *NOTE: refer also to the EU ICSR IG and GVP Module VI (revision 2) for EU specific requirements on nullFlavors*

nullFlavors

Code	Name	Definition
NI	No Information	• No information whatsoever can be inferred from this exceptional value • This is the most general exceptional value • It is also the default exceptional value Example: C.1.9.1 "Other Case Identifiers in Previous Transmissions"
MSK	Masked	• There is information on this item available - it has not been provided by the sender due to security, privacy or other reasons • Its primary purpose is for those circumstances where it is necessary to inform the receiver that the information does exist without providing any detail Example: e.g. C.2.r.1.2 "Reporter's Given Name"

nullFlavors

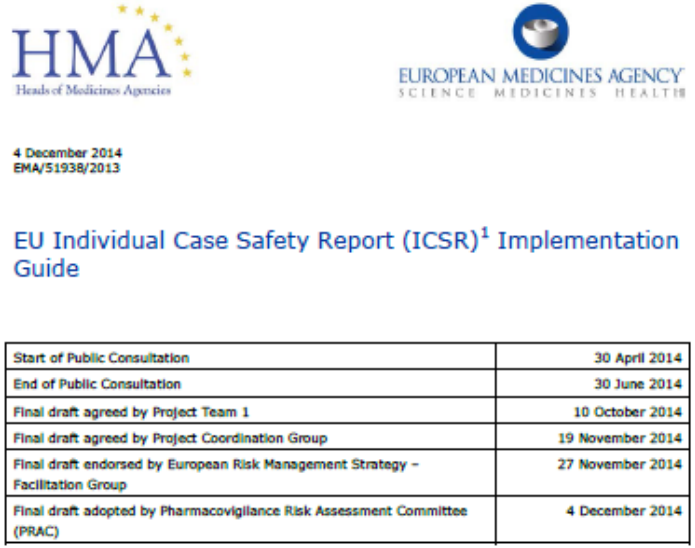
Code	Name	Definition
UNK	Unknown	• A proper value is applicable, but not known Example: C.2.r.2.7 "Reporter's Telephone"
NA	Not applicable	• No proper value is applicable in this context Example: last menstrual period for a male
ASKU	Asked but Unknown	Information was sought but not found Example: C.5.2 "Study Name"

nullFlavors

Code	Name	Definition
NASK	Not Asked	• This information has not been sought Example: C.5.3 “Sponsor Study Number”
NINF	Negative Infinity	• Negative infinity of numbers Example: F.r.3.2 “Test Result (value / qualifier)”
PINF	Positive Infinity	• Positive infinity of numbers Example: F.r.3.2 “Test Result (value / qualifier)”

EU ICSR Implementation Guide

Please carefully review the EU ICSR IG



HMA
Heads of Medicines Agencies

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

4 December 2014
EMA/51938/2013

EU Individual Case Safety Report (ICSR)[1] Implementation Guide

Start of Public Consultation	30 April 2014
End of Public Consultation	30 June 2014
Final draft agreed by Project Team 1	10 October 2014
Final draft agreed by Project Coordination Group	19 November 2014
Final draft endorsed by European Risk Management Strategy – Facilitation Group	27 November 2014
Final draft adopted by Pharmacovigilance Risk Assessment Committee (PRAC)	4 December 2014

- We are now going to discuss important principles and changes to the business rules for the validation of ICSRs which are reported electronically to EudraVigilance in line with the ISO/ICH E2B(R3) format

NOTE: ensure that your pharmacovigilance system is aligned with the new business rules when processing ICSRs in the new format

EU ICSR Implementation Guide

- Attachments
- Use of local language
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- Batch/Lot Number
- nullFlavor
- Characterisation of Drug Role “Drug Not Administered”
- Literature references - Digital Object Identifiers (DOI)
- Business Rules

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EU ICSR Implementation Guide – Attachments

- Main use for attachments will be the provision of literature articles and any associated translation of the literature article into English (if requested by the Agency)
- Other documents made available by a primary source (e.g. autopsy reports, ECG strips, chest X-ray, or photographs, etc.) can also be provided as attachments using the same method
- Additional documents should not be routinely attached to ICSRs:
  - Either be at the request of the receiver on a case by case basis or
  - Where the correct medical interpretation of the ICSR cannot be made without access to the attachment(s)

EU ICSR Implementation Guide – Attachments

- Within one ICSR, multiple document titles (C.1.6.1.r) and literature titles (C.4.r.1) can be provided, as well as the associated materials
- In line with GVP module VI, if a literature article refers to more than one ICSR then the literature article should be attached to the first ICSR created only and all the associated ICSRs should be linked to the first ICSR through the linked report number (C.1.10.r)
- Table 9 “Supported file types in the EU” of the EU ICSR IG provides an overview of portable document formats

EU ICSR Implementation Guide – Attachments

- Because documents might not be ready for transmission at the time of ICSR reporting, attachments can be transmitted separately from the ICSR transmission
- When the sender transmits an attachment later, the original ICSR should be retransmitted along with the attachment
- Data element C.1.11.1 should be completed as an 'amendment' along with the reason for amendment in data element C.1.11.2 i.e. transmission of attachment(s)
- If additional documents are subsequently received by the sender and contain medically relevant information a follow-up case containing the additional information should be created and submitted

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EU ICSR Implementation Guide – Use of local language in Reaction/Event section and case summary section

- EU requirements for use of languages in ICSRs

Primary Source Country	Sender	Language
EEA	NCA	Local language • Case translation shall be provided by the NCA when requested by the Agency or other Member States for the evaluation of potential signals
EEA	MAH	English language + Reaction/Event as reported by the primary source in Narrative Language (Ei.1.1a) + Reporter's comments Text (H.5.r.1a) in local language
Non-EEA	MAH	English

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EU ICSR Implementation Guide – Data elements for Causality Assessments

- *For SUSAR reporting* medicinal products classified as suspect or interacting should have *at least one method of assessment*
- The *binary decision method* detailed in the CIOMS Working Group VI report for each event/reaction reported in the ICSR should be used
- This method of assessment should be characterised:
  - With the value '1' in the data element = *EU Method of Assessment* (G.k.9.i.2.r.2.EU.1)
  - With the data element EU Source of Assessment (G.k.9.i.2.r.1.EU.1) and
  - With the data element EU Result of the Assessment (G.k.9.i.2.r.3.EU.1) (1,2)
- The *use of other methods of causality assessment is optional* and can be provided in accordance with the ICH E2B(R3) Implementation Guide

EU ICSR Implementation Guide – Data elements for Causality Assessments

NOTE: In SUSARs where a medicinal product is classified as "drug not administered" causality assessments are not required for that specific drug

EU ICSR Implementation Guide – Data elements for Causality Assessments

G.k.9.i.2.r.1.EU.1- EU Source of Assessment:

- Values: Investigator [1], Sponsor [2], NCA [3], MAH [4], Healthcare professional [5], non-Healthcare professional [6]
- Business Rule(s): Mandatory if G.k.9.i.2.r.2.EU.1 = '1'
  - For reports sent to EVCTM, the value must be [1-3]
  - For reports sent to EVHUMAN, the value must be [3-6]

EU ICSR Implementation Guide – Data elements for Causality Assessments

G.k.9.i.2.r.3.EU.1 - *EU Result of Assessment*

EU Result of Assessment	Value
Reasonable possible	1
No reasonable possibility	2

- Each MedDRA LLT code reported in the data element E.i.2.1b should have an assessment provided by the Investigator AND/OR by the Sponsor for each reported medicinal product classified as suspect or interacting
- Failure to comply with this requirement generates an error acknowledgement

EU ICSR Implementation Guide – Data elements for Causality Assessments

- Any initial ICSR submitted to EVCTM should contain at least one reaction with a causality assessment ‘Reasonable possibility’ to at least one of the reported medicinal products classified as suspect or interacting
- This rule is not applied to follow-up ICSRs submitted to EVCTM in order to allow sponsors the possibility to downgrade the causality of an initial ICSR
- When the sponsor is sending the report at an early stage and does not have sufficient information to assign causalities, a ‘Reasonable possibility’ of causal association should be considered until further information is available to confirm or downgrade the initially reported causality

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EU ICSR Implementation Guide – Biological Products requiring Batch Number

G.k.4.r.7 - Batch / Lot Number

- Data element should be completed with a value or an appropriate null flag for all suspect or interacting drugs being biologics
- The nullflavor “ASKU” should be completed for biological products where the primary source has been contacted for this information but was unable to provide it
- For all other situations the nullflavor “UNK” should be used when this information is missing

EU ICSR Implementation Guide

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EU ICSR Implementation Guide – nullFlavors

- In the EU the ICH E2B(R3) IG is generally followed for the usage of nullflavor flags
- Usually, for specific data fields which are required in the EU for an ICSR to be considered valid, nullflavor flags are not permitted
- There are situations where the use of a nullflavor is required in the EU, which is not foreseen in the ICH E2B(R3) IG
- A summary of the exceptions between the EU and ICH E2B(R3) ICSR IG is provided as follows

EU ICSR Implementation Guide – nullFlavors

Nullflavor flag- Exceptions

ICH E2B(R3) field	Description
C.2.r.4 - Qualification	• The **reporter qualification** is mandatory for all reporters • The use of a nullflavor is not permitted
C.4.r.1 - Literature Reference(s)	• For a **literature report**, the literature reference must be provided • The use of a nullflavor is not permitted

EU ICSR Implementation Guide – nullFlavors

Nullflavor flag- Exceptions

ICH E2B(R3) field	Description
C.5.1.r.2 - Study Registration Country	• To identify EU registration numbers and the EudraCT number, the study registration country code must be provided • The use of a nullflavor is not permitted
G.k.4.r.7 - Batch / Lot Number	• The nullflavors “UNK” & “ASKU” should be provide for each reported suspect or interacting drug if no information is available

EU ICSR Implementation Guide – nullFlavors

- The ICH E2B(R3) IG foresees the use of the nullflavor “MSK”, which indicates to the receiver of an ICSR that the sender of the ICSR holds this information but is unable to send this information due to data protection / privacy reasons
- In the EU ICSR IG, for Patient name or initials (D.1) or Date of Birth (D.2.1) the “MSK” flag can be used
- In other E2B(R3) fields the use of the “MSK” flag is not considered valid for use in the EU as those fields would not lead to the direct identification of an individual
  - The EU exceptions are summarised and provided as follows

EU ICSR Implementation Guide – nullFlavors

Data elements where the use of "MSK" is not allowed in the EU

ICH E2B(R3) field code	ICH E2B(R3) field Description
D.5	Patient Sex
D.6	Patient Last Menstrual Period Date
D.7.1.r.2	Medical History Start Date
D.7.1.r.3	Medical History Continuing
D.7.1.r.4	Medical History End Date
D.7.2	Text for Relevant Medical History and Concurrent Conditions (not including reaction / event)
D.8.r.4	Relevant Past Drug History Start Date
D.8.r.5	Relevant Past Drug History End Date
D.9.1	Date of Death
D.10.3	Last Menstrual Period Date of Parent
D.10.6	Sex of Parent
D.10.7.1.r.2	Relevant Medical History and Concurrent Conditions of Parent Start Date

ICH E2B(R3) field code	ICH E2B(R3) field Description
D.10.7.1.r.3	Relevant Medical History and Concurrent Conditions of Parent Continuing
D.10.7.1.r.4	Relevant Medical History and Concurrent Conditions of Parent End Date
D.10.8.r.4	Relevant Past Drug History of Parent Start Date
D.10.8.r.5	Relevant Past Drug History of Parent End Date
E.i.4	Date of Start of Reaction / Event
E.i.5	Date of End of Reaction / Event
G.k.4.r.4	Date and Time of Start of Drug
G.k.4.r.5	Date and Time of Last Administration

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EU ICSR Implementation Guide – Characterisation of Drug Role "Drug Not Administered"

G.k.1= 4- Drug not administered

- For ***clinical trials***, in accordance with section 7.11.4 of the *"Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use"* ('CT-3'), this type of report should not be submitted as a SUSAR

EU ICSR Implementation Guide – Characterisation of Drug Role "Drug Not Administered"

G.k.1= 4- Drug not administered

- ***Medication error***: If the patient did not receive the actual prescribed drug but another one: Repeatable Sections G should be completed with
  - the information about the prescribed drug (selecting the characterisation of drug role as "Drug Not Administered") and
  - the information on the dispensed drug as the 'suspect' drug

  The appropriate medication error LLT should be captured with the appropriate MedDRA LLT code for the associated reaction/event in Section E.i "Reaction(s) / Event(s)"

EU ICSR Implementation Guide

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- **Literature references - Digital Object Identifiers (DOI)**
- Business Rules

EU ICSR Implementation Guide – Literature references and the use of Digital Object Identifiers (DOI)

- For a literature report, literature reference should be provided in the data field *Literature Reference(s)* (*C.4.r.1) in* 'Vancouver style' developed by the International Committee of Medical Journal Editors
- The EU IG also requires the Digital Object Identifier (DOI) for the article to be included where available

  Example: International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med 1997; 336:309-15. ***doi:10.1056/NEJM199701233360422***

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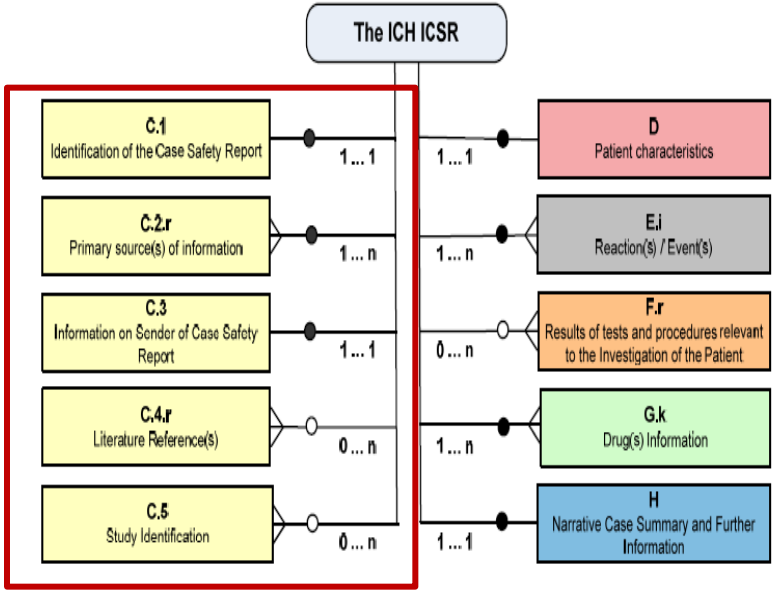
The ICH E2B(R3) ICSR – EudraVigilance Business Rules

- The following slides provide an overview of the most important changes of the EudraVigilance business rules with the move from the ICH E2B(R2) ICSR format to the ICH E2B(R3) format

- Always consult the reference documents for detailed requirements and specifications
  - For ICH E2B(R2): Note for guidance – EudraVigilance Human – Processing of safety messages and individual case safety reports (ICSRs) Revision 2
  - For ICH E2B(R3): European Union individual case safety report (ICSR) implementation guide

The ICH E2B(R3) ICSR – EudraVigilance Business Rules



ICH E2B(R3)

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
C.1.6.1	Are additional documents available? Boolean (false/true)	Optional	Mandatory
C.1.6.1.r.1	Documents held by sender	100 AN	2000 AN Mandatory if C.1.6.1 ='true' or if C.1.6.1r.2 contains a file
C.1.7	Does this case fulfil local criteria for an expedited report? Boolean (false/true; nullFlavor: NI*)	Optional	Mandatory *'nullFlavor' only allowed when sender is retransmitting a case that was first received ICH E2B (R2) format, where the equivalent data element for C.1.7 was optionally not populated; in other cases, only 'false'or 'true' should be used.

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
C.1.9.1	Other case identifiers in previous transmissions Boolean (true; nullFlavor: NI)	Optional	Mandatory
C.1.9.1.r.1	Source(s) of the case identifier	N/A	Mandatory if C.1.9.1. = "true"
C.1.9.1.r.2	Case identifier(s)	N/A	Mandatory if C.1.9.1. = "true"
C.1.11.2	Reason for Nullification/Amendment	200 AN Optional	2000 AN Mandatory if it is a nullification or amendment report (C.1.11.1 is populated) (Conditional-Mandatory)

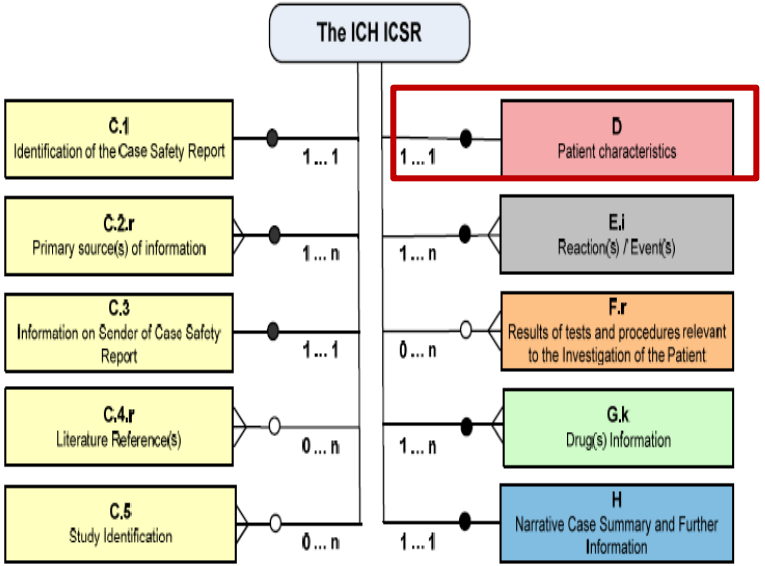
The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
C.2.r.3	Reporter's country code	Look up ISO 3166 At least one reporter family name, organization, postcode, country, literature reference or study name.	Mandatory if C.2.r.5. =1 ISO 3166-1 alpha-2, **value EU not accepted**
C.2.r.5	Primary source for regulatory purposes	N/A	Mandatory for one and only one instance of this element

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
C.3.2	Sender's organization	60 AN Mandatory	100 AN Mandatory if sender type C.3.1 = Pharmaceutical Company or Regulatory authority
C.4.r.1.	Literature reference(s)	At least one reporter family name, organization, postcode, country, literature reference or study name	Mandatory if a document is embedded in section C.4.r.2 Vancouver Style should be used

The ICH E2B(R3) ICSR – EudraVigilance Business Rules



ICH E2B(R3)

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
D.1	Patient (name or initials)	10 AN (only initials)	60 AN At least one of D.1: D.1.1.1, D.1.1.2, D.1.1.3, D.1.1.4, D.2.1, D.2.2a, D.2.2.1a, D.2.3 or D.5 (Note 9)
D.2.1	Date of Birth	At least one of initials, medical record number, specialist record number, hospital record number, investigation number, birth day, age, gestation period, age group, patient sex	Minimum precision required is the day (i.e. 'CCYYMMDD'). At least one of D.1: D.1.1.1, D.1.1.2, D.1.1.3, D.1.1.4, D.2.1, D.2.2A, D.2.2.1a, D.2.3 or D.5 (Note 5 & 9)

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

NOTE 5:

- *No date/time value should exceed the current UK GMT time plus 12 hours*
- *Failure of the validation of the date format generates an error*
- *All dates should be inferior or equal to the EudraVigilance Gateway date plus 12 hours*
- *Failure of this validation generates an error*

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

NOTE 9:

- *At least one patient identifier is required to indicate that a patient exists this is meet through the completion of at least one of the following fields D.1, D.1.1.1, D.1.1.2, D.1.1.3, D.1.1.4, D.2.1, D.2.2A, D.2.2.1a, D.2.3 or D.5. The use of "UNK", "ASKU" or "NASK" nullflavors in any of the patient identifier fields does not indicate that a patient exists*
- *If due to data privacy the name or initials of the patient is known but cannot be provided the nullflavor "MSK" can be used and will pass the validation rules*
- *If nullflavor "MSK" is used in the date of birth field then either the patient age or patient age group should be completed, if not an error message will be generated*

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
D.2.2.a	Age at time of onset of reaction/event (number)	If not null, should not be > 150 years	Mandatory if D.2.2b is populated Should not be > 150 years (Note 3) At least one of D.1: D.1.1.1, D.1.1.2, D.1.1.3, D.1.1.4, D.2.1, D.2.2A, D.2.2.1a, D.2.3 (Note 5 & 9)

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

NOTE 3:

- *If the patient/parent's age, height or weight value is above the allowed upper limit, the relevant ICH E2B(R3) data element should remain empty and the information should be reported in the data element Case Narrative (ICH E2B(R3) H.1)*
- *Reported values above the upper limits generate an error message*

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
D.2.2b	Age at time of onset of reaction/event (unit)	Mandatory if B.1.2.2.a is not null	50 AN UCUM Year, Month, Week, Day, Hour and {Decade} Mandatory if D.2.2a is populated (Note 9)
D.2.2.1.b & (G.k.6.b Gestation period at time of exposure)	Gestation period when reaction was observed in the Foetus (unit)	3N 802 = Month 803= week 804 = day 805 = Trimester	50 AN (UCUM) Month, Week, Day and Trimester Mandatory if D.2.2.1a is populated

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
D.2.3	Patient Age Group (as per reporter)	[1-6] 1= Neonate 2= Infant 3= Child 4= Adolecent 5= Adult 6=Elderly	[0-6] 0=Foetus 1= Neonate 2= Infant 3= Child 4= Adolecent 5= Adult 6=Elderly At least one of D.1: D.1.1.1, D.1.1.2, D.1.1.3, D.1.1.4, D.2.1, D.2.2A, D.2.2.1a, D.2.3 or D.5 (Note 9)

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

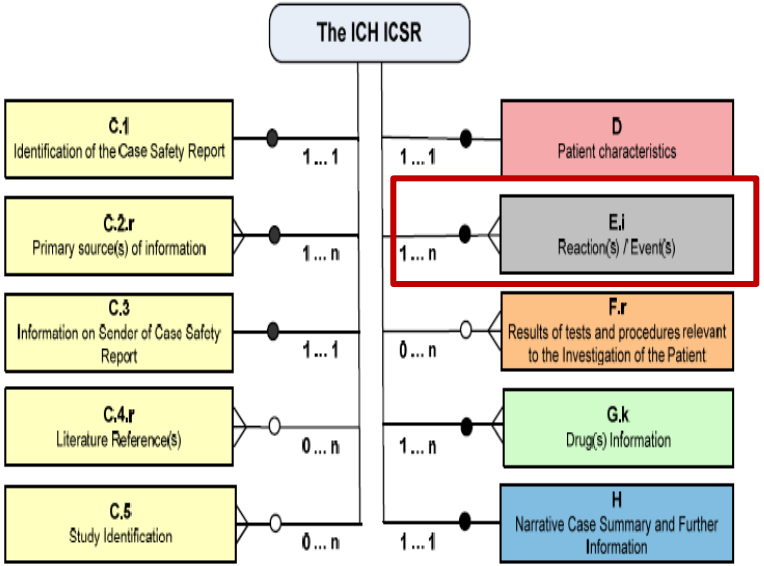
Data element	Description	ICH E2B(R2)	ICH E2B(R3)
D.7.1.r.1.a.	MedDRA version for Medical history	8 AN (x.x) Mandatory if B.1.7.1a.2 Is not NULL	4 AN (N.N) Mandatory if D.7.1.r.1.b is populated Numeric values and the decimal point only (Note 1)
D.7.1.r.1.b.	MedDRA history (disease/ procedure/etc) MedDRA Code	250 AN (Look up MedDRA LLT)	Mandatory if D.7.1.r.1.a is populated

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

NOTE 1:

- *The supported MedDRA versions are related to the EV environment (EV compliance testing environment or production environment) that is the recipient of the Safety Message transmission*
- *It also relates to the current MedDRA version officially published by the MedDRA Maintenance Support Service Organisation (MSSO)*
- *The EV compliance testing environment supports MedDRA version 4.0 and higher*
- *The EV production environment supports the previous and the current MedDRA version*
- *The validation process of the ICSRs accepts only current lower level term (LLT) numeric codes of the supported MedDRA versions*
- *All stakeholders should follow the recommendations of the MedDRA MSSO regarding the switch to a new MedDRA version*
- *The latest supported MedDRA versions in line with the official semi-annual releases are posted on the EudraVigilance website*
- *The use of non-valid or non-current numeric MedDRA LLT codes generates an error message in the validation process*

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

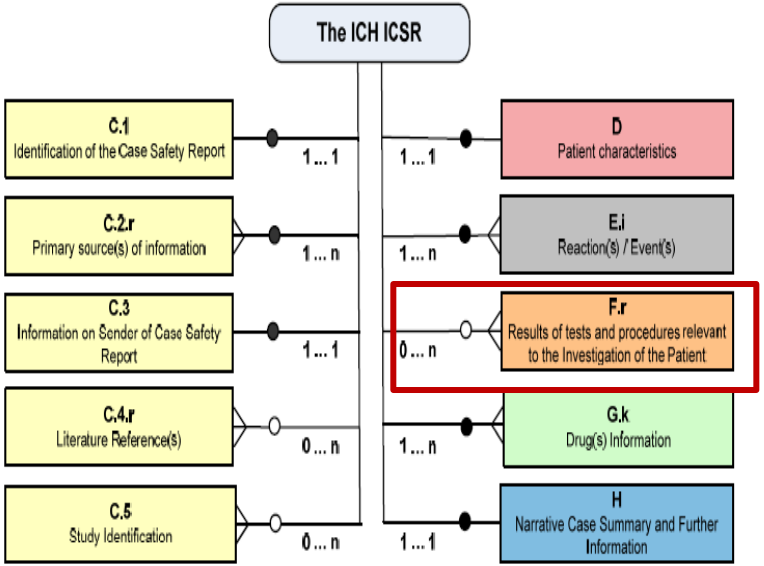


ICH E2B(R3)

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
E.i.9	Identification of the country where the reaction occurred	ISO 3166	ISO 3166-1 alpha 2, including value EU

The ICH E2B(R3) ICSR – EudraVigilance Business Rules



ICH E2B(R3)

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
F.r.1	Test date	Optional	Date/Time CCYY minimum Mandatory if F.r.2.2.b (Test name MedDRA) or F.r.2.1(test name free text) is populated Nullflavor "UNK" is supported (Note 5)

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
F.r.2.2b	Test name (MedDRA code)	A valid MedDRA LLT name or code The failure of a successful match with MedDRA lookup generates an error If necessary, test names and results can be provided in free text in the data element "result test procedures"	Mandatory if F.r.2.2a is populated or if F.r.1 is populated

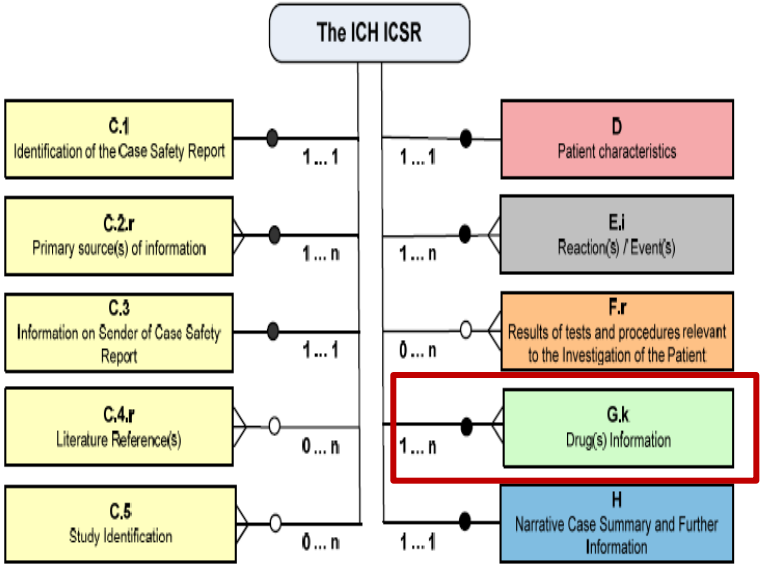
The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
F.r.3.1	Test result (code) 1= positive 2= negative 3= borderline 4= inconclusive	N/A	Mandatory if F.r.2.2b (test name MedRA) is populated, and F.r.3.2 (test result value), or F.r.3.4 (Result Unstructured Data) is not populated
F.r.3.2	Test Result (value/qualifier)	Optional	Madatory if F.r.2.2.b (test name MedDRA) is populated, and F.r.3.1 (test result code), or F.r.3.4 (Result Unstructured Data) is not populated

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
F.r.3.4	Result Unstructured Data	2000 AN Optional	2000 AN Mandatoy if F.r.2.2b (test name MedDRA) is populated, and F.r.3.1 (test result code), or F.r.3.2 (test result value) is not populated

The ICH E2B(R3) ICSR – EudraVigilance Business Rules



ICH E2B(R3)

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
G.k.1	Characterisation of Drug Role	Mandatory 1= suspect 2= concomitant 3= interacting	Mandatory [1-4] 1= suspected 2= concomitant 3= interacting 4= Drug not administered At least one iteration of the Drug section G.k must have the value 1, 3 or 4

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
G.k.2.2	Medicinal Product Name as reported by the Primary Source	70 AN At least one between medicinal product or active substances.	250 AN Mandatory
G.k.2.3.r.1	Substance name	100 AN Mandatory for any transmission to EVCTM (error) or EVPM (warning) when characterisation of drug role is suspected or interacting	250 AN Optional

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
G.k.2.4	Identification of the country where the drug was obtained	ISO 3166	ISO3166-1 alpha-2, including value EU
G.k.3.2	Country of authorisation/ application	ISO 3166	ISO3166-1 alpha-2, including value EU

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
G.k.4.r.1a	Dose (number)	8N	8N Mandatory if G.k.4.r.1b is populated
G.k.4.r.1b (same for G.k.5b Cumulative Dose to First Reaction (unit)	Dose (Unit)	3N [001-032] Mandatory if dose number is not null	50AN UCUM Mandatory if G.k.4.r.1a is populated

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
G.k.4.r.2	Number of units in the interval	3N	4N Mandatory if G.k.4.r.3 is populated unless the definition of the time interval unit (G.k.4.r.3) is 'cyclical', 'as necessary', or 'total'
G.k.4.r.3	Definition of the time interval unit	3 AN (year, week, day, hour, minute, second trimester, cyclical, as necessary, total)	50 AN Mandatory if G.k.4.r.2 is populated

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
G.k.4.r.6a	Dose (number)	8N	8N Mandatory if G.k.4r.6b (Dose Unit) is populated
G.k.4r.6b	Dose (unit)	3N [001-032] Mandatoty if dose number is not null.	50AN UCUM Mandatory if G.k.4.r.6a (Dose number) is populated

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
G.k.4.r.7	Batch / Lot number	35 AN	35 AN Mandatory for all suspected or interacting drugs Field should be completed with a value or an appropiate null flag
G.k.4.r.8	Dosage Text	100 AN	2000 AN
G.k.4.r.9.1	Pharmaceutical dosage form (free text)	100 AN Lookup on dosage forms (Warning)	60 AN

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
G.k.4.r.10.1	Route of administration (free text)	3N	60 AN
G.k.4.r.10.2a (same for G.k.4.r.11.2a)	Route of administration termID version date/ number	N/A	4 (N.N) E2B (R2) 10 AN (free text) E2B R3 Mandatory if G.k.4.r.10.2b is populated; numeric values and the decimal point only
G.k.4.r.10.2b (same for G.k.4.r.11.2b)	Route of administration term ID	N/A	3N (RoA) E2B(R2) 100 AN (RoAID) E2B (R3) Mandatory if G.k.4.r.10.2a is populated

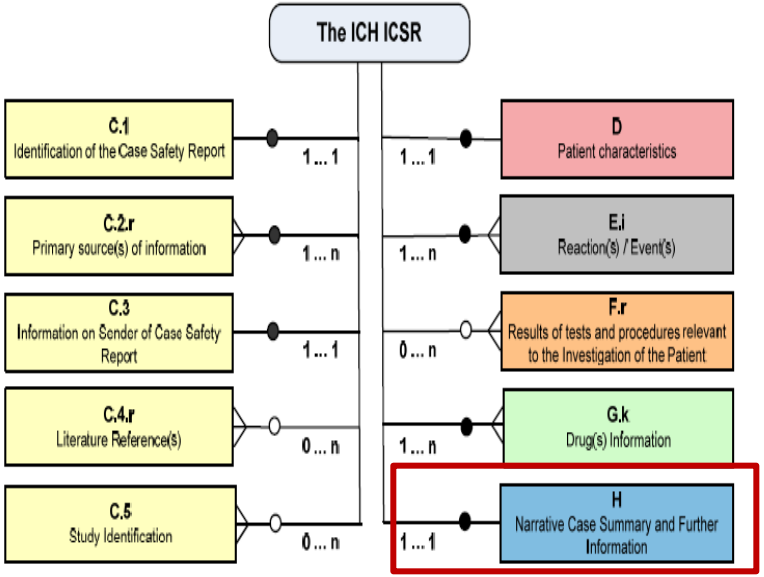
The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
G.k.7.r.1	Indication reported by the primary source	N/A	250AN
G.k.7.r.2a	MedDRA version for indication	8 AN (X.X) Mandatory if B.4.k.11 (Indication MedDRA code) is not null	4AN N.N Mandatory if G.k.7.r.2.b (Indication MedDRA code) is populated Numeric values and the decimal point only (Note 1)

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
G.k.7.r.2b	Indication (MedDRA code)	250 N (Lookup on MedDRA LLT)	8N MedDRA Mandatory if G.k.7.r.2a or G.k.7.r.1 is populated (Note 1)

The ICH E2B(R3) ICSR – EudraVigilance Business Rules



ICH E2B(R3)

The ICH E2B(R3) ICSR – EudraVigilance Business Rules

Data element	Description	ICH E2B(R2)	ICH E2B(R3)
H.1	Case Narrative Including Clinical Course, Therapeutic Measures, Outcome and Additional Relevant Information	20000 AN	100000 AN
H.2	Reporter's comments	500 AN	20000 AN
H.4	Sender's comments	2000 AN	20000 AN

Session summary: What are the key changes for the operation of pharmacovigilance?

In this session you learned:

- To recognise the key changes that will occur with the use of the ICH E2B(R3)/ISO ICSR standard in comparison with the ICH E2B(R2)guideline /M2 format
- To define the areas where adaptation to your pharmacovigilance system and business processes will be required
- To discuss each ICSR section and modifications that have been introduced as part of the ICH ICSR IG
- To describe the main changes as regards the business rules to be applied for the electronic transmission of ICSRs as set out in the EU ICSR IG

Session summary: What are the key changes for the operation of pharmacovigilance?

NOTE 1: training module PhV-G2 will describe the main changes that will be introduced as part of revision 2 of the guideline on Good Pharmacovigilance Practices, Module VI, which will provide guidance on how to use the ICH E2B(R3) format for adverse reaction reporting in the EU

NOTE 2: training module IT-M1 will describe the aspects to be taken into account by IT developers for the ISO ICSR standards implementation

Overview Module PhV-M2a

- Introduction to this training module
- What is the origin of the ISO ICSR and ICH E2B(R3) guideline?
- What are the legal basis and benefits for the use of the new ICSR standard?
- What are the key changes for the operation of pharmacovigilance?
- **How can I get supporting information?**

Session summary: How I can I get supporting information?

In this session you will learn:

- What documents are essential for you to prepare for the implementation of the ISO ICSR standard based on the ICH E2B(R3) Implementation Guide and the EU ICSR Implementation Guide
- How to contact the Service Desk in case you require support or further information

Supporting Documents (1)

Documentation	Description
Guideline on good pharmacovigilance practices (GVP) Module VI – Management and reporting of adverse reactions to medicinal products (Rev 1) *Revision 2 in draft*	• Addresses the legal requirements detailed in Title IX of Directive 2001/83/EC and chapter 3 of Regulation (EC) No 726/2004 as regards the collection, data management and reporting of suspected adverse reactions (serious and non-serious) associated with medicinal products for human use authorised in the European Union (EU).

Supporting Documents (2)

Documentation	Description
EudraVigilance stakeholder change management plan	Details the changes taking place in the EudraVigilance system and to the process of reporting Individual Case Safety Reports (ICSRs)

Supporting Documents (3)

Documentation	Description
European Union individual case safety report (ICSR) implementation guide	• This guidance describes the EU-specific requirements to generate a valid ICSR safety and acknowledgment messages in the international format EN ISO ICSR 27953-2:2011 in accordance with ICH E2B(R3) guidance. • This guidance should be read in conjunction with the ICH E2B(R3) implementation guide and related materials published on the ICH website.
Implementation of the ISO IDMP standards webpage of the Agency	
EudraVigilance webpage of the Agency	

Supporting Documents (4)

Documentation	Description
EU ICSR implementation guide business rules spreadsheet	• This spreadsheet includes all the ICH E2B(R3) and EU specific business rules in a format to help system developers.
EU backwards forwards conversion element mapping spreadsheet	• This document describes the relationship between EU specific data elements in E2B(R3) and E2B(R2). This document is an addition to the ICH backwards-forwards conversion rules. It covers additional EU-specific rules for the conversion back and forth between E2B(R2) and E2B(R3).

Supporting Documents (5)

Documentation	Description
Draft EU BFC conversion	• The ICH backwards-forwards conversion tool updated to include additional EU-specific data fields.
EU E2B(R3) code lists	• The list of codes for EU-specific data fields.
EU reference instances	• ICH reference instances amended to include EU-specific data fields.

Reference: EudraVigilance webpage

Supporting Documents (6)

Documentation	Description
EU example instances	Additional example instances to be used for testing E2B(R3) transmissions to the EudraVigilanceEudraVigilance A centralised European database of suspected adverse reactions to medicines that are authorised or being studied in clinical trials in the European Economic Area (EEA).

Supporting Documents (7)

Documentation	Description
ICH Implementation guide package	• A set of documents including the ICH ICSR implementation guide, backwards and forwards compatibility recommendations and element mapping
ICH E2B(R3) Questions and answers	• A question-and-answer document relevant for technical E2B questions

Supporting Documents (8)

Documentation	Description
Note for guidance – EudraVigilance Human – Processing of safety messages and individual case safety reports (ICSRs) Revision 2	The purpose of this guidance is to describe the aspects of the message processing and acknowledgment generation implemented in EudraVigilance (EV) based on the use of the ICH E2B(R2) guideline
Maintenance of the ICH guideline on clinical safety data management: Data elements for transmission of individual case safety reports E2B(R2)	The purpose of this document is to describe the data elements for the electronic reporting of Individual Case Safety Reports (to be read with the ICH ICSR M2 Version 2.3 Specification Document)

Where can I get support if needed?

EudraVigilance Registration

- Email - eudravigilanceregistration@ema.europa.eu
- Tel - 44 (0) 20 3660 7523

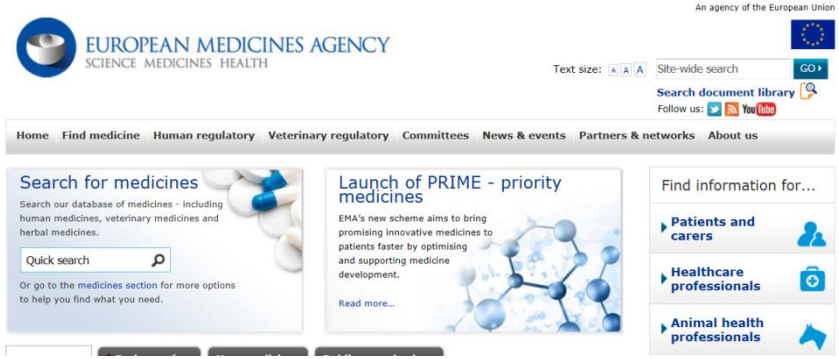
EudraVigilance Operations and IT Operations

- Visit the EMA Service Desk portal: https://servicedesk.ema.europa.eu
- U**rgent** helpline for technical enquiries: +44 (0)20 3660 8520

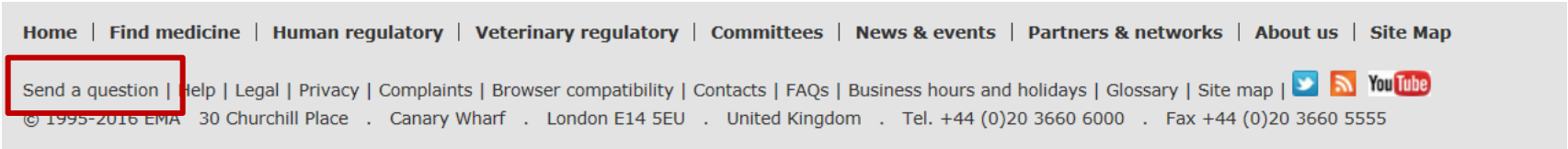
Where can I get support if needed?

Pharmacovigilance operations

- Send a question to EMA (accessible from the EMA homepage)



Web address:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/landing/ask_ema_landing_page.jsp&mid=WC0b01ac05806499f0



Session summary: How I can I get supporting information?

In this session you have learned:

- What documents are essential for you to prepare for the implementation of the ISO ICSR standard based on the ICH E2B(R3) Implementation Guide and the EU ICSR Implementation Guide
- How to contact the Service Desk in case you require support or further information

Overview Module PhV-M2a

- Introduction to this training module
- What is the origin of the ISO ICSR and ICH E2B(R3) standard?
- What are the legal basis and benefits for the use of the new ICSR standard?
- What are the key changes for the operation of pharmacovigilance?
- How can I get supporting information?

Summary of PhV-M2a

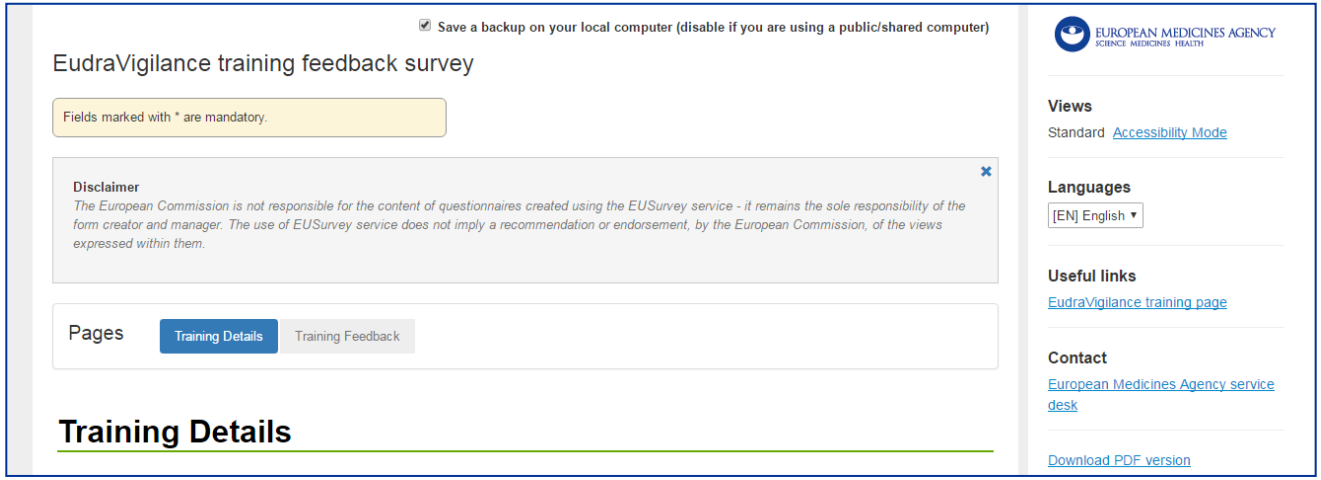
We are now at the end of the training module PhV-M2a, which provided you to basis for:

- Understanding the origin of the ISO ICSR and ICH E2B(R3) standard and the ICH E2B(R3) Implementation Guide (IG)
- Describe the legal basis and the benefits for the use of the ISO ICSR/ICH E2B(R3) guideline
- Recognise the impact on pharmacovigilance with the move from the ICH E2B(R2)guideline /M2 format to the E2B(R3) guideline/ISO ICSR standard
- Describe changes to the business rules as outlined in the EU ICSR IG
- Understand where to obtain supporting information

Feedback

- Please provide us with feedback on this E-learning module and any attendant guidance documents you have viewed by taking the EMA training survey.

- The survey is accessible via this link.



Acronyms (1)

Acronym	Description
CDISC	Clinical Data Interchange Consortium
CEN	European Committee for Standardization
CV	Controlled Vocabulary
EEA	European Economic Area
EU	European Union
EV	EudraVigilance
HL7	Health Level 7

Acronyms (2)

Acronym	Description
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICSR	Individual Case Safety Reports
IDMP	Identification of Medicinal Products
IHTSDO	International Health Terminology Standards Development Organisation
IG	Implementation Guide
ISO	International Organization for Standardization

Acronyms (3)

Acronym	Description
MAH	Marketing authorisation holder
MedDRA	Medical Dictionary for Regulatory Activities
MPID	Medicinal Product Identifier
NCA	National competent authority
OID	Object Identifier
PHPID	Pharmaceutical Product Identifier
PhV	Pharmacovigilance

Acronyms (4)

Acronym	Description
SDO	Standards Development Organisation
UCUM	Unified Code for Units of Measure

Thank you for your attention

Further information

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