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ICH E2B Implementation Working Group

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

E2B(R3) Data Elements and Message Specification

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Table of Contents

INTRODUCTION **14**

1.0 Purpose **15**

1.1 Scope 15

1.2 Business Case 15

2.0 Background **16**

2.1 General Background and History of ICH 16

2.1.1 The ICH and its Partners 16

2.1.2 History of ICH ICSR guidelines 16

2.1.3 The Process of Revision in ICH 17

2.2 Development of ICSR Standard under Joint Initiative 17

2.3 Background of Message Standard 18

2.4 Representation of the Electronic ICSR 18

2.4.1 Why Standardisation and Electronic ICSR Exchange are Needed 18

2.4.2 How ICSRs Are Presently Transmitted and the Advantages of Electronic Submissions 19

3.0 Essential Components **21**

3.1 ICH ICSR Relational Diagrams 21

3.2 Code Sets, Terminologies and Vocabularies for E2B(R3) 23

3.2.1 Terminologies and Vocabularies Employed by the ICSR Message 23

3.2.2 ICH Maintained Code Sets and Object Identifiers (OIDs) Created for the ICH ICSR 27

3.2.3 International Standard Code Sets 30

3.3 ICH E2B(R3) Specifications for the Transmission of ICSRs 32

3.3.1 Minimum Information 32

3.3.2 Definition of Data Elements within a Message 32

3.3.3 General Principles 33

3.3.4 Retransmission of cases 33

3.3.5 Notes on Format of Data Elements 34

3.3.6 General rules for Data Entry 35

3.3.7 Details of ICH E2B(R3) Data Elements 39

3.4 ICH E2B(R3)DATA ELEMENTS 41
N.1 ICH ICSR Transmission Identification (batch wrapper) 41
N.1.1 Type of Messages in Batch 41
N.1.2 Batch Number 41
N.1.3 Batch Sender Identifier 42
N.1.4 Batch Receiver Identifier 42
N.1.5 Date of Batch Transmission 42
N.2.r ICH ICSR Message Header (message wrapper) (repeat as necessary) 43
N.2.r.1 Message Identifier 43
N.2.r.2 Message Sender Identifier 44
N.2.r.3 Message Receiver Identifier 44
N.2.r.4 Date of Message Creation 44
C.1 Identification of the Case Safety Report 45
C.1.1 Sender's (case) Safety Report Unique Identifier 46
C.1.2 Date of Creation 47
C.1.3 Type of Report 48
C.1.4 Date Report Was First Received from Source 48
C.1.5 Date of Most Recent Information for This Report 49
C.1.6 Additional Available Documents Held by Sender 49
C.1.6.1 Are Additional Documents Available? 49
C.1.6.1.r Documents Held by Sender (repeat as necessary) 50
C.1.7 Does This Case Fulfil the Local Criteria for an Expedited Report? 50
C.1.8 Worldwide Unique Case Identification 51
C.1.8.1 Worldwide Unique Case Identification Number 51
C.1.8.2 First Sender of This Case 52
C.1.9 Other Case Identifiers 52
C.1.10.r Identification Number of the Report Linked to This Report (repeat as necessary) 54
C.1.11 Report Nullification / Amendment 54

C.2.r Primary Source(s) of Information (repeat as necessary) 56
C.2.r.1 Reporter's Name 57
C.2.r.2 Reporter's Address and Telephone 58
C.2.r.3 Reporter's Country Code 60
C.2.r.4 Qualification 61
C.2.r.5 Primary Source for Regulatory Purposes 61
C.3 Information on Sender of Case Safety Report 62
C.3.1 Sender Type 62
C.3.2 Sender's Organisation 63
C.3.3 Person Responsible for Sending the Report 63
C.3.4 Sender's Address, Fax, Telephone and E-mail Address 65
C.4.r Literature Reference(s) (repeat as necessary) 68
C.4.r.1 Literature Reference(s) 68
C.4.r.2 Included Documents 68
C.5 Study Identification 69
C.5.1.r Study Registration (repeat as necessary) 69
C.5.1.r.1 Study Registration Number 69
C.5.1.r.2 Study Registration Country 70
C.5.2 Study Name 70
C.5.3 Sponsor Study Number 70
C.5.4 Study Type Where Reaction(s) / Event(s) Were Observed 71
D Patient Characteristics 72
D.1 Patient (name or initials) 76
D.1.1 Patient Medical Record Number(s) and Source(s) of the Record Number 76
D.2 Age Information 78
D.2.1 Date of Birth 78
D.2.2 Age at Time of Onset of Reaction / Event 79
D.2.2.1a Gestation Period When Reaction / Event Was Observed in the Foetus 79
D.2.3 Patient Age Group (as per reporter) 81
D.3 Body Weight (kg) 81
D.4 Height (cm) 82

D.5 Sex 82
D.6 Last Menstrual Period Date 82
D.7 Relevant Medical History and Concurrent Conditions (not including reaction / event) 83
D.7.1.r Structured Information on Relevant Medical History (repeat as necessary) 83
D.7.2 Text for Relevant Medical History and Concurrent Conditions 85
D.7.3 Concomitant Therapies 86
D.8.r Relevant Past Drug History (repeat as necessary) 86
D.8.r.1 Name of Drug as Reported 88
D.8.r.2 Medicinal Product Identifier (MPID) 88
D.8.r.3 Pharmaceutical Product Identifier (PhPID) 89
D.8.r.4 Start Date 89
D.8.r.5 End Date 89
D.8.r.6 Indication (MedDRA code) 90
D.8.r.7 Reaction (MedDRA code) 90
D.9 In Case of Death 91
D.9.1Date of Death 91
D.9.2.r Reported Cause(s) of Death (repeat as necessary) 91
D.9.2.r.1b Reported Cause(s) of Death (MedDRA code) 91
D.9.2.r.2 Reported Cause(s) of Death (free text) 92
D.9.3 Was Autopsy Done? 92
D.9.4.r Autopsy-determined Cause(s) of Death (repeat as necessary) 92
D.10 For a Parent-child / Foetus Report, Information Concerning the Parent 94
D.10.1 Parent Identification 94
D.10.2 Parent Age Information 94
D.10.2.1 Date of Birth of Parent 94
D.10.2.2 Age of Parent 95
D.10.3 Last Menstrual Period Date of Parent 95
D.10.4 Body Weight (kg) of Parent 95
D.10.5 Height (cm) of Parent 96
D.10.6 Sex of Parent 96
D.10.7 Relevant Medical History and Concurrent Conditions of Parent 96

D.10.7.1.r Structured Information of Parent (MedDRA code) (repeat as necessary) 96
D.10.7.2 Text for Relevant Medical History and Concurrent Conditions of Parent..... 98
D.10.8.r Relevant Past Drug History of Parent (repeat as necessary) 98
D.10.8.r.1 Name of Drug as Reported 98
D.10.8.r.2 Medicinal Product Identifier (MPID) 99
D.10.8.r.3 Pharmaceutical Product Identifier (PhPID) 99
D.10.8.r.4 Start Date 99
D.10.8.r.5 End Date 100
D.10.8.r.6 Indication (MedDRA code) 100
D.10.8.r.7 Reactions (MedDRA code) 101
E.i REACTION(S)/EVENT(S) (REPEAT AS NECESSARY) 102
E.i.1 Reaction / Event as Reported by the Primary Source 103
E.i.1.1 Reaction / Event as Reported by the Primary Source in Native Language 103
E.i.1.2 Reaction / Event as Reported by the Primary Source for Translation 103
E.i.2.1 Reaction / Event (MedDRA code) 104
E.i.3.1 Term Highlighted by the Reporter 104
E.i.3.2 Seriousness Criteria at Event Level (more than one can be chosen) 104
E.i.3.2a Results in Death 105
E.i.3.2b Life Threatening 105
E.i.3.2c Caused / Prolonged Hospitalisation 105
E.i.3.2d Disabling / Incapacitating 105
E.i.3.2e Congenital Anomaly / Birth Defect 106
E.i.3.2f Other Medically Important Condition 106
E.i.4 Date of Start of Reaction / Event 106
E.i.5 Date of End of Reaction / Event 107
E.i.6 Duration of Reaction / Event 107
E.i.7 Outcome of Reaction / Event at the Time of Last Observation 108
E.i.8 Medical Confirmation by Healthcare Professional 108
E.i.9 Identification of the Country Where the Reaction / Event Occurred 109
F.r Results of Tests and Procedures Relevant to the Investigation of the Patient (repeat as necessary) 109

F.r.1 Test Date 110
F.r.2 Test Name 110
F.r.2.1 Test Name (free text) 110
F.r.2.2 Test Name (MedDRA code) 111
F.r.3 Test Result 111
F.r.3.1 Test Result (code) 111
F.r.3.2 Test Result (value / qualifier) 112
F.r.3.3 Test Result (unit) 112
F.r.3.4 Result Unstructured Data (free text) 113
F.r.4 Normal Low Value 114
F.r.5 Normal High Value 114
F.r.6 Comments (free text) 114
F.r.7 More Information Available 115
G.k DRUG(S) INFORMATION (REPEAT AS NECESSARY) 116
G.k.1 Characterisation of Drug Role 119
G.k.2 Drug Identification 120
G.k.2.1 Medicinal Product Unique Identifier/Pharmaceutical Product Unique Identifier 121
G.k.2.2 Medicinal Product Name as Reported by the Primary Source 122
G.k.2.3.r Substance / Specified Substance Identifier and Strength (repeat as necessary) . 122
G.k.3 Holder and Authorisation / Application Number of Drug 125
G.k.3.1 Authorisation / Application Number 125
G.k.3.2 Country of Authorisation / Application 126
G.k.3.3 Name of Holder / Applicant 126
G.k.4.r Dosage and Relevant Information (repeat as necessary) 126
G.k.4.r.1a Dose (number) 127
G.k.4.r.1b Dose (unit) 127
G.k.4.r.2 Number of Units in the Interval 127
G.k.4.r.3 Definition of the Time Interval Unit 127
G.k.4.r.4 Date and Time of Start of Drug 128
G.k.4.r.5 Date and Time of Last Administration 128
G.k.4.r.6 Duration of Drug Administration 128

G.k.4.r.7 Batch / Lot Number 129
G.k.4.r.8 Dosage Text 129
G.k.4.r.9 Pharmaceutical Dose Form 131
G.k.4.r.10 Route of Administration 132
G.k.4.r.11 Parent Route of Administration (in case of a parent child / foetus report) 133
G.k.5 Cumulative Dose to First Reaction 134
G.k.6 Gestation Period at Time of Exposure 134
G.k.7.r Indication for Use in Case (repeat as necessary) 135
G.k.7.r.1 Indication as Reported by the Primary Source 135
G.k.7.r.2 Indication (MedDRA code) 135
G.k.8 Action(s) Taken with Drug 136
G.k.9.i Drug-reaction(s) / Event(s) Matrix (repeat as necessary) 136
G.k.9.i.1 Reaction(s) / Event(s) Assessed 137
G.k.9.i.2 Assessment of Relatedness of Drug to Reaction(s)/Event(s) 138
G.k.9.i.3 Time Interval between Beginning of Drug Administration and Start of Reaction / Event ... 139
G.k.9.i.4 Did Reaction Recur on Re-administration? 140
G.k.10.r Additional Information on Drug (coded) (repeat as necessary) 140
G.k.11 Additional Information on Drug (free text) 141
H NARRATIVE CASE SUMMARY AND FURTHER INFORMATION 142
H.1 Case Narrative Including Clinical Course, Therapeutic Measures, Outcome and Additional Relevant Information 142
H.2 Reporter's Comments 143
H.3.r Sender's Diagnosis (MedDRA code) (repeat as necessary) 143
H.4 Sender's Comments 144
H.5.r Case Summary and Reporter’s Comments in Native Language (repeat as necessary) 144
H.5.r.1a Case Summary and Reporter’s Comments Text 144
H.5.r.1b Case Summary and Reporter’s Comments Language 144
3.5 DOCUMENT ATTACHMENTS 145
3.5.1 User Guidance 145
3.5.2 Technical specification 145
3.5.3 Examples of XML instances 146

4.0 THE ICSR ACKNOWLEDGEMENT TRANSACTION 147
4.1 Acknowledgement Message in HL7 147
4.2 ICH ICSR Acknowledgement Message 147
ACK.M / A ICH ICSR Batch Acknowledgement 149
ACK.M.1 Acknowledgement Batch Number 149
ACK.M.2 Acknowledgement Batch Sender Identifier 149
ACK.M.3 Acknowledgement Batch Receiver Identifier 150
ACK.M.4 Acknowledgement Date of Batch Transmission 150
ACK.A.1 ICSR Batch Number 151
ACK.A.2 Acknowledgement Local Message Number 151
ACK.A.3 Date of ICSR Batch Transmission 151
ACK.A.4 Transmission Acknowledgement Code 152
ACK.A.5 Batch Validation Error 152
ACK.B ICH ICSR Message Acknowledgement 152
ACK.B.r.1 ICSR Message Number 152
ACK.B.r.2 Local Report Number 152
ACK.B.r.3 ICSR Message ACK Receiver 153
ACK.B.r.4 ICSR Message ACK Sender 153
ACK.B.r.5 Date of ICSR Message Creation 153
ACK.B.r.6 Acknowledgement Code for a ICSR Message 154
ACK.B.r.7 Error / Warning Message or Comment 154
APPENDICES 155
APPENDIX I – PREPARING AND SENDING ICH ICSRS: 155
Appendix I (A) – ICH ICSR SCHEMAs 155
1. List of schemas for ICH ICSR messages and ICSR Acknowledgement messages 155
2. User Guidance for each ICH ICSR schemas 156
Appendix I (B) – Backwards & Forwards Compatibility 160
Appendix I (C) – Schema files 160
Appendix I (D) – Reference Instances for ICH ICSR message and ICSR Acknowledgement message 160
Appendix I (E) – Example Instances of report cases 160
Appendix I (F) – ICH E2B code lists 161

Appendix I (G) – Technical Information..... 161
Appendix I (H) – SGML & XML conversion..... 161
APPENDIX II – DATE / TIME 162
Appendix II (A) Date / Time..... 162
Appendix II (B) Time Zone..... 163
Appendix II (C) ISO 8601 Compliant XML Examples 163
APPENDIX III - ABBREVIATIONS and GLOSSARY OF TERMS..... 164
Appendix III (A)ABBREVIATIONS..... 164
Appendix III (B) GLOSSARY of TERMS 166

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Introduction

This document is a guide for implementing the standard adopted by the ICH[1] for electronic transmission of *Individual Case Safety Reports* (ICSRs) according to the ICH E2B(R3) message standard. This *Implementation Guide* (IG) was jointly developed by the ICH E2B(R3) and M2 *Expert Working Groups* (EWGs). The ICH E2B(R3) EWG provided business requirements and the M2 EWG provided technical content for this IG. These two EWGs were reconstituted as the ICH E2B(R3) EWG in November 2010.

Conceptually, an ICSR is a report of information describing adverse event(s) / reaction(s) experienced by an individual patient.

This ICH IG focuses on medicinal products and therapeutic biologics for human use. However, the ICH is aware of other regional applications of the messaging standard that have a wider scope, such as pharmacovigilance activities related to vaccines, herbal products, cosmetics, veterinary products or medical devices. The primary ICH application is for the exchange of pharmacovigilance information between and among the pharmaceutical industry and regulatory authorities.

This IG is also intended to support the implementation of software and tools for creating, editing, sending and receiving electronic ICSR messages.

This IG is not intended to serve as a reference for proper pharmacovigilance practices nor is it intended to explain the underlying scientific or medical issues that support the collation, categorisation or analysis of medicinal product safety information. It is also not intended to explain the rationale that underlies proper case safety reporting.

The focus of this ICH IG is on technical implementation. Thus, the 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. This IG provides the information necessary to support the development of adequate informatics tools (e.g., forms and interfaces for end user data entry) as well as technical requirements to design style sheets, conduct data transformations and code well-formed messages. However, this IG does not provide or infer guidance or recommendations for any particular database technology or software platform. Instead, this IG describes the technical requirement to generate valid *eXtensible Markup Language* (XML) code according to the standard outlined in this IG.

Subsequent sections of this IG provide explanatory text concerning the business context for electronic ICSR messaging, including ICH documentation, and application to pharmacovigilance transactions.

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[1]The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) http://www.ich.org/

1.0 Purpose

The business objective of this ICH IG is to standardise the definitions of the data elements used in the electronic transmission of different types of ICSRs, regardless of source and destination. This IG describes data elements for ICSRs for both the pre- and post-authorisation periods, and addresses both adverse drug reaction reports and adverse event reports. The technical objective of this IG is to assist reporters and recipients (including pharmaceutical companies, regulatory authorities and non-commercial sponsors) in implementing systems to construct transmittable ICSR messages. The representation of the ICSR follows an international standard that is platform-, application-, and vendor-independent.

1.1 Scope

The representation of the ICSR in this IG, in its format and content, is made up of a large number of data elements, allowing precise reporting of medical content to most business partners, including regulatory authorities. For example, the data elements and their format are suitable to describe several types of case reports including those without adverse events or adverse drug reactions, such as medicinal product administration during pregnancy, overdose, medication error, or potential lack of efficacy. Therefore, in order to maintain the integrity and usability of the standard, requests for inclusion of additional local data should not be necessary and should be avoided as much as possible. The scope of this IG for the ICH E2B(R3) ICSR does not include the definition of database structures, the design of a paper report form, quality control/quality assurance aspects, or technical security issues.

1.2 Business Case

Because of national and international agreements, rules, regulations, and the protection of patient safety, there is a need to expedite the exchange of safety information (e.g., ICSRs):

- from identified reporting sources to regulatory authorities and pharmaceutical companies;
- between regulatory authorities;
- between pharmaceutical companies and regulatory authorities;
- between pharmaceutical companies;
- from clinical investigators, via the sponsor of a clinical trial, to ethics committees; or
- from authorities to the World Health Organisation (WHO) Collaborating Centres for International Drug Monitoring.

The exchange of safety information is based on paper-based formats (e.g., Yellow Cards, CIOMS I forms, MedWatch forms, etc.) or electronic media (e.g., on-line access, tape, CD, etc.). Considering the large number of potential participants in a world-wide exchange of information, there should be a standard format that is capable of accommodating direct database-to-database transmission using standardised message transfers. Successful electronic transmission of information relies on the consistent and uniform interpretation of definitions for common data elements and standard transmission procedures, such as those provided in this document.

Over the last decade as the number of case reports has increased, exchange of ICSRs has increasingly shifted from paper-based to electronic reports and electronic transmission of case safety information has become an important component of global pharmacovigilance. The ICH released a consensus electronic standard for ICSRs in 1997 and this standard has undergone a number of revisions since it was first adopted. The ICH E2B(R2) standard has been used for regulatory compliance purposes for several years and, indeed, is now mandatory in some ICH regulatory jurisdictions and is widely accepted.

Development of the standard described in this IG represents a change of the ICH process, as the messaging standard was developed through a partnership with external *Standards Development Organisations* (SDOs). Prior to the message standard described in this IG, ICH electronic messaging standards were developed by the ICH M2 EWG for *Electronic Standards for the Transmission of Regulatory Information* (ESTRI). Specifically, the current message standard was developed through a collaborative relationship between the ICH and the *Joint Initiative Council* (JIC); the JIC is a partnership of the *International Organisation for Standardisation* (ISO), the *Health Level Seven* (HL7), the *European Committee for Standardisation* (CEN), the *Clinical Data Interchange Standards Consortium* (CDISC), the *International Health Terminology Standards Development Organisation* (IHTSDO), and GS1[2]. The ICSR standard named "*ISO / HL7 27953-2: 2011 Health informatics -- Individual case safety reports (ICSRs) in pharmacovigilance -- Part 2: Human pharmaceutical reporting requirements for ICSR"* is available at the ISO website (http://www.iso.org/iso/store.htm).

2.0 BACKGROUND

2.1 General Background and History of ICH

2.1.1 The ICH and its Partners

The ICH brings together regulatory authorities and the pharmaceutical industry to harmonise scientific and technical aspects of drug registration.
Further information about ICH and its work products is available from the ICH website.

2.1.2 History of ICH ICSR guidelines

The first ICH E2B guideline, *Data Elements for Transmission of Individual Case Safety Reports*, was endorsed on July 17, 1997. It was modified in November 2000, and then published with minor editorial changes in February 2001 as the ICH *Step 4* E2B(M) guideline. As part of an ICH document management initiative, the *Step 4* E2B(M) guideline was retitled as the E2B(R2) guideline in May 2005; there was no change in business content. The ICH M2 EWG prepared the *Electronic Transmission of Individual Case Safety Reports Message Specification* guideline

[2]GS1 is an international not-for-profit association dedicated to the design and implementation of global standards and solutions to improve the efficiency and visibility of supply and demand chains globally and across sectors.

in 2001 to standardise the data elements for the electronic transmission of ICSRs by identifying and defining the core elements for an ICSR, regardless of source or destination.

2.1.3 The Process of Revision in ICH

Considering the high volume of data and the large number of potential participants involved with the world-wide exchange of safety information, there is an ongoing need for efficient transmission of safety reports in a format that can be generated and processed nearly automatically by a transactional database. This need has led to periodic revisions of the E2B document, as described in Section 2.1.2 (above). The E2B(R3) message represents an iteration of the electronic ICSR that has evolved in a controlled fashion over more than a decade.

Successful electronic transmission of ICSRs relies on standard common data elements and syntactical definition of the electronic message. Therefore, the adoption of a standardised electronic message across regions, regulatory agencies, and other participants is of paramount importance. In 2006, the ICH decided to pursue an alternative model for the development of the third revision of E2B that engaged SDOs. This IG describes the messaging standard for the implementation of the E2B(R3) message developed through this new process.

In order to broaden the ICH's outreach and be able to develop a global, harmonised and implementable electronic messaging standard, the ICH Steering Committee, which is the body that governs the ICH, made a decision to align its development efforts with SDOs. The ISO, HL7, CEN, CDISC and IHTSDO, along with their respective *technical committees* (TCs) and stakeholders for health informatics standardisation, have collectively identified an opportunity to collaborate, coordinate, and cooperate so their efforts will support the creation of global electronic health informatics standards that can be integrated into the broader healthcare environment.

To that end, the SDOs noted above have formed a *Joint Initiative* to address and resolve issues of gaps, overlaps, and counter-productive standardisation efforts through an agreed-upon decision process. Governance of the Joint Initiative is via a *Joint Initiative Council* (JIC), which has representation from each member SDO. This approach facilitates a single best standard for each problem with mutual recognition and endorsement of standards by participating SDOs. For the ICH, working with SDOs to leverage resources for electronic standards development and avoid overlapping, counter-productive, or counter-acting standards is critical to achieving and maintaining its own harmonisation goals.

2.2 Development of ICSR Standard under Joint Initiative

The ICH's original New Work Item Proposal to ISO for the ICSR standard was accepted as an ISO Project activity, *ISO 27953*, and was subsequently endorsed as a Joint Initiative project in February 2008. The ICSR standard was considered a candidate for SDO harmonisation because of global interest in improving patient safety through the electronic exchange of unambiguous, structured data to support regulatory and patient safety needs.

The ISO 27953 consolidates content and messaging specifications based on ISO New Work Item Proposal N545 (*Pharmacovigilance - Structure and Data Elements of Individual Case Safety Report*), HL7 ICSR Release 1 Normative Standard, and HL7 ICSR Release 2 *Draft Standard for Trial Use* (DSTU). The ICSR standard was developed through the ISO ballot process, *Draft International Standard*, *Final Draft International Standard*, and *International Standard* (IS). The standard was published by ISO as the IS in November 2011.

2.3 Background of Message Standard

The HL7 *version 3* (V3) messaging standard deals with a static model of health care information as viewed within the scope of HL7 standards development activities. ISO recognises HL7 as an accredited partnering organisation for mutually issuing standards. The first mutually published standard was *ISO/HL7 21731:2006 Health informatics -- HL7 version 3 -- Reference Information Model -- Release 1*[3]. HL7 V3 was developed to address the complex needs of health information technology. The HL7 *Reference Information Model* (RIM) is the cornerstone of HL7 V3 and the essential model from which all HL7 messages are derived. The RIM defines data content needed in a specific context and provides an explicit representation of the semantic and lexical connections that exist between the information carried in the elements of a message. HL7 V3 supports development of specifications that facilitate interoperability between systems. The HL7 model-driven methodology is used to develop consensus-based standards for healthcare system interoperability and information exchange. HL7 V3 messages are based on an XML encoding syntax. To learn more about HL7 V3, refer to "*Understanding Version 3: A primer on the HL7 Version 3 Healthcare Interoperability Standard – Normative Edition,"* by Andrew Hinchley. The ISO / HL7 27953-2 standard is built upon the HL7 ICSR Release 3 standard (or HL7 ICSR R3). The HL7 ICSR R3 standard is a particular message based on the HL7 V3.

A framework of ICSR standard published as "*ISO / HL7 27953-1:2011 Health informatics -- Individual case safety reports (ICSRs) in pharmacovigilance -- Part 1: Framework for adverse event reporting"* supports message transmissions in drugs, medical devices, veterinary drugs, cosmetic, and dietary supplements. The ICH E2B(R3) message standard is founded on the ISO / HL7 27953-2 standard, which is constrained from ISO / HL7 27953-1 to provide an "ICH sub-set" of the standard supporting electronic messaging for the ICH E2B(R3) data elements. Although this standard is the "ICH sub-set", it can be applied to regions and business cases beyond the narrower use described in this ICH E2B(R3) IG. Elements of the ISO / HL7 27953-2 standard which solely relate to use cases outside the remit of ICH will not be addressed within this document. Detailed information about ISO/HL7 27953-2 can be obtained from ISO web site: http://www.iso.org/iso/home/store.htm.

2.4 Representation of the Electronic ICSR

2.4.1 Why Standardisation and Electronic ICSR Exchange are Needed

[3] Available from the HL7 Website, at http://www.hl7.org

ICSRs are exchanged primarily to enhance patient safety thereby promoting public health. Furthermore, ICSRs need to be transmitted across stakeholder communities throughout the health product lifecycle, during clinical investigation as well as for continued safety monitoring once authorised for marketing. Electronic reporting facilitates the transfer of information and makes safety data readily available for further processing and analysis. These advantages allow regulators, MAHs, *healthcare professionals* (HCPs) and consumers to make better-informed decisions regarding the use of health products.

Without harmonization, the existence of a multiplicity of message and / or content standards across regions and regulatory jurisdictions would result in diseconomies of scale and increase the burden for reporters. A lack of harmonisation might lead to difficulties in reconciling ICSRs on the global level. A harmonised standard should stimulate vendors to develop "off-the-shelf" tools that are interoperable due to the standard itself. A harmonised standard will also help maximise forward compatibility of data and minimise the complexities of backward compatibility. For these reasons, health authorities and the pharmaceutical industry are moving in unison toward a meaningful, harmonised standard for use by all constituents.

2.4.2 How ICSRs Are Presently Transmitted and the Advantages of Electronic Submissions

To support the ICH E2B guideline, the ICH M2 EWG published the "*Electronic Transmission of Individual Case Safety Reports Message Specification (ICH ICSR DTD Version 2.1), Final Version 2.3"* in February of 2001. At that time, prior work on the standardisation of an electronic message by HL7 and *Electronic Data Interchange for Administration, Commerce and Transport* (EDIFACT) was considered, but the ICH selected *Standard Generalised Markup Language* (SGML, ISO 8879:1986) as the preferred alternative because SGML was the de facto standard for the interchange of information. SGML also supported the multi-lingual character sets needed across ICH regions.

In spite of this fact, the SGML-based *Document Type Definition* (DTD) approach is no longer the optimal solution. As a result, the current messaging standard herein now relies upon XML schemas. The reasoning is explained below.

2.4.2.1 Markup Languages[4]

First published in 1988, SGML is an ISO standard (ISO 8879) designed to describe the structure and content of electronic documents, with an original purpose of enabling the exchange of electronic documents between business entities that need information to be available for extended periods of time (archived). It serves as a basis for XML, which is simpler than SGML yet maintains the most useful parts of SGML.

[4] "Co-existence of Traditional EDI with XML-EDI", Skip Stein, Management Systems Consulting, Inc., http://www.msc-inc.net/

SGML requires that structured documents reference a DTD to be valid. The DTD is the tool used to create and describe the expected SGML or XML. Simply, a DTD specifies the syntax (the elements, attributes, entities, and notations) required in a document authored in SGML or XML. Once a DTD is created and a document is written based on that DTD, the document is then compared to the DTD. This is referred to as validation. If the document follows the rules listed in the DTD, then the document is said to be valid. SGML/XML documents that do not follow the rules in their DTDs are categorised as invalid.

The DTD specifies the required structure and format of a particular document. XML is more flexible than SGML and allows for the concept of "well-formed" data – content that meets the basic vocabulary and 'grammatical' requirements of XML but does not reference a DTD for a specific set of attributes or list of required elements. XML contains a further concept called a schema. An XML schema introduces both the ability to apply more complex constraints and the ability to have more flexibility in well-formed data.

In general, DTDs perform well when applied to documents or text-intensive information. XML schema work best for data-intensive information[5]. One challenge with DTDs is that they represent two different things at the same time: a grammar and a schema. Because XML syntax is "fixed", it does not need "grammar" to properly access the information content. In addition, XML schemas can be manipulated, stored, and indexed, which is a practical advantage[6].

Another advantage to XML is that Unicode is universally present in all XML parsers. Except for more recent ones, most SGML parsers do not provide Unicode support[7]. Unicode provides a "unique" code (a number) for each character. Thus, characters are represented in an abstract way while the visual rendering (size, shape, font or style) is left to other applications, such as a web browser or word processor. In this way, translation between languages is built into the use of XML[8].

2.4.2.2 Advantages to Electronic Submissions

The ICH chose to adopt an XML schema for the ICSR as it is more suitable for the intended purpose: XML is portable and non-proprietary. It can be used to store and share information electronically across platforms. XML is used for encapsulating information to be passed between two computing systems which might otherwise be unable to communicate. It provides a common

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[5] Tittel, Ed, Pitts, Natanya, and Boumphrey, Frank.XML for Dummies. New York: Wiley Publishing, Inc., 2002.

[6] "Beyond the SGML DTD", François CHAHUNEAU, Directeur Général / General Manager, AIS S.A., 15-17 rue Rémy Dumoncel, 75014, Paris, FRANCE, http://xml.coverpages.org/chahuneauXML.html

[7] "XML: What HTML Wanted to Be!", Norma Haakonstad, National Accounts Manager, Arbortext, Inc., 1000 Victors Way, Ann Arbor (Michigan) 48108

[8] "Unicode". Wikipedia<http://en.wikipedia.org/wiki/Unicode>, 18SEP2008.

envelope for inter-process communication (messaging). It is supported by an international standard and will, therefore, remain accessible[9].

The ICH ICSR enhances electronic adverse event reporting and analysis by facilitating the efficient reporting of suspected product-related adverse events / reactions. The electronic environment:

- improves the ability to efficiently exchange and process ICSR data;
- facilitates the transfer of information to organisations who need it;
- enables incoming messages to be automatically routed and processed;
- facilitates aggregation of safety data for analysis; and
- allows minimising resources required for data (re-)entry activities.

3.0 ESSENTIAL COMPONENTS

Developing software specifications to support business needs, such as those specified in E2B(R3), calls for an approach where the functional and procedural requirements are well understood and reflected accurately in the electronic message. The electronic message must not only contain an accurate definition of the data elements (XML schema), but also maintain any required relationships between the elements for efficient information exchange. The development of relational diagrams, attribute lists, numeric codes, and a constrained ICH ICSR schema are all parts of the process of developing the software specifications to facilitate electronic transmission of ICSRs. The ICH ICSR message allows for the preparation of adverse event / reaction data sets that can accurately maintain and represent the intended purpose of the E2B(R3) document. Section 3 of this IG lists the exact E2B(R3) data elements and essential components to develop usable and exchangeable ICH ICSR messages. Necessary schemas for the ICH ICSR message are listed in Appendix I (A).

3.1 ICH ICSR Relational Diagrams

Figure 1 below illustrates the relationship between the main sections defined in E2B(R3) for the ICH ICSR message and XML descriptors. Each box in the diagram represents a related section of the E2B(R3) data element structure, and all the data elements in that block are listed in the attribute list (Section 3.4). For example, box C.1 in the diagram *Identification of the Case Safety Report* represents the complete C.1 section of the E2B(R3) data elements and the C.1 block of elements listed in the ICH E2B(R3) data element list.

The E2B(R3) specification defines inter-relationships between data elements allowing for various mandatory / required, optional, unique, or repeatable sections (information blocks). Relationships between elements vary, as indicated by:

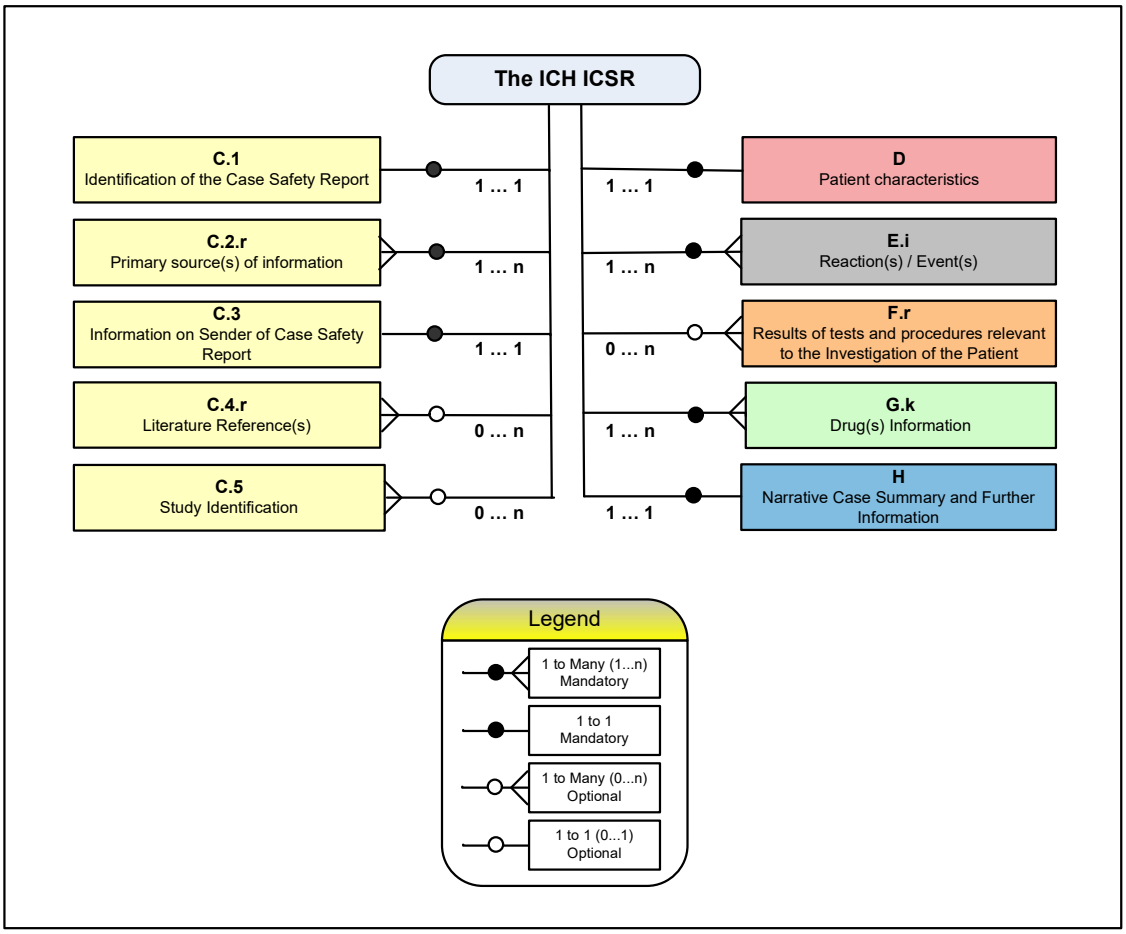
- 1 ..1 (unique and mandatory);
- 0 ..1 (unique and optional);

[9] The XML FAQ, Version 4.56 (8 August 2007), Edited by Peter Flynn, Frequently-Asked Questions about the Extensible Markup Language, http://xml.silmaril.ie/

- 1 ..n (one to many and mandatory); or
- 0 ..n (one to many and optional).

Diagrams in Section 3.4 provide the next level of detail and are intended to help business users understand how the various portions of the ICSR relate to one another, while helping application developers understand how to populate an XML message designed and developed to meet the E2B(R3) specification.

Figure 1: The ICH ICSR Structure



3.2 Code Sets, Terminologies and Vocabularies for E2B(R3)

There are several terminologies and controlled vocabularies that are used to describe or code information within an ICSR. Some of these terminologies or code sets are general and are used by many applications, such as units for mass or time, or country codes. Others are specific to the medical section, such as *Medical Dictionary for Regulatory Activities* (MedDRA). Still others are specific code lists created for the ICH. This section will address the code sets, terminologies and vocabularies used in this IG. Specific guidance is provided in Section 3.4 for each individual element.

Although the technical specifications for the code sets (e.g., Data Types) are provided in Section 3.4, these are current as of printing this IG. Specifications may evolve over time to adapt to new technologies and new business needs. Ultimately, the validation specifications of code sets (e.g., technical format and values allowed) are defined by the organisation that maintains the terminology, and those organisations should be consulted to obtain the most current specifications for their code sets.



Code set specifications (e.g., technical format and values allowed) are defined by the organisation that maintains the terminology. As they may evolve at a different pace than the publication of this IG, those organisations should be consulted to obtain their most current specifications.

An *Object Identifier* (OID) is a sequence of numbers to uniquely identify an object. The numbers represent a hierarchically-assigned namespace, formally defined using the *International Telecommunications Union ASN.1* standard. These numbers are written either as a string of digits separated by dots or as a list of named "branches". For example, the MedDRA dictionary of terms is identified by the OID 2.16.840.1.113883.6.163 which also represents the branch "joint-iso-itu-t.country.us.organisation.hl7.external-code-system.MedDRA".

Organizations can obtain an OID by requesting an identifier from a registrar, and, if it desires, an organisation can in turn become a registrar and subsequently generate child OIDs to its internal objects. The ICH is implementing OIDs to identify code systems used in ICSR message exchange.

Tables 1 through 7 in this section of the IG list all the OIDs used to *code* the data elements of the ICH ICSR. A list of OIDs registered by ICH is available on the ICH website. In addition to OIDs in the tables 1 to 7, some OIDs registered by HL7 are used in ICSR messages to differentiate the intended use of some elements (e.g., in data elements F.r.4 and F.r.5 for normal values of test results, different OIDs are used to differentiate between "low" and "high", respectively). Although those HL7 registered OIDs are not described in the tables below, the reference instance in Appendix I (D) provides all OIDs in the context they are used.

3.2.1 Terminologies and Vocabularies Employed by the ICSR Message

3.2.1.1 ISO Identification of Medicinal Products (IDMP)

In collaboration with ICH, ISO developed a set of standards to enhance exchange of information for medicinal products. These include identifiers to allow mapping of international terminologies for routes of administration, dosage forms and units of measurement, as well as controlled identifiers to enable cross-border identification of pharmaceutical products and mapping to their core components, e.g., substances.

The ISO IDMP standards include:

- ISO 11238 Health informatics — Identification of medicinal products—*Data elements and structures for the unique identification and exchange of regulated information on substances*
- ISO 11239 Health Informatics — Identification of medicinal products —*Data elements and structures for the unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging*
- ISO 11240 Health informatics — Identification of medicinal products —*Data elements and structures for the unique identification and exchange of units of measurement*
- ISO 11615 Health Informatics —Identification of medicinal products – *Data elements and structures for the unique identification and exchange of regulated medicinal product information*
- ISO 11616 Health informatics — Identification of medicinal products—*Data elements and structures for the unique identification and exchange of regulated pharmaceutical product information*

The data elements that use ISO IDMP vocabularies are described in Section 3.4 of this document. However, where the ISO IDMP terms and / or identifiers (e.g., codes) are not available, the IG provides instructions for alternate means to code the information.

	Until the controlled vocabularies for the ISO IDMP are available, temporary rules are applied to the data elements. Terms and identifiers (codes) may be provided by each region until the ISO IDMP controlled vocabularies are implemented.

Table 1: E2B (R3) data elements and IDMP OIDs

Element id	Element Name	OID Reference[10]
D.8.r.2b	Medicinal Product Identifier (MPID)	***ISO11615 MPID***
D.8.r.3b	Pharmaceutical Product Identifier (PhPID)	***ISO11616 PhPID***
D.10.8.r.2b	Medicinal Product Identifier (MPID)	***ISO11615 MPID***
D.10.8.r.3b	Pharmaceutical Product Identifier (PhPID)	***ISO11616 PhPID***
G.k.2.1.1b	Medicinal Product Identifier (MPID)	***ISO11615 MPID***
G.k.2.1.2b	Pharmaceutical Product Identifier (PhPID)	***ISO11616 PhPID***
G.k.2.3.r.2b	Substance/Specified Substance TermID	***ISO11238 IDMP Substance***
G.k.4.r.9.2b	Pharmaceutical Dose Form TermID	***ISO11239 IDMP Dosage Forms & Routes of Admin***
G.k.4.r.10.2b	Route of Administration TermID	***ISO11239 IDMP Dosage Forms & Routes of Admin***
G.k.4.r.11.2b	Parent Route of Administration TermID	***ISO11239 IDMP Dosage Forms & Routes of Admin***

3.2.1.2 MedDRA - the Medical Dictionary for Regulatory Activities

MedDRA® - the *Medical Dictionary for Regulatory Activities* - is a medical terminology used to classify adverse event information associated with the use of biopharmaceuticals and other medical products (e.g., medical devices and vaccines). Coding these data to a standard set of MedDRA terms allows health authorities and the biopharmaceutical industry to more readily exchange and analyze data related to the safe use of medical products[11].

MedDRA trademark is owned by the *International Federation of Pharmaceutical Manufacturers and Associations* (IFPMA) on behalf of ICH, and MedDRA was developed by the ICH. The MSSO - *Maintenance and Support Services Organization* - serves as the repository, maintainer, and distributor of MedDRA as well as the source for the most up-to-date information regarding MedDRA and its application within the biopharmaceutical industry and regulators. MedDRA subscribers submit proposed changes to the terminology. The MSSO includes a group of internationally based physicians who review all proposed subscriber changes and provide a timely response directly to the requesting subscriber.

The ICH ICSR utilises MedDRA to code a number of medical concepts, such as adverse reactions or events, indications for drug use, medical history, etc. The following elements require MedDRA coding at the *Lowest Level Term* (LLT). Please note that only one version of MedDRA can be used in a single ICSR.

[10]These will be replaced with the registered OID reference when it is available.

[11] This description of MedDRA is taken from the webpage of the MSSO at http://www.meddramsso.com/. For more information, please see webpage for ICH.

Table 2: E2B (R3) data elements and MedDRA OIDs

Element id	Element Name	OID Reference
D.7.1.r.1b	Medical History (disease / surgical procedure / etc.) (MedDRA code)	***2.16.840.1.113883.6.163***
D.8.r.6b	Indication (MedDRA code)	***2.16.840.1.113883.6.163***
D.8.r.7b	Reaction (MedDRA code)	***2.16.840.1.113883.6.163***
D.9.2.r.1b	Reported Cause(s) of Death (MedDRA code)	***2.16.840.1.113883.6.163***
D.9.4.r.1b	Autopsy-determined Cause(s) of Death (MedDRA code)	***2.16.840.1.113883.6.163***
D.10.7.1.r.1b	Medical History (disease / surgical procedure / etc.) (MedDRA code)	***2.16.840.1.113883.6.163***
D.10.8.r.6b	Indication (MedDRA code)	***2.16.840.1.113883.6.163***
D.10.8.r.7b	Reactions (MedDRA code)	***2.16.840.1.113883.6.163***
E.i.2.1b	Reactions / Event (MedDRA code)	***2.16.840.1.113883.6.163***
F.r.2.2b	Test Name (MedDRA code)	***2.16.840.1.113883.6.163***
G.k.7.r.2b	Indication (MedDRA code)	***2.16.840.1.113883.6.163***
H.3.r.1b	Sender's Diagnosis / Syndrome and / or Reclassification of Reaction / Event (MedDRA code)	***2.16.840.1.113883.6.163***

3.2.2 ICH Maintained Code Sets and Object Identifiers (OIDs) Created for the ICH ICSR

This section contains tables of Code Sets and OIDs relevant to this IG specifically created for the ICH; these code sets are maintained by or for ICH.

Note: The codesystem versions for the E2B code lists used in the ICH E2B(R3) reference instances are not the latest version of the E2B code lists. A sender should update the codesystem version in ICSR messages (xml files) for submission. Acceptable codesystem version(s) are designated by regulatory authorities in each region.

Table 3: E2B (R3) data elements and ICH ICSR message Codes OIDs

Element id	Element Name	ICH OID
N.1.1	Type of Messages in Batch	***2.16.840.1.113883.3.989.2.1.1.1***
C.1.3	Type of Report	***2.16.840.1.113883.3.989.2.1.1.2***
C.1.8.2	First Sender of This Case	***2.16.840.1.113883.3.989.2.1.1.3***
C.1.11.1	Report Nullification / Amendment	***2.16.840.1.113883.3.989.2.1.1.5***
C.2.r.4	Qualification	***2.16.840.1.113883.3.989.2.1.1.6***
C.3.1	Sender Type	***2.16.840.1.113883.3.989.2.1.1.7***
C.5.4	Study Type Where Reaction(s) / Event(s) Were Observed	***2.16.840.1.113883.3.989.2.1.1.8***
D.1.1.1 – D.1.1.4	Source(s) of the Patient Medical Record Number	***2.16.840.1.113883.3.989.2.1.1.4***
D.2.3	Patient Age Group (as per reporter)	***2.16.840.1.113883.3.989.2.1.1.9***
E.i.3.1	Term Highlighted by the Reporter	***2.16.840.1.113883.3.989.2.1.1.10***
E.i.7	Outcome of Reaction / Event at the Time of Last Observation	***2.16.840.1.113883.3.989.2.1.1.11***
F.r.3.1	Test Result (code)	***2.16.840.1.113883.3.989.2.1.1.12***
G.k.1	Characterisation of Drug Role	***2.16.840.1.113883.3.989.2.1.1.13***
G.k.4.r.10.2b, G.k.4.r.11.2b	Route of Administration TermID (E2B(R2))	***2.16.840.1.113883.3.989.2.1.1.14***
G.k.8	Action(s) Taken with Drug	***2.16.840.1.113883.3.989.2.1.1.15***
G.k.9.i.4	Did Reaction Recur on Re-Administration?	***2.16.840.1.113883.3.989.2.1.1.16***
G.k.10.r	Additional Information on Drug (coded) (repeat as necessary)	***2.16.840.1.113883.3.989.2.1.1.17***

Table 4: E2B (R3) data elements and ICH ICSR message Codes OIDs (ICH constrained UCUM codes)

Element id	Element Name	ICH OID
D.2.2b	Age at Time of Onset of Reaction / Event (unit)	***2.16.840.1.113883.3.989.2.1.1.26***
D.2.2.1b	Gestation Period When Reaction / Event Was Observed in the Foetus (unit)	***2.16.840.1.113883.3.989.2.1.1.26***
D.10.2.2b	Age of Parent (unit)	***2.16.840.1.113883.3.989.2.1.1.26***
E.i.6b	Duration of Reaction / Event (unit)	***2.16.840.1.113883.3.989.2.1.1.26***
G.k.2.3.r.3b	Strength (unit)	***2.16.840.1.113883.3.989.2.1.1.25***
G.k.4.r.1b	Dose (unit)	***2.16.840.1.113883.3.989.2.1.1.25***
G.k.4.r.3	Definition of the Time Interval Unit	***2.16.840.1.113883.3.989.2.1.1.26***
G.k.4.r.6b	Duration of the Drug Administration (unit)	***2.16.840.1.113883.3.989.2.1.1.26***
G.k.5b	Cumulative Dose to First Reaction (unit)	***2.16.840.1.113883.3.989.2.1.1.25***
G.k.6b	Gestation Period at Time of Exposure (unit)	***2.16.840.1.113883.3.989.2.1.1.26***
G.k.9.i.3.1b	Time Interval between Beginning of Drug Administration and Start of Reaction / Event (unit)	***2.16.840.1.113883.3.989.2.1.1.26***
G.k.9.i.3.2b	Time Interval between Last Dose of Drug and Start of Reaction / Event (unit)	***2.16.840.1.113883.3.989.2.1.1.26***

There is an exception for F.r.3.3 “Test Result”. ICH does not provide constrained UCUM codes for this field to allow variety of units. UCUM codes can be selected from the original UCUM list and OID is listed in the table 8.

Table 5: E2B (R3) data elements and ICSR message Namespace OIDs

Element id	Element Name	ICH OID
N.1.2	Batch Number	***2.16.840.1.113883.3.989.2.1.3.22***
N.1.3	Batch Sender Identifier	***2.16.840.1.113883.3.989.2.1.3.13***
N.1.4	Batch Receiver Identifier	***2.16.840.1.113883.3.989.2.1.3.14***
N.2.r.2	Message Sender Identifier	***2.16.840.1.113883.3.989.2.1.3.11***
N.2.r.3	Message Receiver Identifier	***2.16.840.1.113883.3.989.2.1.3.12***
C.1.1	Sender's (case) Safety Report Unique Identifier	***2.16.840.1.113883.3.989.2.1.3.1***
C.1.8.1	Worldwide Unique Case Identification Number	***2.16.840.1.113883.3.989.2.1.3.2***
C.1.9.1.r.1, C.1.9.1.r.2	Source(s) of Case Identifier (repeated as necessary) and Case Identifier(s)	***2.16.840.1.113883.3.989.2.1.3.3***
C.5.1.r.1	Study Registration Number	***2.16.840.1.113883.3.989.2.1.3.6***
C.5.3	Sponsor Study Number	***2.16.840.1.113883.3.989.2.1.3.5***
D.1.1.1	Patient Medical Record Number(s)(GP)	***2.16.840.1.113883.3.989.2.1.3.7***
D.1.1.2	Patient Medical Record Number(s)(Specialist)	***2.16.840.1.113883.3.989.2.1.3.8***
D.1.1.3	Patient Medical Record Number(s)(Hospital)	***2.16.840.1.113883.3.989.2.1.3.9***
D.1.1.4	Patient Medical Record Number(s) (Investigation)	***2.16.840.1.113883.3.989.2.1.3.10***
G.k.3.1	Authorisation / Application Number	***2.16.840.1.113883.3.989.2.1.3.4***

Table 6: E2B (R3) data elements and Ack message Namespace OIDs

Element id	Element Name	ICH OID
ACK.M.2	Acknowledgement Batch Sender Identifier	***2.16.840.1.113883.3.989.2.1.3.17***
ACK.M.3	Acknowledgement Batch Receiver Identifier	***2.16.840.1.113883.3.989.2.1.3.18***
ACK.B.r.3	ICSR Message ACK Receiver	***2.16.840.1.113883.3.989.2.1.3.16***
ACK.B.r.4	ICSR Message ACK Sender	***2.16.840.1.113883.3.989.2.1.3.15***

Table 7: ICSR / Ack common technical OIDs

Technical Codes	ICH OID
Action Performed Code	***2.16.840.1.113883.3.989.2.1.1.18***
Observation Identification Codes	***2.16.840.1.113883.3.989.2.1.1.19***
Value Grouping Code	***2.16.840.1.113883.3.989.2.1.1.20***
Role of Assigned Entity Code	***2.16.840.1.113883.3.989.2.1.1.21***
Report Relationship Code	***2.16.840.1.113883.3.989.2.1.1.22***
Report Characterisation Codes	***2.16.840.1.113883.3.989.2.1.1.23***
Attention Line Codes	***2.16.840.1.113883.3.989.2.1.1.24***
Documentation & Reference Organiser Code	***2.16.840.1.113883.3.989.2.1.1.27***

3.2.3 International Standard Code Sets

This section contains information on Code Sets and OIDs relevant to this IG but not specifically created by or for ICH. These code sets are maintained internationally in various places by organisations and entities other than ICH. As such, the value and format allowed is limited to what is defined by the organisation that maintains the code in question.
The external code sets and OIDs used in the message include:

- ISO 3166 Part 1 (alpha-2) – *Codes for the representation of names of countries and their subdivisions – Part 1: Country codes, defines codes for the names of countries, dependent territories, and special areas of geographical interest* (2-letter codes)
- ISO 5218 – Information technology – *Codes for the representation of human sexes*
- ISO 639-2 – *Codes for the Representation of Names of Languages*
- UCUM – *The Unified Code for Units of Measure* (UCUM), case sensitive form[12]

The following table lists the ICSR elements using these external code sets:

[12] More information on UCUM at http://unitsofmeasure.org/

The UCUM standard can be downloaded in xml or html form from http://unitsofmeasure.org/trac/

Table 8: International Standard Code Set OIDs

Element id	Element Name	Coding Scheme Name	OID Reference
C.2.r.3	Reporter's Country Code	ISO 3166 Part 1 (alpha-2)	***1.0.3166.1.2.2***
C.3.4.5	Sender's Country Code	ISO 3166 Part 1 (alpha-2)	***1.0.3166.1.2.2***
C.5.1.r.2	Study Registration Country	ISO 3166 Part 1 (alpha-2)	***1.0.3166.1.2.2***
D.5	Sex	ISO 5218	***1.0.5218***
D.10.6	Sex of Parent	ISO 5218	***1.0.5218***
E.i.1.1b	Reaction / Event as Reported by the Primary Source Language	ISO 639-2/RA (alpha-3)	***1.0.639.2***
E.i.9	Identification of the Country Where the Reaction / Event Occurred	ISO 3166 Part 1 (alpha-2)	***1.0.3166.1.2.2***
F.r.3.3	Test Result (unit)	UCUM	***2.16.840.1.113883.6.8***
G.k.2.4	Identification of the Country Where the Drug Was Obtained	ISO 3166 Part 1 (alpha-2)	***1.0.3166.1.2.2***
G.k.3.2	Country of Authorisation / Application	ISO 3166 Part 1 (alpha-2)	***1.0.3166.1.2.2***
H.5.r.1b	Case Summary and Reporter's Comments Language	ISO 639-2/RA (alpha-3)	***1.0.639.2***

There is one exception not included in the table above. The identifier used in the "Sender's (case) Safety Report Unique Identifier" (C.1.1) and the "Worldwide Unique Case Identification Number" (C.1.8.1), is not listed as it is not exclusively coded using ISO 3166 Part 1. Nevertheless, it does reference the ISO Country Code system in its construction; see the user guidance for C.1.1 for more details.

3.2.3.1 Use of ISO 3166 Country Codes

Multiple data elements within the ICSR identify countries, either in relation to the drug, the event, the sender or the reporter. E2B (R3) references ISO 3166-1 alpha-2 country codes that includes "Officially assigned" country codes plus "EU" in the "Exceptionally reserved" category, in the data elements which capture country codes. The "Unassigned" category should not be used. "Transitionally reserved", "Indeterminately reserved" and "Formerly used" categories may be used when appropriate, e.g., for legacy data.

3.2.3.2 Use of message encoding

ICH M2 recommends to use UTF-8 for XML message encoding in all messages developed based on ICH electronic guidelines.

3.3 ICH E2B(R3) Specifications for the Transmission of ICSRs

The E2B(R3) specification has a detailed breakdown of each data element in the ICH ICSR, as well as notes on transmission and user guidance information.

3.3.1 Minimum Information

The minimum information for valid safety report should include at least:

- one identifiable patient - any one of several data elements is considered sufficient to define an identifiable patient (e.g., initials, age, sex);
- one identifiable reporter - any one of several data elements is considered sufficient to define an identifiable reporter (e.g., initials, address, qualifications);
- one adverse event/reaction (or outcome); and
- one suspect or interacting drug.

Note: Additional validation rules for the required "minimal information" might exist at the regional level.

	Any one of several data elements is sufficient to define an identifiable patient (e.g., initials, age, and sex) or an identifiable reporter (e.g., initials, address, and qualification). The guideline ICH E2D Section 5.1 (http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html) provides further guidance on this topic. It is also recognised that the patient and the reporter can be the same individual and still fulfil the minimum reporting criteria. Due to data privacy legislation in some countries, the patient's initials and other patient identifiers might not be exchanged between countries. However, at least one of the data elements in the section D.1 must be populated and user guidance for this data element is provided.

3.3.2 Definition of Data Elements within a Message

The guidance for transmitting ICSR information includes provisions for transmitting all relevant data useful to assess an individual adverse event / reaction report. The message standard from which this guidance is derived is fully capable of conveying a comprehensive ICSR. However, it is noted that each and every data element will not be available for each and every transmission.

In fact, for most ICSRs, a number of data elements will be unknown, and therefore, not transmitted in the report. Since ICSR information will be transmitted electronically, it is unnecessary to assign values to unknown, optional data elements. However, in certain cases it is important to understand if a data element is null because it is not applicable or because it is unknown or because

it is “protected” by privacy legislation. In those cases, provisions for expressing a null value are included in the message for a data element to indicate the absence of data and reason.

Furthermore, in addition to the minimum information required for an ICSR report (See Section 3.3.1) certain specific administrative information should be provided to properly process the report:

- Sender’s (case) Safety Report Unique Identifier (C.1.1);
- Type of Report (C.1.3);
- Date of Most Recent Information for This Report (C.1.5);
- Dose This Case Fulfil the Local Criteria for an Expedited Report? (C.1.7);
- Worldwide Unique Case Identification (C.1.8);
- Reporter’s Country Code (C.2.r.3);
- Sender’s Organisation (C.3.2); and
- When Type of Report = ‘Report from study’, Study Type Where Reaction(s) / Event(s) Were Observed (C.5.4).

3.3.3 General Principles

While complete information is desirable, a minimum set of information is always required for an ICSR to be valid. This applies to all types of ICSRs including initial case reports, follow-up information, and cases to be amended or nullified.

All the information available should be reported in fully structured format using the relevant E2B(R3) data elements and applicable standard terminologies. Those terminologies include;ISO (country codes, gender codes and language codes), MedDRA (e.g., medical history, indication, and reaction / event), UCUM (units of measurement), and ISO IDMP (see Section 3.2.1.1 for details). Please refer to each standard for further information.

Although the exchange of other unstructured data (e.g., published articles, full clinical records, X-Ray images, etc.) is outside the scope of this IG, the technical solution to transmit attachments is provided in Section 3.5.

3.3.4 Retransmission of cases

Based on regional reporting obligations and business arrangements in pharmacovigilance, an ICSR may be re-transmitted several times between different senders and receivers. During this re-transmission process, medical information ‘received’ on the case should not be omitted or changed during the retransmission when no new information on the case is available to the re-transmitting sender.

There are certain exceptions and the following data elements might be updated:

- Sender’s (case) Safety Report Unique Identifier (C.1.1);
- Date of Creation (C.1.2);

- Date Report Was First Received from Source (C.1.4);
- Date of Most Recent Information for This Report (C.1.5);
- Are Additional Documents Available? (C.1.6.1);
- Does This Case Fulfil the Local Criteria for an Expedited Report? (C.1.7);
- Information on Sender of Case Safety Report (C.3);
- Seriousness Criteria at Event Level (E.i.3.2);
- More Information Available (F.r.7);
- Assessment of Relatedness of Drug to Reaction(s)/ Event(s) (repeat as necessary) (G.k.9.i.2.r);
- Sender's Diagnosis (repeat as necessary) (H.3.r);
- Sender's Comments (H.4); and
- English translation of the free text data elements in the ICSRs.

In addition to these data elements, it is also possible to update MedDRA coded data elements with the most recent version of MedDRA.

There could be situations in which more than one ICSR shares the same "Worldwide Unique Case Identification Number" (C.1.8.1), or due to sequential updates to information in the same case, more than one ICSR could share the same "Date of Most Recent Information" (C.1.5). For these situations, "Date of Creation" (C.1.2) should be used to identify the most recent *version* of the case.

3.3.5 Notes on Format of Data Elements

E2B (R3) data elements have a hierarchical tree structure. It consists of two major sections A and B, where A contains administrative and identification information, and B contains information on the case. The subsidiary sections are categorised by the nature of the data, and are:

- Section A
  - C.1 - Identification of the Case Safety Report;
  - C.2 - Primary Source(s) of Information;
  - C.3 - Information on Sender of Case Safety Report;
  - C.4 - Literature Reference(s);
  - C.5 - Study Identification.
- Section B
  - D - Patient Characteristics;
  - E - Reaction(s)/ Event(s);
  - F - Results of Tests and Procedures Relevant to the Investigation of the Patient;
  - G - Drug(s) Information; and
  - H - Narrative Case Summary and Further Information.

In addition to the letters “i” and “k” indicating iterations of the event (E.i) or the drug (G.k), the letter “r” is used to indicate that the data element or the section is repeatable.

	It is recognised that the numbering scheme for the data elements in this IG is different than the one used in the E2B(R2).

3.3.6 General rules for Data Entry

- Date / Time Format
  HL7 uses a single format to represent dates and times: CCYYMMDDHHMMSS.UUUU[+|-ZZzz]. Complete date time information down to seconds can be reported using this format. This date format makes it possible to provide data to the appropriate degree of precision.

  “Future dates” cannot be transmitted in an ICH ICSR message when transmissions occur across different time zones, senders and receivers should configure their systems (e.g., attach the ZZzz offset to Coordinated Universal Time) to prevent dates and times to be interpreted as “future dates”.

  Please refer to Appendix II in this IG for more detail.

  For E2B(R3), minimum level of date precision for each date data element is specified in Section 3.4.

	A single format (CCYYMMDDHHMMSS.UUUU[+|-ZZzz]) is used to represent dates and times throughout this IG. This format allows for varying degrees of precision to be exchanged for date and time information, from only the year, down to the second. The minimum level of precision for the date data elements is specified in Section 3.4, however, as much information as available (e.g., known) should be provided.

- All free text data elements (with the exception of the “Reaction / Event as Reported by the Primary Source in Native Language” (E.i.1.1a) and the “Case Summary and Reporter’s Comments in Native Language” (H.5.r)) are to be provided in English for international transmission. However, the message control act wrapper supports language codes for regional message exchanges. Please refer to regional implementation guides.
- Metric units should be used exclusively.
- For ICSR reporting, MedDRA is commonly used in the ICH regions. For additional advice on MedDRA coding, refer to the latest edition of the ICH document “MedDRA Term Selection: Points to Consider”.

- In certain instances, provisions have been made for transmission of free text items, including a full text case summary narrative. Text data elements are intended to provide additional information that cannot be provided in structured format using reference standard terminology.
- Only one version of MedDRA can be used to code the relevant data elements within a single ICSR. Therefore, the same MedDRA version should be identified each time a MedDRA term is populated. However, multiple ICSRs are submitted in a single batch, different ICSRs can refer to different MedDRA version.

	For all data elements that reflect a MedDRA coded value, the same MedDRA version should be used for all data elements in a single ICSR. However, when multiple ICSRs are submitted in a single batch, different ICSRs can refer to different MedDRA version.

It should be noted that:

- The data type for each element will be described as follows:
  - A = Alpha: This data type is primarily used within the ICSR for certain data elements that require controlled vocabulary, such as the "Reporter's Country Code" (C.2.r.3) - 2A, to accommodate the ISO3166 code. The string data elements that require the Alpha data type can contain only upper and lower case alphabetic characters, e.g., "JP". Numbers and special characters, such as ". " , ^ " are not allowed;
  - AN = AlphaNumeric: String data element that can contain alphabetic, numerical and special characters. Example: "AB-19.990115 ' " ^ ". Regarding all aspects of XML, the W3C standards should be followed as published at http://www.w3.org/. In principle, ICH "AN" data type accepts all characters, including space and some special characters listed in UTF8, but some characters are not allowed with XML message. For example, when the XML special characters >, < and & occur in text, data elements they should always be replaced by > < and & respectively. ICH data elements with the ICH "AN" data type may not always have a one-to-one mapping with the data type in ISO / HL7 27953- 2 ICSR message standard. The representation of the data can vary across implementations. For example, ICH F.r.4 Normal Low Value and ICH F.r.5 Normal High Value. These data elements specify use of the ICH AN data type; however, the ISO / HL7 27953-2 message specification restricts allowable XML schema values using the HL7 xsi:type code designation Physical Quantity (PQ). The HL7 PQ data type is expressed as two XML schema attributes: value and unit; value has HL7 REAL data type and units are expressed as UCUM codes. For the use and information of the HL7 data type, please refer to the ISO / HL7 27953-2 Informative Annex F: *HL7 Data Type Specification*. In the Business Rule section for the related data elements, the ICH ICSR IG provides information and examples for representing the ICH "AN" data type with HL7 data type in transmission; or

- N = numeric: String data element that contains only the characters “0-9 . E + - ” used to represent an integer or floating point numbers, including scientific notation. Example: “1.23E-1” or “34192” or “32.12”. Commas are not permitted.
- Date: See Appendix II (A)
- Boolean: Boolean values are represented by:
  - ***“false”*** which can also equate to “no”;
  - ***“true”*** which can also equate to “yes”*;
  - “nullflavor” which can have different meanings in different scenarios. HL7 refers to these as “null flavors”. (See below)

    * For the purposes of this IG, there is one exception to this rule for the ‘Investigational Product Blinded’ (G.k.2.5) where “true” = “blinded”.

- All mandatory data elements must always be part of the ICSR message, however optional elements do not have to be transmitted. A blank optional element may not appear in the XML code. A blank mandatory element needs to appear in the XML code for the message to be valid.
  - Some elements might need to be transmitted as part of a *valid* ICSR yet might need to be *empty* of content for specific reasons. In HL7 messaging it is possible to transmit an empty element *and* to code the element to explain the reason for the lack of data. This allows for the creation of valid messages containing mandatory elements without transmitting content. This reason for a blank element is referred to as the “flavor” of the null value.
  - nullFlavors: ICH ICSR uses the following codes from the HL7 Messaging Standard to categorise exceptions. For further information, please see the standard ISO / HL7 27953-2. Not all nullFlavors are valid for all data types. For ICH ICSR, the nullFlavors “NINF” (negative infinity of numbers) and “PIMF” (positive infinity of numbers) are used only for the data element *F.r.3.2 Test Result*, and only when the element describes a range (e.g., data type IVL<…>) with an (unknown) infinity. For example, the concept of “equal or greater to 3” can be represented as the range from “3” to “positive infinity”, e.g., any (unknown) number greater than 3.

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

The following examples demonstrate how a nullFlavor can be used to code values in the ICH ICSR. In these examples, the name of the data element appears after each coded value in a <!--comment tag-->:

Example 1. 'Masked' is expressed by nullFlavor =MSK.

```
<component typeCode="COMP">
   <adverseEventAssessment classCode="INVSTG" moodCode="EVN">
      <subject1 typeCode="SBJ">
         <primaryRole classCode="INVSBJ">
            <player1classCode="PSN" determinerCode="INSTANCE">
               <name nullFlavor="MSK"/>
               <!-- D.1:  Patient (name or initials) -->
               <administrativeGenderCode code="D.5" codeSystem="1.0.5218"/>
               <!-- D.5 Sex [1] Male [2]Female-->
               <birthTime value="19200101"/>
```

```
<!-- D.2.1: Date of Birth -->
<deceasedTime value="20090101"/>
```

Example 2. 'Unknown' is expressed by nullFlavor=UNK.

```
<role classCode="PRS">
  <code code="PRN" codeSystem="2.16.840.1.113883.5.111"/>
    <associatedPerson determinerCode="INSTANCE" classCode="PSN">
      <name nullFlavor="UNK"/>
      <!-- D.10.1:  Parent Identification-->
      <administrativeGenderCode code="D.10.6" codeSystem="1.0.5218"/>
      <!-- D.10.6: Sex of Parent [1]Male [2]Female-->
      <birthTime value="19730101"/>
      <!-- D.10.2.1: Date of Birth of Parent -->
    </associatedPerson>
```

3.3.7 Details of ICH E2B(R3) Data Elements

All of the E2B(R3) data elements and message specifications are described in tables in Section 3.4. The E2B(R3) data element table contains:

- the data element number;
  - For the purpose of this IG, data elements for the Acknowledgement message will be preceded by the letters ACK, for example:
    - data element N.1.2 refers to the "Batch Number" as detailed in Section 3.4; and
    - ACK.M.1 refers to the "Acknowledgement Batch Number" in the Acknowledgement transaction.
- the data element name;
- a definition appears under "User Guidance" to provide information on how to populate correctly each E2B (R3) data element;
- "Conformance" indicates if a value for the data element is mandatory / required or optional. Some data elements are required for "technical" reasons (e.g., to parse the message correctly) and will generate an error when omitted. A list of required elements is provided in Appendix I (G) the Technical Information.
- "Data Type" and data element length — each data element will use a number to denote the width of a data element followed by A for alpha, N for numeric, or AN for alphanumeric. For data elements referencing a code set (e.g., not a free text data element), the organisation that maintains the terminology should be consulted to obtain the most current specifications;
- an Object Identifier ("OID") — identifies if a specific code list or namespace applies to the data element. The OIDs provided in this IG should be used in XML messages for the ICH ICSR;
- "Value Allowed" indicates possible values for the data element; and
- "Business Rule(s)" provide additional details on validation rules for some data elements.

The messaging specifications in this IG are the agreed, harmonised rules used by the ICH parties. These are the validation conditions applied to 'inbound' ICH ICSR XML messages (e.g., applied by "receivers"). Therefore, this IG should be used to verify the accuracy and compliance of data entry when preparing an "outbound" ICH ICSR XML message.

It is recognised that the information in "Value Allowed" printed in this document for some code lists may become outdated or incomplete. This information will be maintained outside this IG. For a list of the most recent codes, please see the code lists in Appendix I (F).

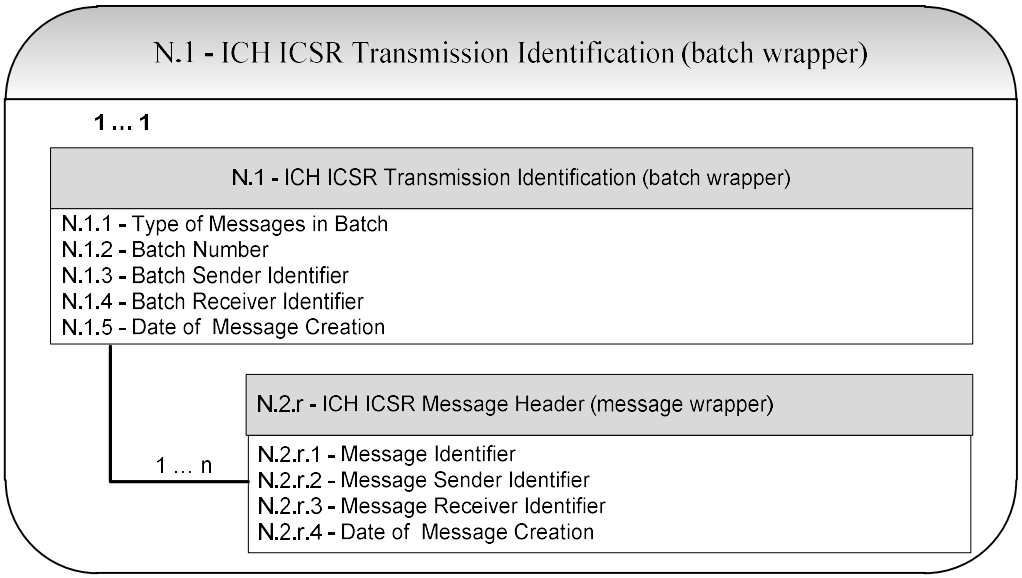
	The specifications in the ICH E2B(R3) data element in Section 3.4 are the harmonised data validation rules in ICH. These data elements should be consulted to verify the accuracy and compliance of data entry when preparing outbound ICH ICSR XML messages.

	For codes in 'Value Allowed', please see the most recent code lists in Appendix I (F) ICH code lists.

3.4 ICH E2B(R3) Data Elements

N.1 ICH ICSR TRANSMISSION IDENTIFICATION (BATCH WRAPPER)

Unlike the information in ICSR sections C to F, the "wrapper" information is intended for routing purposes only (e.g., "from" –> "to") and is not usually stored or archived. An assumption is made that an *Electronic Data Interchange* (EDI) trading partnership agreement is established to define the Message number, Sender ID, Receiver ID, and Message date conventions.



N.1.1 Type of Messages in Batch

User Guidance	This data element contains information on the type of information being transmitted. One ICH ICSR batch can contain one or more safety reports (ICSRs).
Conformance	Required
Data Type	2N
OID	2.16.840.1.113883.3.989.2.1.1.1
Value Allowed	1 = ichicsr
Business Rule(s)	
	Other codes may be used regionally.

	One Batch can contain one or more ICSR messages. Each ICSR message contains one ICSR.

N.1.2 Batch Number

User Guidance	This data element, also called a "Batch Wrapper", contains a unique tracking number assigned by the sender to each outbound ICH ICSR batch file. The batch number is unique only to the sender.

Conformance	Required
Data Type	100AN
OID	2.16.840.1.113883.3.989.2.1.3.22
Value Allowed	Free text
Business Rule(s)	
	The following notation will be used to represent N.1.2: <id extension="batch number" root="2.16.840.1.113883.3.989.2.1.3.22"/> The root indicates the namespace of N.1.2, the actual batch number i populated at id extension.

N.1.3 Batch Sender Identifier

User Guidance	This data element identifies the origin of the ICSR reports (creator of ICH ICSR batch file), e.g., company name or regulatory authority. The identifier is unique to the receiver.
Conformance	Required
Data Type	60AN
OID	2.16.840.1.113883.3.989.2.1.3.13
Value Allowed	Free text
Business Rule(s)	
	The following notation will be used to represent N.1.3: <id extension="sender identifier" root="2.16.840.1.113883.3.989.2.1.3.13"/> The root indicates the namespace of N.1.3, the actual batch sender identifier is populated at id extension. The sender identifier should be agreed between trading partners.

N.1.4 Batch Receiver Identifier

User Guidance	This data element identifies the intended destination of the ICSR batch file. The identifier is unique to the sender.
Conformance	Required
Data Type	60AN
OID	2.16.840.1.113883.3.989.2.1.3.14
Value Allowed	Free text
Business Rule(s)	
	The following notation will be used to represent N.1.4: <id extension="receiver identifier" root="2.16.840.1.113883.3.989.2.1.3.14"/> The root indicates the namespace of N.1.4, the actual batch receiver identifier is populated at id extension. The receiver identifier should be agreed between trading partners.

N.1.5 Date of Batch Transmission

User Guidance	This data element contains the date on which the ICH ICSR batch file was transmitted.
Conformance	Required
Data Type	Date / Time

OID	None
Value Allowed	See Appendix II for further information.
Business Rule(s)	
	The full precision of date and time must be recorded down to the second. (i.e., "CCYYMMDDhhmmss[+/-ZZzz]"). The date specified cannot refer to a future date. The date should be local time at point of transmission of ICSR message.

N.2.r ICH ICSR MESSAGE HEADER (MESSAGE WRAPPER) (REPEAT AS NECESSARY)

N.2.r.1 Message Identifier

User Guidance	This data element contains the message identifier (also called the Message Wrapper). It is a unique tracking identifier assigned to a specific ICH ICSR message transmitted by the sender. One ICH ICSR message contains one and only one ICSR.
Conformance	Required
Data Type	100AN
OID	2.16.840.1.113883.3.989.2.1.3.1
Value Allowed	Free text
Business Rule(s)	
	The value is the same as C.1.1. Therefore the notation would be: <id extension="message identifier" root="2.16.840.1.113883.3.989.2.1.3.1"/>

N.2.r.2 Message Sender Identifier

User Guidance	This data element identifies the sender of the ICSR reports (creator of ICH ICSR message).
Conformance	Required
Data Type	60AN
OID	2.16.840.1.113883.3.989.2.1.3.11
Value Allowed	Free text
Business Rule(s)	
	The following notation will be used to represent N.2.r.2: <id extension="message sender identifier" root="2.16.840.1.113883.3.989.2.1.3.11"/> The root indicates the namespace of N.2.r.2, the actual message sender identifier is populated at id extension. The sender identifier should be agreed between trading partners.

N.2.r.3 Message Receiver Identifier

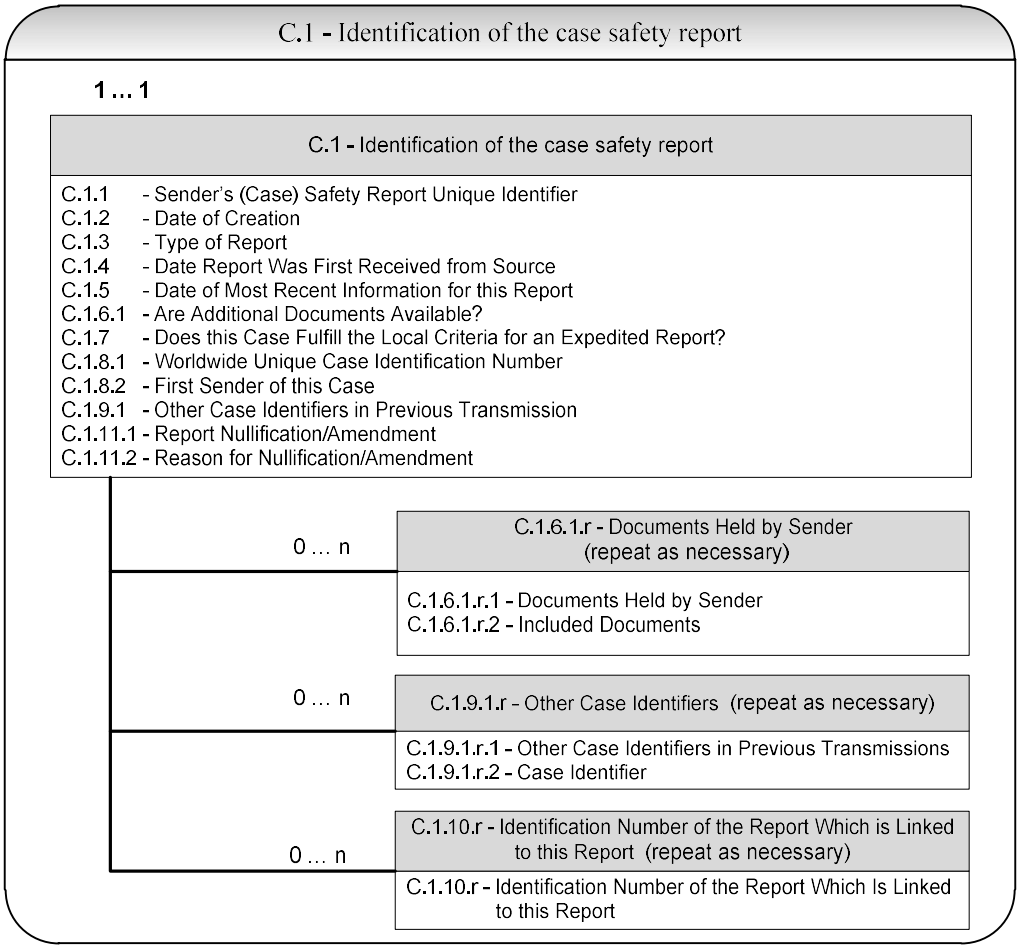
User Guidance	This data element identifies the intended recipient of the transmission of the ICSR message.
Conformance	Required
Data Type	60AN
OID	2.16.840.1.113883.3.989.2.1.3.12
Value Allowed	Free text
Business Rule(s)	
	The following notation will be used to represent N.2.r.3: <id extension="message receiver identifier" root="2.16.840.1.113883.3.989.2.1.3.12"/> The root indicates the namespace of N.2.r.3, the actual message receiver identifier is populated at id extension. The receiver identifier should be agreed between trading partners.

N.2.r.4 Date of Message Creation

User Guidance	This data element contains the date on which the ICH ICSR message was created in the sender's database.
Conformance	Required
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information.
Business Rule(s)	
	The value must be the same as C.1.2. The full precision of date and time must be recorded down to the second (i.e., "CCYYMMDDhhmmss[+/-ZZzz]").

C.1 IDENTIFICATION OF THE CASE SAFETY REPORT

This section corresponds to the root of the case safety report. An ICH ICSR *message* file contains one and only one ICSR; an ICH ICSR *batch* file contains one or more ICH ICSR messages. Therefore, there must be one and only one "subject" element within "controlActProcess" in the ICSR message file.



C.1.1 Sender's (case) Safety Report Unique Identifier

User Guidance	This data element contains an identifier for the ICSR that is unique. The value should be a concatenation of 3 segments separated by a dash / hyphen: "country code-company or regulator name-report number". *Country code* is the 2-letter ISO 3166 part 1 code (ISO 3166-1 alpha-2) corresponding to the country of the primary source of the report (C.2.r.3). The *company or regulator name* is an internationally unique abbreviation or code for the sender's organisation; the use of a "-" (dash / hyphen) should be avoided in this segment. The *report number* is the organisation's international case number. For example, a report transmitted from a company to a regulatory authority concerning a case from France would populate C.1.1 with "FR-companyname-12345" where 12345 is that company's unique case report number. When the *same* sender retransmits the same case (e.g., to transmit follow-up information), C.1.1 *usually* remains constant. Exceptions are: • In the case of an organisational change, (e.g., a merger between companies or a name change), follow-up reports can be identified in C.1.1 by the identifier of the newly named organisation. • In the case of changes of country code for primary source for regulatory purposes (C.2.r.3) or the country where the reaction occurred (E.i.9), C.1.1 can be changed. However, the "Worldwide Unique Case Identification Number" (C.1.8.1) used in any previous transmissions of the case should always remain the same (See the user guidance for C.1.8). Other retransmitters should replace this value with their own unique identifier.
Conformance	Required
Data Type	100AN
OID	2.16.840.1.113883.3.989.2.1.3.1
Value Allowed	Free text (country code-company or regulator name-report number)
Business Rule(s)	
	A two character country code will be used in all instances for the country component of the Unique Identifier. The country code EU exists in the ISO 3166 country code list as an exceptional reservation code to support any application that needs to represent the name European Union. In this case, "EU" will be accepted as the country code. The format of C.1.1 ensures a unique report identifier for the sender of particular ICSR. The use of a "-" (dash / hyphen) should be avoided in the "company or regulator name". Both the "Sender's (case) Safety Report Unique Identifier" (C.1.1) and the "Worldwide Unique Case Identification Number" (C.1.8.1) data elements are mapped to the repeatable XML attribute <id> in the

	"investigationEvent" entity in the HL7 ICSR model (See Appendix I (D) the Reference Instances). ICH uses two values – "2.16.840.1.113883.3.989.2.1.3.1" and "2.16.840.1.113883.3.989.2.1.3.2" – in the root portion of the investigationEvent.id to distinguish C.1.1 and C.1.8.1. The following notation will be used to represent C.1.1: <id extension="country code-company name-report no" root="2.16.840.1.113883.3.989.2.1.3.1"/> The following notation will be used to represent C.1.8.1: <id extension="country code-company name-report no" root="2.16.840.1.113883.3.989.2.1.3.2"/>

C.1.2 Date of Creation

User Guidance	This data element has the function of a timestamp and represents the equivalent of a version number for the ICSR. Every ICSR and every iteration (e.g., version) of an ICSR in a safety message must have a different value for Date of Creation. The most recent version of an ICSR will have the most recent date; previous versions of an ICSR will have older dates.
Conformance	Required
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information.
Business Rule(s)	
	Minimum precision required is date and time to the second. The date specified cannot refer to a future date; the time zone may have to be specified. (i.e., "CCYYMMDDhhmmss[+/-ZZzz]")

C.1.3 Type of Report

User Guidance	This data element captures the type of report independently of its source; a separate element for the designation of the source is covered in item C.4 and is not duplicated in this section. For example, if a case in the literature arises from spontaneous observations, "type of report" should be ***Spontaneous report***. If a case in the literature arises from a study, "type of report" should be ***Report from study*** and the differentiation between types of studies (e.g., clinical trials or others) should be given in Section C.5.4 (See the user guidance for C.5.4). If it is unclear from the literature report whether or not the case(s) cited are spontaneous observations or whether they arise from a study, then this item should be ***Other***. The ***Not available to sender*** option allows for the transmission of information by a secondary sender (e.g., regulatory authority) where the initial sender did not specify the type of report; it differs from ***Other,*** which indicates that the sender knows the type of report but cannot fit it into the categories provided.
Conformance	Required
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.2
Value Allowed	1 = Spontaneous report 2 = Report from study 3 = Other 4 = Not available to sender (unknown)
Business Rule(s)	

C.1.4 Date Report Was First Received from Source

User Guidance	For organisations transmitting an initial case, this data element should be the date when the information was received from the primary source *and* fulfilling the 4 minimum criteria, as described in the Section 3.3.1. When retransmitting information received from another regulatory agency or another company or any other secondary source, C.1.4 should be the date the retransmitter first received the information.
Conformance	Required
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information.
Business Rule(s)	
	Minimum precision required is the day (i.e., "CCYYMMDD"). The date specified cannot refer to a future date.

C.1.5 Date of Most Recent Information for This Report

User Guidance	This data element captures the date each time follow-up information is received by the sender from a primary source. In the case that a sender has only first-received information, and the date of first-received information and the date of most recent information are the same, a sender enters the date correspond to C.1.4 in C.1.5. However, if the case is amended for any other reason (e.g., after internal review by the sender) this date should not be changed, and the data element C.1.11.1 should be populated with the value 'amendment,' indicating that the case was amended by the sender (See the user guidance for C.1.11.1).
Conformance	Required
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information.
Business Rule(s)	
	Minimum precision required is the day (i.e., "CCYYMMDD"). The date specified cannot refer to a future date.

	The "Date of Most Recent Information for this Report" should be changed each time follow-up information is received by the sender.

	The date originally reported in C.1.5 should not be changed in an amended or nullified report if no new information on the case has been *received*.

C.1.6 Additional Available Documents Held by Sender

The documents received from the primary source (e.g., clinical records, hospital records, autopsy reports, ECG strips, chest X-ray, photographs) should be listed individually. List all the documents held by the sender, even if they are not actually forwarded to the receiver. Literature reference documents, when available, are described in Section C.4, and are not duplicated in C.1.6.

C.1.6.1 Are Additional Documents Available?

User Guidance	When retransmitting information, the sender (retransmitter) indicates 'true' in this data element only if they have the documents available.
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	false true
Business Rule(s)	
	For further information on how to attach documents to an ICSR, please see Section 3.5.

C.1.6.1.r Documents Held by Sender (repeat as necessary)

C.1.6.1.r.1 Documents Held by Sender

User Guidance	A description of the documents held by the sender relevant to this ICSR (e.g., clinical records, hospital records, autopsy reports, ECG strips, chest X-ray, or photographs) should be listed individually in this data element.
Conformance	Optional, but required if C.1.6.1 is "true".
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rule(s)	

C.1.6.1.r.2 Included Documents

User Guidance	This data element contains the actual content of C.1.6.1.r.1 if the sender chooses to send the document.
Conformance	Optional
Data Type	N/A
OID	None
Value Allowed	Media type: e.g., Application / PDF, image / jpeg, application / DICOM, text / plain Representation: e.g., B64 Compression: e.g., DF
Business Rule(s)	
	For further information on how to attach documents to an ICSR, please see Section 3.5. Because a receiver's system may have particular configurations on handling attachments, "Value Allowed" is defined by each region.

C.1.7 Does This Case Fulfil the Local Criteria for an Expedited Report?

User Guidance	The definition of expedited is dependent upon the sender's local regulatory requirements. This data element should be used by the sender to indicate whether the case fulfils the local expedited requirements. When the countries of the sender and receiver differ, the receiver should be aware that this information might not be applicable to the receiver's country's regulatory requirements.
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	false true nullFlavor: NI*
Business Rule(s)	
	* "nullFlavor" is 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.

C.1.8 Worldwide Unique Case Identification

Both C.1.8.1 and C.1.8.2 should always be populated and should never be changed in any subsequent retransmission.

When a sender has not previously received the ICSR in an electronic format (e.g., the information was taken from a paper CIOMS, journal article, etc.) and thus creates the 'initial' electronic ICSR, the identifiers (content and format) in C.1.1 and C.1.8.1 are identical.

Retransmitters should use their own sender's (case) safety report unique identifier in data element C.1.1, but not change the values in data elements C.1.8.1 and C.1.8.2.

When a regulator is the initial sender, C.1.8.2 should be flagged as 1 = Regulator.

When an entity other than a regulator is the initial sender, C.1.8.2 should be flagged as 2 = Other.

C.1.8.1 Worldwide Unique Case Identification Number

User Guidance	See Section C.1.8. Because the data elements used to generate this identification number may change over time (e.g., country code may become non-current), the receiver should accept the value in this data element as is and not apply particular business validation rules.
Conformance	Required
Data Type	100AN
OID	2.16.840.1.113883.3.989.2.1.3.2
Value Allowed	Free text (See C.1.1 user guidance for format)
Business Rule(s)	
	Both the "Sender's (case) Safety Report Unique Identifier" (C.1.1) and the "Worldwide Unique Case Identification" (C.1.8) data elements are mapped to the repeatable XML attribute <id> in the "investigationEvent" entity in the HL7 ICSR model (See the Reference Instance). ICH uses two values - "2.16.840.1.113883.3.989.2.1.3.1" and "2.16.840.1.113883.3.989.2.1.3.2" in the root portion of the investigationEvent.id to distinguish C.1.1 and C.1.8. The following notation will be used to represent C.1.1: <id extension="country code-company name-report no" root=" 2.16.840.1.113883.3.989.2.1.3.1 "/> The following notation will be used to represent C.1.8: <id extension="country code-company name-report no" root=" 2.16.840.1.113883.3.989.2.1.3.2"/> Although the attribute <id> can repeat in the message, but there must be a single instance of the <id> attribute with the root value of "2.16.840.1.113883.3.989.2.1.3.2" for a particular case safety report.

	Retransmitters should use their own "Sender's (case) Safety Report Unique Identifier" (C.1.1), but must not change C.1.8.1 and C.1.8.2.

C.1.8.2 First Sender of This Case

User Guidance	This data element is used to identify the type of sender that created and transmitted the original electronic ICSR. When a regulator is the initial sender, C.1.8.2 should be flagged as "Regulator". When an entity other than a regulator is the initial sender, C.1.8.2 should be flagged as "Other".
Conformance	Required
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.3
Value Allowed	1 = Regulator 2 = Other
Business Rule(s)	

C.1.9 Other Case Identifiers

C.1.9.1 Other Case Identifiers in Previous Transmissions

User Guidance	In the event that the ICSR either has been exchanged by the two parties in the past using a different identifier or that it is exchanged simultaneously with a different identifier, this other identifier should be listed in data element C.1.9.1.r.2 and the organisations name should be captured in data element C.1.9.1.r.1. In this scenario, C.1.9.1 should be populated with "True". In all other cases, provide the nullFlavor.
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	
	False is not a value allowed for this data element. This mandatory data element should either be "true" or "nullFlavor".

C.1.9.1.r Source(s) of the Case Identifier(s) (repeat as necessary)

C.1.9.1.r.1 Source(s) of the Case Identifier

User Guidance	This repeatable data element should be used in conjunction with C.1.9.1.r.2 to provide all sources (organisation's name) of electronic transmissions for this case. If the case has been received from another sender, all other case identifiers included in C.1.9.1.r.1 (and C.1.9.1.r.2) should be retransmitted. In addition, the case identifier assigned by the previous sender in C.1.1 should be included here by the retransmitter.
Conformance	Optional, but required if C.1.9.1 = "true".
Data Type	100AN
OID	2.16.840.1.113883.3.989.2.1.3.3
Value Allowed	Free text
Business Rule(s)	
	The following notation will be used to represent C.1.9.1.r.1: <id assigningAuthorityName="C.1.9.1.r.1" extension="C.1.9.1.r.2" root="2.16.840.1.113883.3.989.2.1.3.3"/> The root indicates the namespace of C.1.9.1, the actual "Source of the Case Identifier" (C.1.9.1.r.1) and the "Case Identifier" (C.1.9.1.r.2) are populated at id and extension, respectively.

C.1.9.1.r.2 Case Identifier(s)

User Guidance	This repeatable data element should be used in conjunction with C.1.9.1.r.1 to provide all other case identifiers for this case used in ICH ICSR *electronic* transmissions. If the case has been received from another sender, all other case identifiers included in C.1.9.1.r.1 (and C.1.9.1.r.2) should be retransmitted. In addition, the case identifier assigned by the previous sender in C.1.1 should be included here by the retransmitter.
Conformance	Optional, but required if C.1.9.1 = "true".
Data Type	100AN
OID	2.16.840.1.113883.3.989.2.1.3.3
Value Allowed	Free text (See C.1.1 user guidance for format)
Business Rule(s)	
	The following notation will be used to represent C.1.9.1.r.2: <id assigningAuthorityName="C.1.9.1.r.1" extension="C.1.9.1.r.2" root="2.16.840.1.113883.3.989.2.1.3.3"/> The root indicates the namespace of C.1.9.1, the actual "Source of the Case Identifier" (C.1.9.1.r.1) and the "Case Identifier" (C.1.9.1.r.2) are populated at id and extension, respectively.

C.1.10.r Identification Number of the Report Which Is Linked to This Report (repeat as necessary)

User Guidance	This data element captures an identifier of another report or case that warrants being evaluated together with this ICSR. This includes, but is not limited to, a mother / parent-child pair where both had events / reactions, siblings with common exposure, several reports involving the same patient, an ICSR previously sent via paper without a conformant E2B *Worldwide Unique Case Identification Number*, or several similar reports from same reporter (cluster). The reason for the linkage between ICSRs should be provided in H.4. For example, if a sender wishes to reference (link) an ICSR A to ICSR B, then the sender populates the data element C.1.10.r in both reports: **ICSR** / **C.1.8.1** / **C.1.10.r** A123 / cc-MAHy-A123 / cc-MAHy-B456 B456 / cc-MAHy-B456 / cc-MAHy-A123 This data element should be populated in both ICSRs when possible, although there are cases in which one case may not have an E2B *Worldwide Unique Case Identification Number* (e.g., legacy paper report never transmitted in ICH E2B).
Conformance	Optional
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	

C.1.11 Report Nullification / Amendment

C.1.11.1 Report Nullification / Amendment

User Guidance	This data element should be used to indicate that a previously transmitted ICSR is either considered completely void (nullified) (for example when the whole case was found to be erroneous), or amended (for example when, after an internal review or according to an expert opinion, some items have been corrected, such as adverse event / reaction terms, seriousness, seriousness criteria or causality assessment). In case of amendment it is important to use the same "Sender's (case) Safety Report Unique Identifier" (C.1.1) and "Worldwide Unique Case Identification" (C.1.8) previously submitted (See exceptions in C.1.1). If it becomes necessary to submit a report that has been previously nullified, a new "Sender's (case) Safety Report Unique Identifier" (C.1.1) and "Worldwide Unique Identifier" (C.1.8.1) should be assigned. The date originally reported in C.1.5 should not be changed in an amended or nullified report if no new information on the case has been received from a primary source.
Conformance	Optional
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.5

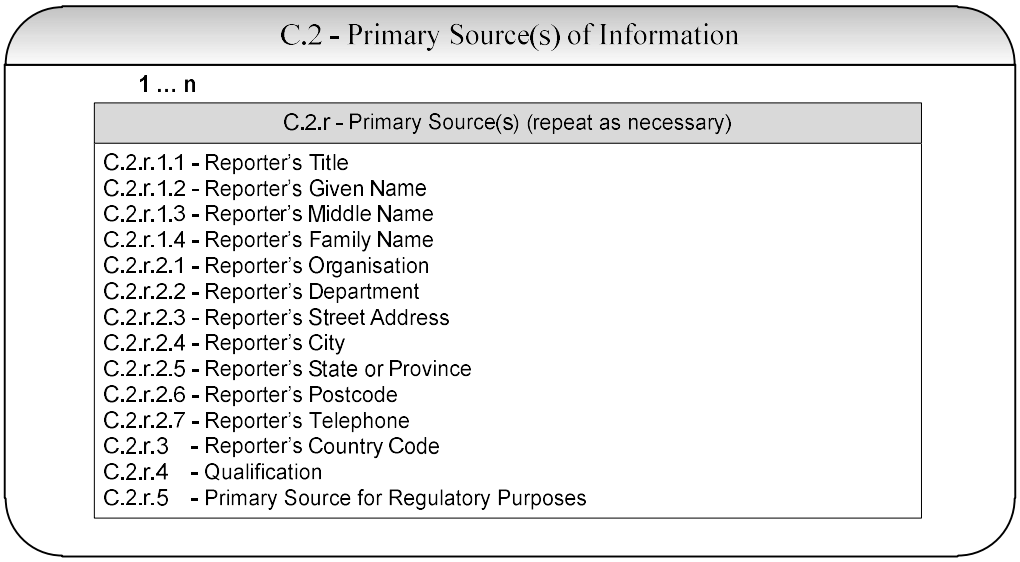
Value Allowed	1 = Nullification 2 = Amendment
Business Rule(s)	

C.1.11.2 Reason for Nullification / Amendment

User Guidance	This item should be used to indicate the reason why a previously transmitted ICSR is either considered completely void (nullified) (for example when the whole case was found to be erroneous), or amended (for example when, after an internal review or according to an expert opinion, some items have been modified, such as adverse reaction / event terms, seriousness, seriousness criteria or causality assessment). It is important to use the same Worldwide Unique Identifier previously submitted in C.1.8.1. The date originally reported in C.1.5 should not be changed in an amended report.
Conformance	Optional, but required when C.1.11.1 is populated.
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rule(s)	

C.2.r PRIMARY SOURCE(S) OF INFORMATION (REPEAT AS NECESSARY)

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 retransmitters; the latter is captured in Section C.3.



	Reporter's Name	**Reporter's Address and Telephone**	**Reporter's Country Code**	**Qualification**	**Primary Source for Regulatory Purposes**
Data Element	C.2.r.1.1 C.2.r.1.2 C.2.r.1.3 C.2.r.1.4	C.2.r.2.1 C.2.r.2.2 C.2.r.2.3 C.2.r.2.4 C.2.r.2.5 C.2.r.2.6 C.2.r.2.7	C.2.r.3	C.2.r.4	C.2.r.5
User Guidance	The identification of the reporter (primary source) could be prohibited by certain national or regional confidentiality requirements. The information should be provided when it is in conformance with confidentiality requirements. However, at least one subsection for each Primary Source should be completed to ensure that it is an identifiable reporter. When an ICSR is forwarded by a Health Authority with no information on the primary source, C.2.r should identify the Health Authority as the primary source. C.2.r.4 should be populated with nullFlavor "UNK". Additionally,				

	C.1.3 may be populated with a code of "4" (Not available to sender (unknown), if appropriate. If only the name of the reporter is known and confidentiality requirements prohibit transmission of the reporter's full name or initials, the data elements C.2.r.1.2, C.2.r.1.3, and / or C.2.r.1.4 can be masked and "populated" with a nullFlavor as appropriate, in compliance with confidentiality requirements or reporter request. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.
Business Rule(s)	
	Each ICSR shall have one primary reporter (primary source) identified in conformance with regional confidentiality requirements. Depending on the local legal requirements regarding confidentiality, it might be necessary to mask some of the elements used to identify the reporter in the transmitted message. If the elements that are being used to identify the reporter are known to the sender but cannot be transmitted due to data privacy requirements, then those data elements should be left blank with nullFlavor = MSK. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

C.2.r.1 Reporter's Name

C.2.r.1.1 Reporter's Title

User Guidance	This data element captures the reporter's title.
Conformance	Optional
Data Type	50AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK, UNK
Business Rule(s)	
	See the business rules for C.2.r.

C.2.r.1.2 Reporter's Given Name

User Guidance	This data element captures the reporter's given name.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Seethe business rules for C.2.r.

C.2.r.1.3 Reporter's Middle Name

User Guidance	This data element captures the reporter's middle name.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Seethe business rules for C.2.r. ISO / HL7 27953-2 does not support the concept of "middle name", thus to transmit this in the message it is necessary to repeat the "given name" tag. The first "given name" tag captures reporter's given name and the second "given name" tag captures reporter's middle name. The order of the tags indicate the order of the names. <name> <prefix>**C.2.r.1.1**</prefix> <!--C.2.r.1.1: Reporter's Title #1 --> <given>**C.2.r.1.2**</given> <!--C.2.r.1.2: Reporter's Given Name #1 --> <given>**C.2.r.1.3**</given> <!--C.2.r.1.3: Reporter's Middle Name #1 --> <family>**C.2.r.1.4**</family> <!--C.2.r.1.4: Reporter's Family Name #1 --> </name>

C.2.r.1.4 Reporter's Family Name

User Guidance	This data element captures the reporter's family name.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	See the business rules for C.2.r.

C.2.r.2 Reporter's Address and Telephone

C.2.r.2.1 Reporter's Organisation

User Guidance	This data element captures the reporter's organisation's name.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK

Business Rule(s)	
	See the business rules for C.2.r.

C.2.r.2.2 Reporter's Department

User Guidance	This data element captures the reporter's department name.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	See the business rules for C.2.r.

C.2.r.2.3 Reporter's Street

User Guidance	This data element captures the reporter's street name.
Conformance	Optional
Data Type	100AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	See the business rules for C.2.r.

C.2.r.2.4 Reporter's City

User Guidance	This data element captures the reporter's city name.
Conformance	Optional
Data Type	35AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	See the business rules for C.2.r.

C.2.r.2.5 Reporter's State or Province

User Guidance	This data element captures the reporter's State or Province.
Conformance	Optional
Data Type	40AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	See the business rules for C.2.r.

C.2.r.2.6 Reporter's Postcode

User Guidance	This data element captures the reporter's postcode.
Conformance	Optional
Data Type	15AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	See the business rules for C.2.r.

C.2.r.2.7 Reporter's Telephone

User Guidance	This data element captures the reporter's telephone number, including the country code and any extension. Numbers should be entered in a fashion that allows for international dialling (e.g., +cc) and not include any domestic trunk prefix. For example, in countries where the leading zero is used domestically, the local 0xx-yyy-zzzz becomes international +cc-xx-yyy-zzzz. Also, the phone number should not include *domestic* international dialling prefixes (also known as country exit codes, such as 00 in Europe, 011 in US, 010 in Japan). Begin with the *International Telecommunications Union* plus sign (+) notation followed by the country code appropriate for the location of the telephone number. Additional visual separators for human readability are not required. If used these characters should be limited to dashes "-" or dots ".".
Conformance	Optional
Data Type	33AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	See the business rules for C.2.r.

C.2.r.3 Reporter's Country Code

User Guidance	This data element captures the two letter ISO 3166 Part 1 code (ISO 3166-1 alpha-2) to represent the name of the reporter's country.
Conformance	Optional, but required if C.2.r.5 = 1.
Data Type	2A
OID	1.0.3166.1.2.2
Value Allowed	ISO 3166-1 (alpha 2), EU
Business Rule(s)	
	A two character country code will be used in all instances. The country code EU exists in the ISO 3166 country code list as an exceptional reservation code to support any application that needs to represent the name European Union. In this case, "EU" will be accepted as the country code.

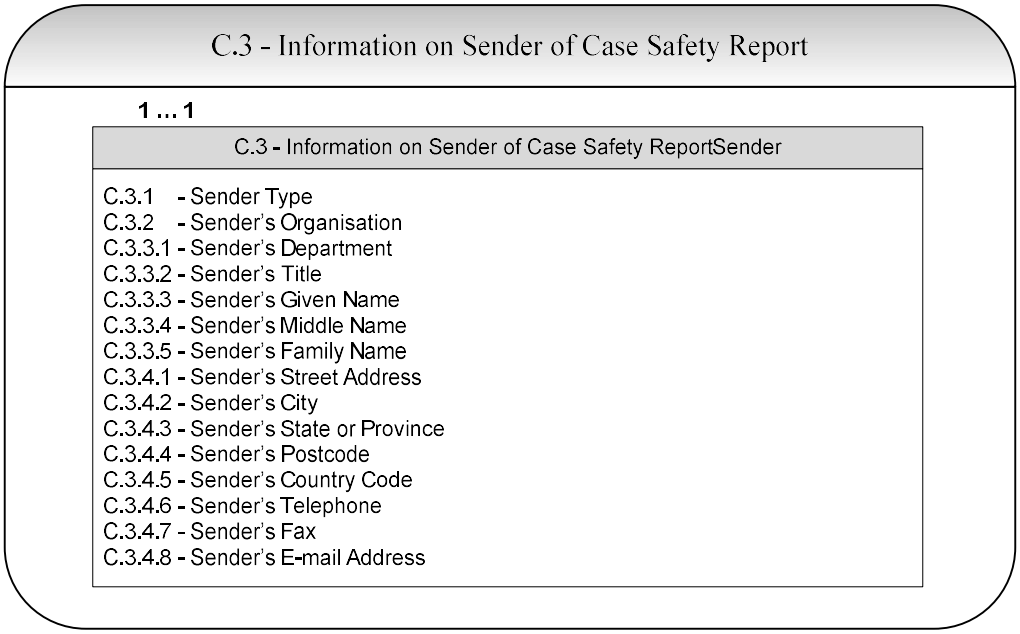
C.2.r.4 Qualification

User Guidance	This data element captures the reporter qualification.
Conformance	Optional, but required if C.2.r.5 = 1.
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.6
Value Allowed	1 = Physician 2 = Pharmacist 3 = Other health professional 4 = Lawyer 5 = Consumer or other non health professional nullFlavor: UNK
Business Rule(s)	
	If the reporter's qualification is unknown to the sender, this data element should be left blank with nullFlavor = UNK. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

C.2.r.5 Primary Source for Regulatory Purposes

User Guidance	This data element identifies which primary source to use for regulatory purposes and in case of multiple sources, it identifies the source of the *World Wide Case Unique Identification* number; this source should identify *where* the case occurred. The data element determines where the case will be reported as a "domestic" case and where the case will be reported as a "foreign" case. The primary source should be distinguished from senders and retransmitters. Information on the sender and retransmitters is captured in section C.3. When retransmitting an electronic ICSR received from another sender, such as a regulatory authority, partner company, or other source in E2B format, the Primary Source information in the initial transmission should reflect the reporter with first-hand information on the case and this should not be changed. The reporter identified as "Primary Source for Regulatory Purposes" in the original transmission should remain unchanged in all subsequent retransmission of the case.
Conformance	Required for one and only one instance of this element.
Data Type	1N
OID	None
Value Allowed	1 = primary
Business Rule(s)	
	It is required that one Primary Source of Information (C.2) be flagged as *Primary source for regulatory purposes*. Therefore this data element must be set to "1" once, and only once, for one C.2 block in each ICH ICSR message. Do not use this element to rank sources either sequentially, chronologically, or hierarchically.

C.3 INFORMATION ON SENDER OF CASE SAFETY REPORT



C.3.1 Sender Type

User Guidance	This data element captures the type of sender organisation or individual. In this context, "Pharmaceutical company" includes biotechnology companies, market authorisation holders and other manufacturers required to submit ICSRs.
Conformance	Required
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.7
Value Allowed	1 = Pharmaceutical Company 2 = Regulatory Authority 3 = Health Professional 4 = Regional Pharmacovigilance Centre 5 = WHO collaborating centres for international drug monitoring 6 = Other (e.g., distributor or other organisation) 7 = Patient / Consumer
Business Rule(s)	

C.3.2 Sender's Organisation

User Guidance	This data element captures the sender's organisation name (e.g., company name or regulatory authority name).
Conformance	Required if the "Sender Type" (C.3.1) is not coded as 7 (Patient / Consumer).
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	

C.3.3 Person Responsible for Sending the Report

	Sender's Department	**Sender's Title**	**Sender's Given Name**	**Sender's Middle Name**	**Sender's Family Name**
Data Element	C.3.3.1	C.3.3.2	C.3.3.3	C.3.3.4	C.3.3.5
User Guidance	The name of person in the company or agency who is responsible for the authorisation of report dissemination. This would usually be the same person who signs the covering memo for paper submissions. The identification of the person responsible for sending the ICSR could be prohibited by certain national or international confidentiality requirements. The information should be provided when it is in conformance with confidentiality requirements.				
Business Rule(s)					
	Depending on the local legal requirements regarding confidentiality, it might be necessary to omit some of the elements used to identify the person responsible for sending the report in the transmitted message.				

C.3.3.1 Sender's Department

User Guidance	This data element captures the name of the sender's department.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	See the business rules for C.3.3.

C.3.3.2 Sender's Title

User Guidance	This data element captures the sender's title.
Conformance	Optional
Data Type	50AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	See the business rules for C.3.3.

C.3.3.3 Sender's Given Name

User Guidance	This data element captures the sender's given name.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	See the business rules for C.3.3.

C.3.3.4 Sender's Middle Name

User Guidance	This data element captures the sender's middle name.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	ISO / HL7 27953-2 does not support the concept of "middle name", thus to transmit this in the message it is necessary to repeat the "given name" tag. The first "given name" tag captures sender's given name and the second "given name" tag captures sender's middle name. The order of the tags indicate the order of the names. <name> <prefix>**C.3.3.2**</prefix> <!--C.3.3.2: Sender's Title #1 --> <given>**C.3.3.3**</given> <!--C.3.3.3: Sender's Given Name #1 --> <given>**C.3.3.4**</given> <!--C.3.3.4: Sender's Middle Name #1 --> <family>**C.3.3.5**</family> <!--C.3.3.5: Sender's Family Name #1 --> </name> See the business rules for C.3.3.

C.3.3.5 Sender's Family Name

User Guidance	This data element captures sender's family name.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	See the business rules for C.3.3.

C.3.4 Sender's Address, Fax, Telephone and E-mail Address

	Sender's Street Address	Sender's City	Sender's State or Province	Sender's Postcode	Sender's Country Code	Sender's Telephone	Sender's Fax	Sender's E-mail Address
Data Element	C.3.4.1	C.3.4.2	C.3.4.3	C.3.4.4	C.3.4.5	C.3.4.6	C.3.4.7	C.3.4.8
User Guidance	The sender's contact information should be provided in conformance with local or international confidentiality requirements.							
Business Rule(s)								
	See the business rules for C.3.3.							

C.3.4.1 Sender's Street Address

User Guidance	This data element captures the sender's street address.
Conformance	Optional
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	See the business rules for C.3.3.

C.3.4.2 Sender's City

User Guidance	This data element captures the sender's city.
Conformance	Optional
Data Type	35AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	See the business rules for C.3.3.

C.3.4.3 Sender's State or Province

User Guidance	This data element captures the sender's state or province.
Conformance	Optional
Data Type	40AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	See the business rules for C.3.3.

C.3.4.4 Sender's Postcode

User Guidance	This data element captures the sender's postcode.
Conformance	Optional
Data Type	15AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	See the business rules for C.3.3.

C.3.4.5 Sender's Country Code

User Guidance	This data element captures the two letter ISO 3166 Part 1 code (ISO 3166-1 alpha-2) to represent the name of the sender's country.
Conformance	Optional
Data Type	2A
OID	1.0.3166.1.2.2
Value Allowed	ISO 3166-1 alpha-2
Business Rule(s)	
	See the business rules for C.3.3.

C.3.4.6 Sender's Telephone

User Guidance	This data element captures the sender's telephone number, including the country code and any extension. Numbers should be entered in a fashion that allows for international dialling (e.g., +cc) and not include any domestic trunk prefix. For example, in countries where the leading zero is used domestically, the local 0xx-yyy-zzzz becomes international +cc-xx-yyy-zzzz. Also, the phone number should not include domestic international dialling prefixes (also known as country exit codes, such as 00 in Europe, 011 in US, 010 in Japan). Begin with the International Telecommunications Union plus sign (+) notation followed by the country code appropriate for the location of the telephone number. Additional visual separators for human readability are not required. If used these characters should be limited to dashes "-" or dots ".".
Conformance	Optional
Data Type	33AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	See the business rules for C.3.3.

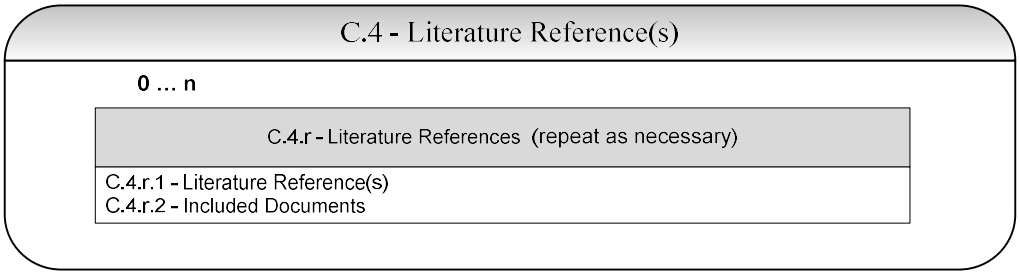
C.3.4.7 Sender's Fax

User Guidance	This data element captures the sender's fax number, including the country code and any extension. Numbers should be entered in a fashion that allows for international dialling (e.g., +cc) and not include any domestic trunk prefix. For example, in countries where the leading zero is used domestically, the local 0xx-yyy-zzzz becomes international +cc-xx-yyy-zzzz. Also, the phone number should not include *domestic* international dialling prefixes (also known as country exit codes, such as 00 in Europe, 011 in US, 010 in Japan). Begin with the *International Telecommunications Union* plus sign (+) notation followed by the country code appropriate for the location of the telephone number. Additional visual separators for human readability are not required. If used these characters should be limited to dashes "-" or dots ".".
Conformance	Optional
Data Type	33AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	See the business rules for C.3.3.

C.3.4.8 Sender's E-mail Address

User Guidance	This data element captures the sender's email address.
Conformance	Optional
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	See the business rules for C.3.3.

C.4.r Literature Reference(s) (repeat as necessary)



C.4.r.1 Literature Reference(s)

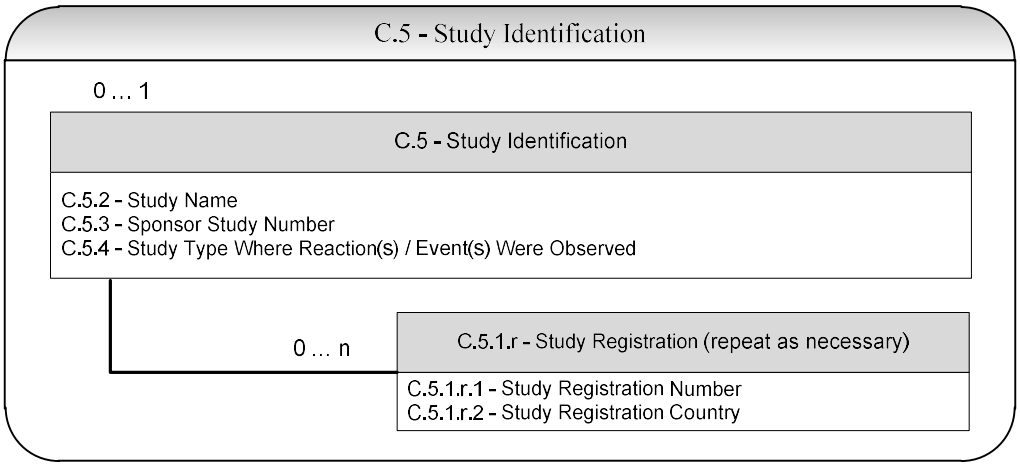
User Guidance	This data element should be used for literature article(s) that describe individual case(s), but not for articles used for data analysis. Citations should be provided in the style specified by the Vancouver Convention, known as "Vancouver style", which has been developed by the *International Committee of Medical Journal Editors*. The conventional styles, including styles for special situations, can be found in the following reference: International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med 1997; 336:309-15.
Conformance	Optional
Data Type	500AN
OID	None
Value Allowed	Free text nullFlavor: ASKU, NASK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

C.4.r.2 Included Documents

User Guidance	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.
Conformance	Optional
Data Type	N/A
OID	None
Value Allowed	Media type: e.g., Application / PDF, image / jpeg, application / DICOM, text / plain Representation: e.g., B64 Compression: e.g., DF
Business Rule(s)	
	For further information on how to attach documents to an ICSR, please see Section 3.5. Because a receiver's system may have particular configurations on handling attachments, "Value Allowed" is defined by each region.

	The standard format to be used for literature citations, as well as formats for special situations, can be found in the reference above, which is in the Vancouver style.

C.5 Study Identification



C.5.1.r Study Registration (repeat as necessary)

C.5.1.r.1 Study Registration Number

User Guidance	This repeatable data element should be populated with the study registration number as assigned in a reporting region, e.g., EudraCT number for reporting in the *European Economic Area* (EEA). Refer to regional implementation guides for details.
Conformance	Optional
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.3.6
Value Allowed	Free text nullFlavor: ASKU, NASK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information. The following notation will be used to represent C.5.1.r.1: <id extension="study registration number" root="2.16.840.1.113883.3.989.2.1.3.6"/> The root indicates the namespace of C.5.1.r.1, the actual study registration number is populated at id extension.

C.5.1.r.2 Study Registration Country

User Guidance	This data element should be populated with the country that assigned the Study Registration Number presented in C.5.1.r.1. Use the two letter ISO 3166 Part 1 code (ISO 3166-1 alpha-2) to represent the names of the country.
Conformance	Optional
Data Type	2A
OID	1.0.3166.1.2.2
Value Allowed	ISO 3166-1 alpha-2, EU nullFlavor: ASKU, NASK
Business Rule(s)	
	A two character country code will be used in all instances. The country code EU exists in the ISO 3166 country code list as an exceptional reservation code to support any application that needs to represent the name European Union. In this case, "EU" will be accepted as the country code. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

C.5.2 Study Name

User Guidance	This data element should be populated with the study name as registered in the jurisdiction where the ICSR is reported.
Conformance	Optional
Data Type	2000AN
OID	None
Value Allowed	Free text nullFlavor: ASKU, NASK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

C.5.3 Sponsor Study Number

User Guidance	This data element should be completed only if the sender is the study sponsor or has been informed of the study number by the sponsor.
Conformance	Optional
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.3.5
Value Allowed	Free text nullFlavor: ASKU, NASK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information. The following notation will be used to represent C.5.3: <id extension="sponsor study number" root="2.16.840.1.113883.3.989.2.1.3.5"/> The root indicates the namespace of C.5.3, the actual sponsor study number is populated at id extension.

C.5.4 Study Type Where Reaction(s) / Event(s) Were Observed

User Guidance	This information should be provided if the "Type of Report" (C.1.3) has been populated with "Report from study".
Conformance	Optional, but required if C.1.3 = 2 (Report from study).
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.8
Value Allowed	1 = Clinical trials 2 = Individual patient use *(*e.g., "*compassionate use" or "named patient basis")* 3 = Other studies *(*e.g., *pharmacoepidemiology, pharmacoeconomics, intensive monitoring)*
Business Rule(s)	

D PATIENT CHARACTERISTICS

This section describes the singular subject who experienced one or several adverse events / reactions. As many patient characteristics as available (e.g., known) should be provided. However, at least one data element in Section D must be populated with a meaningful value or masked to fulfil the criteria 'one identifiable patient' (See Section 3.3.1).



At least one of the data elements in Section D must be populated with a meaningful value or masked to fulfil the criteria "one identifiable patient".

In cases where a foetus or breast-feeding infant is exposed to one or several drugs through the parent *and* experienced one or several adverse events / reactions, information on both the parent and the child / foetus should be provided. Reports of these cases are referred to as parent-child / foetus reports. The following general principles should be used for filing these reports.

- If there has been no event / reaction affecting the child / foetus, the parent-child / foetus report does not apply; e.g., the data elements in Section D apply only to the parent (mother or father) who experienced the adverse reaction / event.

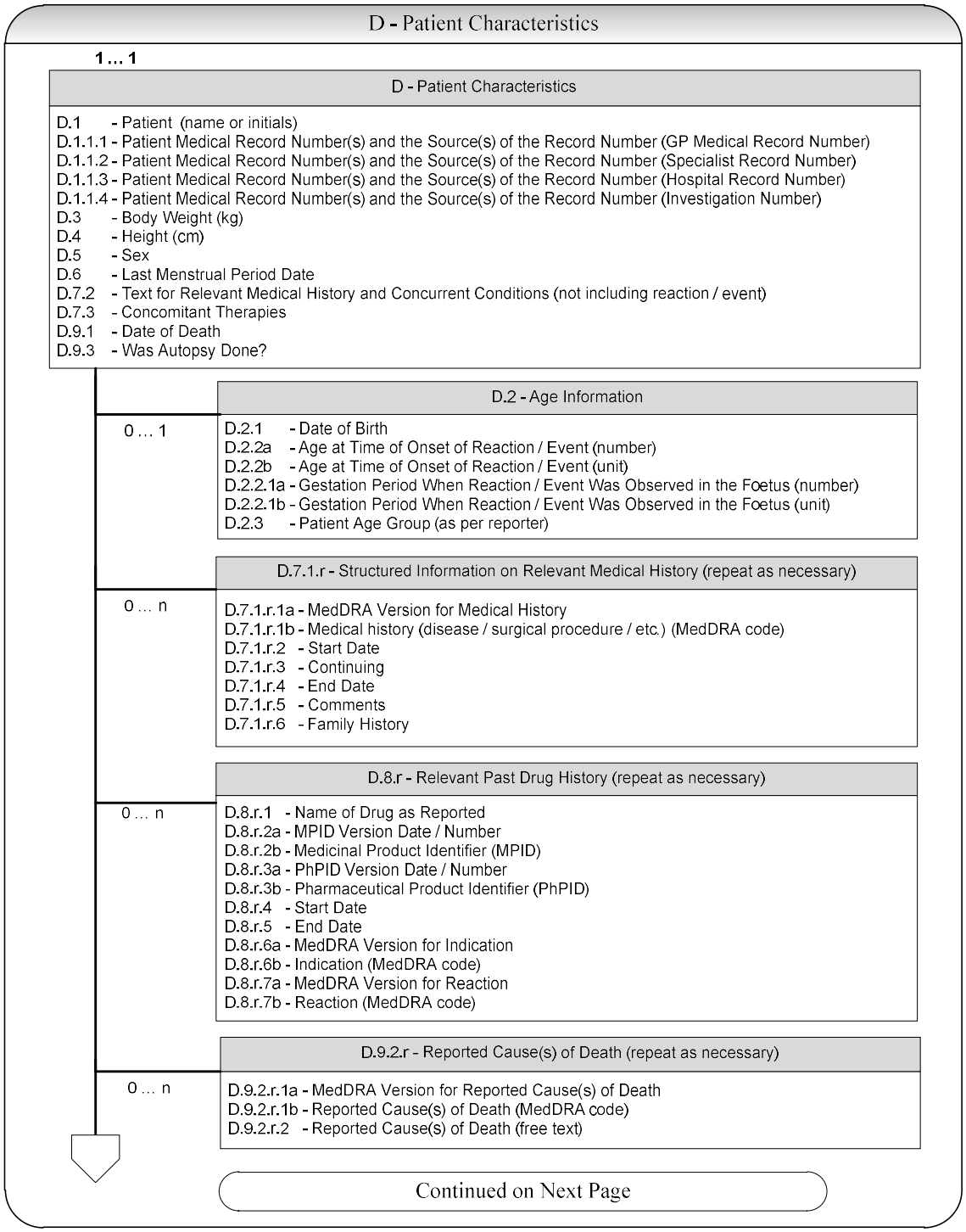
  Example: Mother suffers from pre-eclampsia and the child has no adverse reaction. Only one ICSR should be completed for the mother, with the adverse event / reaction of pre-eclampsia. No events / reactions are reported for the child, therefore a linked ICSR for the child is not applicable.
- For those cases describing miscarriage, stillbirth or early spontaneous abortion, only a mother report is applicable, e.g., the data elements in Section D apply to the mother. However, if suspect drug(s) were taken by the father, this information should be indicated in the data element G.k.10.r.
- If both the parent and the child / foetus sustain adverse event(s) / reaction(s), two separate reports, e.g., one for the parent (mother or father) and one for the child / foetus, should be provided and should be linked by using the data element C.1.10.r in each report.

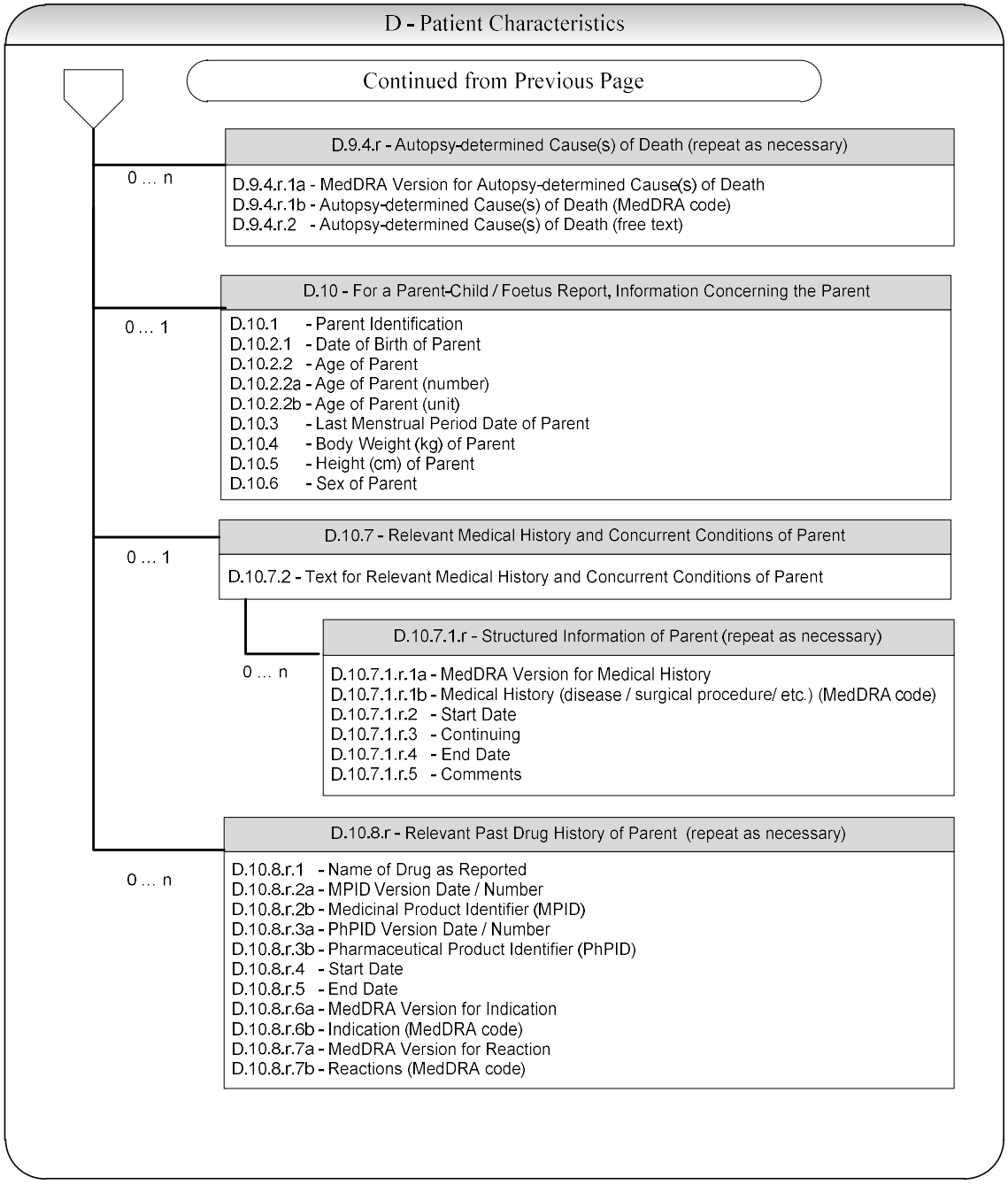
  Example: Mother suffers from pre-eclampsia and, at parturition, the baby had a low birth weight and club foot. Two linked ICSRs should be submitted: The mother's report should have the adverse event / reaction of pre-eclampsia; the report for the baby should have event / reaction terms for low birth weight and club foot. The term pre-eclampsia would only apply to the mother's case. The data element C.1.10.r should be completed for both cases (e.g., the mother's and baby's).
- If only the child / foetus has an adverse event / reaction (other than early spontaneous abortion / foetal demise) the information provided in this section applies only to the child / foetus, and characteristics concerning the parent (mother or father) who was the source of exposure to the suspect drug should be provided in Section D.10.

  Example: A report of foetal distress, where the mother delivered via a Caesarean section. There will be one ICSR for the baby, with the adverse event / reaction of foetal distress.

The Caesarean section should not be considered an adverse event / reaction for the mother. The mother's characteristics should be captured in Section D with the Caesarean section as relevant medical history (D.10.7).

- If both parents are the suspect source of exposure to the suspect drug(s) then the case should reflect the mother's information in Section D.10 and the case narrative (Section H.1) should describe the entire case, including the father's information.


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?
0 ... 1
D.2 - Age Information
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)
0 ... n
D.7.1.r - Structured Information on Relevant Medical History (repeat as necessary)
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
0 ... n
D.8.r - Relevant Past Drug History (repeat as necessary)
D.8.r.1 - Name of Drug as Reported
D.8.r.2a - MPID Version Date / Number
D.8.r.2b - Medicinal Product Identifier (MPID)
D.8.r.3a - PhPID Version Date / Number
D.8.r.3b - Pharmaceutical Product Identifier (PhPID)
D.8.r.4 - Start Date
D.8.r.5 - End Date
D.8.r.6a - MedDRA Version for Indication
D.8.r.6b - Indication (MedDRA code)
D.8.r.7a - MedDRA Version for Reaction
D.8.r.7b - Reaction (MedDRA code)
0 ... n
D.9.2.r - Reported Cause(s) of Death (repeat as necessary)
D.9.2.r.1a - MedDRA Version for Reported Cause(s) of Death
D.9.2.r.1b - Reported Cause(s) of Death (MedDRA code)
D.9.2.r.2 - Reported Cause(s) of Death (free text)
Continued on Next Page


D - Patient Characteristics
Continued from Previous Page
D.9.4.r - Autopsy-determined Cause(s) of Death (repeat as necessary)
0 … n
D.9.4.r.1a - MedDRA Version for Autopsy-determined Cause(s) of Death
D.9.4.r.1b - Autopsy-determined Cause(s) of Death (MedDRA code)
D.9.4.r.2 - Autopsy-determined Cause(s) of Death (free text)
D.10 - For a Parent-Child / Foetus Report, Information Concerning the Parent
0 … 1
D.10.1 - Parent Identification
D.10.2.1 - Date of Birth of Parent
D.10.2.2 - Age of Parent
D.10.2.2a - Age of Parent (number)
D.10.2.2b - Age of Parent (unit)
D.10.3 - Last Menstrual Period Date of Parent
D.10.4 - Body Weight (kg) of Parent
D.10.5 - Height (cm) of Parent
D.10.6 - Sex of Parent
D.10.7 - Relevant Medical History and Concurrent Conditions of Parent
0 … 1
D.10.7.2 - Text for Relevant Medical History and Concurrent Conditions of Parent
D.10.7.1.r - Structured Information of Parent (repeat as necessary)
0 … n
D.10.7.1.r.1a - MedDRA Version for Medical History
D.10.7.1.r.1b - Medical History (disease / surgical procedure/ etc.) (MedDRA code)
D.10.7.1.r.2 - Start Date
D.10.7.1.r.3 - Continuing
D.10.7.1.r.4 - End Date
D.10.7.1.r.5 - Comments
D.10.8.r - Relevant Past Drug History of Parent (repeat as necessary)
0 … n
D.10.8.r.1 - Name of Drug as Reported
D.10.8.r.2a - MPID Version Date / Number
D.10.8.r.2b - Medicinal Product Identifier (MPID)
D.10.8.r.3a - PhPID Version Date / Number
D.10.8.r.3b - Pharmaceutical Product Identifier (PhPID)
D.10.8.r.4 - Start Date
D.10.8.r.5 - End Date
D.10.8.r.6a - MedDRA Version for Indication
D.10.8.r.6b - Indication (MedDRA code)
D.10.8.r.7a - MedDRA Version for Reaction
D.10.8.r.7b - Reactions (MedDRA code)

D.1 Patient (name or initials)

User Guidance	It is important that this data element is populated. The identification of the patient might be prohibited by certain national confidentiality laws or directives. The information should be provided when it is in conformance with the confidentiality requirements.
Conformance	Required
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK, UNK
Business Rule(s)	
	If the initials are known to the sender but cannot be transmitted due to data privacy requirements, this data element should be left blank with nullFlavor = MSK. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.1.1 Patient Medical Record Number(s) and Source(s) of the Record Number (if allowable)

Record numbers can include the health professional record(s) number(s), hospital record(s) number(s), or patient / subject identification number in a study. The most appropriate data element should be used in order to indicate the source of the number and facilitate record retrieval when possible and desirable.

The patient identification in a clinical trial can be transmitted below in the "Patient Medical Record Number(s) and Source(s) of the Record Number (Investigation number)" (D.1.1.4). Multiple elements should be extracted from the source database, like Centre ID, Patient ID and a random (check) number, and concatenated in this element to assure a unique patient identification.

A numeric code listed in the ICH code list #4 is required to identify the Medical Record Type for D.1.1.1 through D.1.1.4. For further information, refer to the X-path described in current Appendix I(G) Technical Information and Reference Instances.

D.1.1.1 Patient Medical Record Number(s) and Source(s) of the Record Number (GP Medical Record Number)

User Guidance	See Section D.1.1.
Conformance	Optional
Data Type	20AN
OID	2.16.840.1.113883.3.989.2.1.1.4 and 2.16.840.1.113883.3.989.2.1.3.7
Value Allowed	Free text nullFlavor: MSK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

	The following notation will be used to represent D.1.1.1: <id extension="medical record number" root="2.16.840.1.113883.3.989.2.1.3.7"/> <code code="1" codeSystem="2.16.840.1.113883.3.989.2.1.1.4"/> The root indicates the namespace of D.1.1.1, the actual medical record number is populated at id extension. The code of "GP(gpmrn)" is populated to distinguish from D.1.1.2 to D.1.1.4.

D.1.1.2 Patient Medical Record Number(s) and Source(s) of the Record Number (Specialist Record Number)

User Guidance	See Section D.1.1.
Conformance	Optional
Data Type	20AN
OID	2.16.840.1.113883.3.989.2.1.1.4 and 2.16.840.1.113883.3.989.2.1.3.8
Value Allowed	Free text nullFlavor: MSK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information. The following notation will be used to represent D.1.1.2: <id extension="medical record number" root="2.16.840.1.113883.3.989.2.1.3.8"/> <code code="2" codeSystem="2.16.840.1.113883.3.989.2.1.1.4"/> The root indicates the namespace of D.1.1.2, the actual medical record number is populated at id extension. The code of "Specialist(specialistMrn)" is populated to distinguish from D.1.1.1, D.1.1.3 and D.1.1.4.

D.1.1.3 Patient Medical Record Number(s) and Source(s) of the Record Number (Hospital Record Number)

User Guidance	See Section D.1.1.
Conformance	Optional
Data Type	20AN
OID	2.16.840.1.113883.3.989.2.1.1.4 and 2.16.840.1.113883.3.989.2.1.3.9
Value Allowed	Free text nullFlavor: MSK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information. The following notation will be used to represent D.1.1.3: <id extension=" medical record number " root="2.16.840.1.113883.3.989.2.1.3.9"/> <code code="3" codeSystem="2.16.840.1.113883.3.989.2.1.1.4"/>

	The root indicates the namespace of D.1.1.3, the actual medical record number is populated at id extension. The code of "Hospital record(hospitalMrn)" is populated to distinguish from D.1.1.1, D.1.1.2 and D.1.1.4.

D.1.1.4 Patient Medical Record Number(s) and Source(s) of the Record Number (Investigation Number)

User Guidance	See Section D.1.1.
Conformance	Optional
Data Type	20AN
OID	2.16.840.1.113883.3.989.2.1.1.4 and 2.16.840.1.113883.3.989.2.1.3.10
Value Allowed	Free text nullFlavor: MSK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information. The following notation will be used to represent D.1.1.4: <id extension=" medical record number " root="2.16.840.1.113883.3.989.2.1.3.10"/> <code code="4" codeSystem="2.16.840.1.113883.3.989.2.1.1.4"/> The root indicates the namespace of D.1.1.4, the actual medical record number is populated at id extension. The code of "Investigation" is populated to distinguish from D.1.1.1 to D.1.1.3.

D.2 Age Information

Only one of the elements describing age should be used. The choice should be based upon the most precise information available and in conformance with the regional confidentiality requirements.

D.2.1 Date of Birth

User Guidance	This data element captures the full precision date (e.g., day, month, year) for the date of birth of the patient. If the full date of birth is not known, an approximate age can be captured in Section D.2.2. Alternatively, the "Patient Age Group (as per reporter)" (D.2.3) can be used to indicate the age of the patient.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK
Business Rule(s)	
	Minimum precision required is the day (i.e., "CCYYMMDD").

	The date specified cannot refer to a future date. If the date of birth is known to the sender but cannot be transmitted due to data privacy requirements, this data element should be left blank with nullFlavor = MSK. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.2.2 Age at Time of Onset of Reaction / Event

If several reactions / events are in the report, the age at the time of the first reaction / event should be used. For foetal reaction(s) / event(s), the Gestation Period When Reaction / Event Was Observed in the Foetus (D.2.2.1) should be used.

When providing the age in decades, please note that, for example, 7 decades refers to a person in his / her 60's.

D.2.2a Age at Time of Onset of Reaction / Event (number)

User Guidance	See Section D.2.2.
Conformance	Optional, but required if D.2.2b is populated.
Data Type	5N
OID	None
Value Allowed	Numeric
Business Rule(s)	

D.2.2b Age at Time of Onset of Reaction / Event (unit)

User Guidance	See Section D.2.2.
Conformance	Optional, but required if D.2.2a is populated.
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.1.26
Value Allowed	UCUM codes for Year (a) Month (mo), Week (wk), Day (d), Hour (h), and Decade (10.a).
Business Rule(s)	

	The gestation period at the time of *exposure* is captured in Section G.k.6.

D.2.2.1a Gestation Period When Reaction / Event Was Observed in the Foetus (number)

User Guidance	This data element captures the value (quantity) for the gestation period when the *reaction/event was observed* in the foetus. In a foetus report, regardless whether the exposure was from father or mother, the foetus age information should be provided in D.2.2.1.

	Information concerning the parent should be provided in section D.10.
Conformance	Optional, but required if D.2.2.1b is populated.
Data Type	3N
OID	None
Value Allowed	Numeric
Business Rule(s)	

D.2.2.1b Gestation Period When Reaction/Event Was Observed in the Foetus (unit)

User Guidance	This data element captures the unit for the value of the gestation period when the *reaction/event* was observed in the foetus. In a foetus report, regardless whether the exposure was from father or mother, the foetus age information should be provided in D.2.2.1. Information concerning the parent should be provided in section D.10.
Conformance	Optional, but required if D.2.2.1a is populated.
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.1.26
Value Allowed	UCUM codes for Month (mo), Week (wk), and Day (d) and {Trimester}
Business Rule(s)	

D.2.3 Patient Age Group (as per reporter)

User Guidance	The terms in *Value Allowed* for this data element are not defined in this document and are intended to reflect the term used by the reporter (i.e., as they were reported by the primary source). This section should be completed *only* when the age is not provided with any more precision (e.g., Sections D.2.1 or D.2.2 is blank).
Conformance	Optional
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.9
Value Allowed	0 = Foetus 1 = Neonate (Preterm and Term newborns) 2 = Infant 3 = Child 4 = Adolescent 5 = Adult 6 = Elderly
Business Rule(s)	

D.3 Body Weight (kg)

User Guidance	This data element captures the reported body weight of the patient in kilograms at the time of the event / reaction.
Conformance	Optional
Data Type	6N
OID	None
Value Allowed	Numeric
Business Rule(s)	
	Fractions or decimals are allowed using a period (dot). No commas are allowed in this numeric data element.

D.4 Height (cm)

User Guidance	This data element captures the reported height of the patient in centimetres at the time of the event / reaction.
Conformance	Optional
Data Type	3N
OID	None
Value Allowed	Numeric
Business Rule(s)	
	Provide rounded number. No fractions, decimals, and commas are allowed in this numeric data element.

D.5 Sex

User Guidance	This data element captures the sex of the patient.
Conformance	Optional
Data Type	1N
OID	1.0.5218
Value Allowed	1 = Male 2 = Female nullFlavor: MSK, UNK, ASKU, NASK
Business Rule(s)	
	If the sex is known to the sender but cannot be transmitted due to data privacy requirements, then leave the data element blank and use the nullFlavor element with "MSK" as masked. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.6 Last Menstrual Period Date

User Guidance	This data element captures the date of the last menstrual period of the patient when it is relevant. Imprecise dates can be included (e.g., month and year, or year only). Other information on menopause or conditions related to menopause should be captured in the data element D.7.1.r. If this report is for a child / foetus, then the mother's last menstrual period is captured in the data element D.10.3.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK
Business Rule(s)	
	Minimum precision required is the year (i.e., "CCYY"). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.7 Relevant Medical History and Concurrent Conditions (not including reaction / event)

D.7.1.r Structured Information on Relevant Medical History (repeat as necessary)

Medical judgment should be exercised in completing this section. Only information pertinent to understanding the case is desired (such as diseases, conditions such as pregnancy, surgical procedures, psychological trauma, risk factors, etc.). In case of prematurity, the birth weight when known should be recorded in the data element "Comments" (D.7.1.r.5). If precise dates are not known and a text description is pertinent to understanding the medical history, or if concise additional information is helpful in showing the relevance of the past medical history, such information can be included in the "Comments" (D.7.1.r.5). In order to identify *relevant* medical information of the family (e.g., hereditary diseases), the data element "Family History" (D.7.1.r.6) should be set to "true" (Yes) for the appropriate medical history of the patient.

If there is no relevant medical history and no concurrent conditions for inclusion in D.7.1, then D.7.2 is required. If the reason is that the relevant medical history is not documented at the time of the report then the value for D.7.2 is "Unknown". This should not be confused with "None". In the first case the nullFlavor is used with the value "UNK" and in the second case the text 'None' will be transmitted.

The designation of "r" in this section indicates that each item is repeatable and that it corresponds to the same 'r' in all subsections. A separate block (r) should be used for each relevant medical history term. For example, if two conditions are reported, the first condition would be described in items D.7.1.1.1 through D.7.1.1.6, and the other condition would be described in items D.7.1.2.1 through D.7.1.2.6.

D.7.1.r.1a MedDRA Version for Medical History

User Guidance	This data element provides the MedDRA version for D.7.1.r.1b.
Conformance	Optional, but required if D.7.1.r.1b is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric and "."(dot)
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. For MedDRA version 15.1 value allowed is "15.1".

D.7.1.r.1b Medical History (disease / surgical procedure / etc.) (MedDRA code)

User Guidance	See Section D.7.1.r.
Conformance	Optional, but required if D.7.1.r.1a is populated.
Data Type	8N
OID	2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	

D.7.1.r.2 Start Date

User Guidance	This data element captures the start date of the patient's medical condition. Imprecise dates can be used for both start and end dates, although the highest precision is desirable.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Minimum precision required is the year (i.e., "CCYY"). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.7.1.r.3 Continuing

User Guidance	This data element indicates if the "medical condition" in D.7.1.r.1b is known to be still present at the time of this report.
Conformance	Optional
Data Type	Boolean
OID	None
Value Allowed	false true nullFlavor: MSK, ASKU, NASK, UNK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.7.1.r.4 End Date

User Guidance	This data element captures the end date of the patient's medical condition. Imprecise dates can be used for both start and end dates, although the highest precision is desirable. Do not provide an End Date if the medical condition is continuing.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Minimum precision required is the year (i.e., "CCYY"). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.7.1.r.5 Comments

User Guidance	This data element provides additional relevant information about the 'medical condition' in D.7.1.r.1b that could not be captured otherwise in a structured data element. For example, in case of prematurity, the birth weight should be recorded here; or in the absence of imprecise dates, a text description that would aid in understanding the medical history (e.g.," since childhood") can also be provided here.
Conformance	Optional
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rule(s)	

D.7.1.r.6 Family History

User Guidance	This data element captures is set to "true when the medical information provided in the "Structured Information on Relevant Medical History"(D.7.1.r) is reported also to be present in another family member (e.g., hereditary diseases). However, this data element is not used when the same medical concept is already provided in the "Relevant Medical History and Concurrent Conditions of Parent" (D.10.7). When this data element is set to "true", detailed information should be provided in the narrative Section H.1.
Conformance	Optional
Data Type	Boolean
OID	None
Value Allowed	True
Business Rule(s)	
	When *Parent* Medical history already is provided in D.10.7, do not set this data element to "true" (Yes) for similar medical concepts also coded for the patient.

D.7.2 Text for Relevant Medical History and Concurrent Conditions (not including reaction / event)

User Guidance	This data element captures information about any other medical history that could not be coded in D.7.1.r. Also, the term "None" should be used here when there is no relevant medical history and no concurrent conditions reported. If relevant medical history is not documented at the time of the report, this data element is set to *unknown* (i.e., nullFlavor=UNK) and should not be confused with "None".
Conformance	Optional, but required if Section D.7.1 is null.
Data Type	10000AN
OID	None
Value Allowed	Free text

	nullFlavor: MSK, ASKU, NASK, UNK
Business Rule(s)	
	If the relevant medical history is unknown to the sender (e.g., not reported), this data element should be left blank with nullFlavor = UNK. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.7. 3 Concomitant Therapies

User Guidance	This data element indicates at the time of the reaction there were concomitant therapies such as radiotherapy, drug class, dietary supplements or other products not otherwise describable in Section G. When this data element is set to 'true', details should be provided in the narrative Section H.1.
Conformance	Optional
Data Type	Boolean
OID	None
Value Allowed	True
Business Rule(s)	



In case of concomitant medication(s) the structured information on the medicinal product(s) should be provided in Section G. In case of other administered therapies that cannot be structured in Section G, then the data element D.7.3 is set to true and details are provided in the narrative Section H.1.

D.8.r Relevant Past Drug History (repeat as necessary)

This section concerns *relevant* drugs previously administered and which have been stopped *before* the Adverse Event onset. It does not concern drugs taken concomitantly or drugs which might have potentially been involved in the current reaction(s) / event(s). Medical judgment should be exercised in completing this section. Medications that have been stopped might be considered suspect based on the elimination half-life of the drug and the known pharmacodynamic effects of the drug in a particular patient (for example, a patient with known renal or liver impairment). Information concerning concomitant and other suspect drugs should be included in Section G. The information provided here can also include previous experience with similar drugs.

Based on the medicinal product name as reported by the primary source, the most specific ISO IDMP identifier - the *Medicinal Product Identifier* (MPID) or the *Pharmaceutical Product Identifier* (PhPID) - should be provided. If a MPID or a PhPID for the reported medicinal product is not available, these data elements should be left blank.

A MedDRA LLT numeric code should be used for the "Indication" (D.8.r.6b) and the "Reaction" (D.8.r.7b). In the event of previous exposure to drug(s) or vaccine(s) without reaction, the

MedDRA code “No adverse effect” should be used in the Reaction column. Imprecise dates can be used for both start and end dates.

The designation of “r” in this section indicates that each item is repeatable and that it corresponds to the same “r” in all subsections. A separate block (r) should be used for each relevant drug term. For example, if two drugs are reported, the first drug would be described in items D.8.1.1 through D.8.1.7 and the other drug would be described in items D.8.2.1 through D.8.2.7.

Overall, a conservative approach should be taken and if there is any doubt, the product should be considered a suspect drug. If there are critical or controversial issues to be discussed in regard to this judgment they can be briefly mentioned in a narrative in Section H.

	As a general principle all drugs that were completed / discontinued *before* the start of the treatment with the suspect(ed) drug(s) should be included in the “Relevant Past Drug History” section (D.8). Any drug(s) that are not suspected of causing the event or reaction and that are administered to the patient at the time of the reaction should be listed as concomitant medication in Section G.

	A history of allergy to a *specific* drug is preferably reported in Section D.8 “Relevant Past Drug History”, using the suspect drug name and MedDRA terms in the indication and reaction data elements. These data elements are often searchable in most databases and thus this is the preferred option. When a non-specific allergy is reported (e.g., “sulfa” allergy is reported, but unknown if to a sulphonamide antibiotic or to a sulfa-containing diuretic), this information could be reported in Section D.7.1 “Structured information on relevant medical history” by using the LLT “Drug hypersensitivity” (or a more descriptive LLT) under “Disease / surgical procedure / etc.”, and the name of the drug under “comments”.

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

User Guidance	This data element captures the name of the medicinal product as used by the reporter. It is recognized that a single product can have different proprietary names in different countries, even when it is produced by a single manufacturer. Trade name, generic name or class of drug can be used.
Conformance	Optional, but required by the schema if any data element in section D.8.r is used.
Data Type	250AN
OID	None
Value Allowed	Free text nullFlavor: UNK, NA
Business Rule(s)	
	NullFlavor = NA should be used when there is no previous exposure to a drug or vaccine. NullFlavor = UNK is allowed when there is previous drug history but the name of the drug or vaccine is not known.

D.8.r.2a MPID Version Date/Number

User Guidance	This data element provides the version date for D.8.r.2b.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	None
Value Allowed	As per ISO IDMP.
Business Rule(s)	

D.8.r.2b Medicinal Product Identifier (MPID)

User Guidance	This data element captures MPID. If an MPID for the reported medicinal product is not available, this data element should be left blank.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	As per ISO IDMP.
Value Allowed	As per ISO IDMP.
Business Rule(s)	
	Any given drug entry may have either MPID or PhPID, but NOT both.

D.8.r.3a PhPID Version Date/Number

User Guidance	This data element provides the version date for D.8.r.3b.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	None
Value Allowed	As per ISO IDMP.
Business Rule(s)	

D.8.r.3b Pharmaceutical Product Identifier (PhPID)

User Guidance	This data element captures the PhPID. If a PhPID for the reported medicinal product is not available, this data elements should be left blank.
Conformance	Optional Not allowed if D.8.r.2 is populated.
Data Type	As per ISO IDMP.
OID	As per ISO IDMP.
Value Allowed	As per ISO IDMP.
Business Rule(s)	
	Any given drug entry may have either MPID or PhPID, but NOT both.

D.8.r.4 Start Date

User Guidance	This data element captures the start date of the medicinal product. Imprecise dates can be used for both start and end dates.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Minimum precision required is the year (i.e., “CCYY”). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.8.r.5 End Date

User Guidance	This data element captures the start date of the medicinal product. Imprecise dates can be used for both start and end dates.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Minimum precision required is the year (i.e., “CCYY”). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.8.r.6a MedDRA Version for Indication

User Guidance	This data element provides the MedDRA version for D.8.r.6b.
Conformance	Optional, but required if D.8.r.6b is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric and “.”(dot)
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. For MedDRA version 15.1 value allowed is “15.1”.

D.8.r.6b Indication (MedDRA code)

User Guidance	This data element captures the MedDRA LLT code for the indication of the medicinal product.
Conformance	Optional, but required if D.8.r.6a is populated.
Data Type	8N
OID	2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	

D.8.r.7a MedDRA Version for Reaction

User Guidance	This data element provides the MedDRA version for D.8.r.7b.
Conformance	Optional, but required if D.8.r.7b is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric and “.”(dot)
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. For MedDRA version 15.1 value allowed is “15.1”.

D.8.r.7bReaction (MedDRA code)

User Guidance	Medical judgment should be exercised in completing this data element. The information provided here describes previous experience with the drug described in D.8.r. See Section D.8.r. A MedDRA LLT code should be used.
Conformance	Optional, but required if D.8.r.7a is populated.
Data Type	8N
OID	2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	

D.9 In Case of Death

D.9.1 Date of Death

User Guidance	This data element captures the reported date of death for the patient. An imprecise date can be used.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Minimum precision required is the year (i.e., "CCYY"). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.9.2.r Reported Cause(s) of Death (repeat as necessary)

The designation of "r" in this section indicates that each item is repeatable and that it corresponds to the same "r" in all subsections. A separate block (r) should be used for each cause of death term. For example, if two causes of death are reported, the first cause would be described in items D.9.2.1.1 through D.9.2.1.2 and the other cause would be described in items D.9.2.2.1 through D.9.2.2.2.

D.9.2.r.1a MedDRA Version for Reported Cause(s) of Death

User Guidance	This data element captures the MedDRA version for D.9.2.r.1b.
Conformance	Optional, but required if D.9.2.r.1b is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric and "."(dot)
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. For MedDRA version 15.1 value allowed is "15.1".

D.9.2.r.1b Reported Cause(s) of Death (MedDRA code)

User Guidance	This data element captures the MedDRA LLT code for the reported cause of death.
Conformance	Optional, but required if D.9.2.r.1a is populated.
Data Type	8N
OID	2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	

D.9.2.r.2 Reported Cause(s) of Death (free text)

User Guidance	This data element captures the original reporter's words and / or short phrases used to describe the cause of death. Text should be provided in an English translation for international transmission.
Conformance	Optional, but required if D.9.2.r.1 is populated.
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

D.9.3 Was Autopsy Done?

User Guidance	This data element indicates if an autopsy was done.
Conformance	Optional, but required if D.9.1 is populated.
Data Type	Boolean
OID	None
Value Allowed	false true nullFlavor: ASKU, NASK, UNK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.9.4.r Autopsy-determined Cause(s) of Death (repeat as necessary)

D.9.4.r.1a MedDRA Version for Autopsy-determined Cause(s) of Death

User Guidance	This data element captures the MedDRA version for D.9.4.r.1b.
Conformance	Optional, but required if D.9.4.r.1b is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric and “.”(dot)
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. For MedDRA version 15.1 value allowed is “15.1”.

D.9.4.r.1b Autopsy-determined Cause(s) of Death (MedDRA code)

User Guidance	This data element captures the MedDRA LLT code for the autopsy-determined cause of death.
Conformance	Optional, but required if D.9.4.r.1a is populated.
Data Type	8N
OID	2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	

D.9.4.r.2 Autopsy-determined Cause(s) of Death (free text)

User Guidance	This data element captures the original reporter's words and / or short phrases used to describe the autopsy-determined cause of death. Text should be provided in an English translation for international transmission.
Conformance	Optional, but required if D.9.4.r.1 is populated.
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

D.10 FOR A PARENT-CHILD / FOETUS REPORT, INFORMATION CONCERNING THE PARENT

This section should be used in the case of a parent-child/foetus report where the parent had *no* reaction / event. **Otherwise, this section should not be used**. See the user guidance for Section D.

D.10.1 Parent Identification

User Guidance	See the user guidance for D.1.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK, UNK
Business Rule(s)	
	If the name or initials of the parent are unknown to the sender, this data element should be left blank with nullFlavor = UNK. If the name or initials are known to the sender but cannot be transmitted due to data privacy requirements, this data element should be left blank with nullFlavor = MSK. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.10.2 Parent Age Information

The parent age at the time of reaction / event to the child / foetus should be used. Select only one of the data elements from D.10.2.1 or D.10.2.2. The choice should be based upon the most precise information available and in conformance with the regional confidentiality requirements.

If the full date of birth is not known, an incomplete date can be used. Alternatively, an approximate age can be captured in Section D.10.2.2.

D.10.2.1 Date of Birth of Parent

User Guidance	This data element captures the date of birth of the parent. An incomplete date can be used.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	nullFlavor: MSK, ASKU, NASK
Business Rule(s)	

	Minimum precision required is the year (i.e., “CCYY”). The date specified cannot refer to a future date. If the date of birth is known to the sender but cannot be transmitted due to data privacy requirements, this data element should be left blank with nullFlavor set to “MSK”. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.10.2.2 Age of Parent

D.10.2.2a Age of Parent (number)

User Guidance	This data element captures the age value (quantity) for the parent.
Conformance	Optional, but required if D.10.2.2b is populated.
Data Type	3N
OID	None
Value Allowed	Numeric
Business Rule(s)	

D.10.2.2b Age of Parent (unit)

User Guidance	This data element captures the unit for the age value in D.10.2.2a.
Conformance	Optional, but required if D.10.2.2a is populated.
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.1.26
Value Allowed	UCUM codes for Year (a) and Decade (10.a)
Business Rule(s)	

D.10.3 Last Menstrual Period Date of Parent

User Guidance	This data element captures the date of the last menstrual period for the parent.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Minimum precision required is the year (i.e., “CCYY”). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.10.4 Body Weight (kg) of Parent

User Guidance	This data element captures the weight of the parent in kilograms.
Conformance	Optional
Data Type	6N
OID	None

Value Allowed	Numeric
Business Rule(s)	
	Fractions or decimals are allowed using a period. No commas are allowed in this numeric data element.

D.10.5 Height (cm) of Parent

User Guidance	This data element captures the reported height of the parent in centimetres.
Conformance	Optional
Data Type	3N
OID	None
Value Allowed	Numeric
Business Rule(s)	
	Provide rounded number. No fractions, decimals, and commas are allowed in this numeric data element

D.10.6 Sex of Parent

User Guidance	This data element captures the sex of the parent.
Conformance	Required if any data element in D.10 section is populated.
Data Type	1N
OID	1.0.5218
Value Allowed	1 = Male 2 = Female nullFlavor: UNK, MSK, ASKU, NASK
Business Rule(s)	
	If the sex of the parent is known to the sender but cannot be transmitted due to data privacy requirements, this data element should be left blank with nullFlavor = MSK. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.10.7 Relevant Medical History and Concurrent Conditions of Parent

D.10.7.1.r Structured Information of Parent (repeat as necessary)

D.10.7.1.r.1a MedDRA Version for Medical History

User Guidance	This data element provides the MedDRA version for D.10.7.1.r.1b
Conformance	Optional, but required if D.10.7.1.r.1b is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric and “.”(dot)
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. For MedDRA version 15.1 value allowed is “15.1”.

D.10.7.1.r.1b Medical History (disease / surgical procedure / etc.) (MedDRA code)

User Guidance	This data element captures the MedDRA LLT code for the medical condition of the parent. See Section D.7.1.r.

Conformance	Optional, but required if D.10.7.1.r.1a is populated.
Data Type	8N
OID	2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	

D.10.7.1.r.2 Start Date

User Guidance	This data element captures the start date of the medical condition of the parent.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Minimum precision required is the year (i.e., "CCYY"). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.10.7.1.r.3 Continuing

User Guidance	This data element indicates if the 'medical condition' in D.10.7.1.r is known to be still present at the time of this report.
Conformance	Optional
Data Type	Boolean
OID	None
Value Allowed	false true nullFlavor: MSK, ASKU, NASK, UNK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.10.7.1.r.4 End Date

User Guidance	This data element captures the stop date of the medical condition of the parent. Do not provide an End Date if the medical condition of the parent is continuing.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK, ASKU, NASK
Business Rule(s)	

	Minimum precision required is the year (i.e., “CCYY”). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.10.7.1.r.5 Comments

User Guidance	This data element provides additional relevant information about the ‘medical condition’ in D.10.7.1.r that could not be captured otherwise in a structured data element.
Conformance	Optional
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rule(s)	

D.10.7.2 Text for Relevant Medical History and Concurrent Conditions of Parent

User Guidance	This data element captures information about any other medical history for the parent that could not be coded in D.10.7.1.r.
Conformance	Optional
Data Type	10000AN
OID	None
Value Allowed	Free text
Business Rule(s)	

D.10.8.r Relevant Past Drug History of Parent (repeat as necessary)

D.10.8.r.1 Name of Drug as Reported

User Guidance	This data element captures the name of the medicinal product as reported by the reporter. It is recognised that a single product can have different proprietary names in different countries, even when it is produced by a single manufacturer. See Section D.8.r.
Conformance	Optional
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

D.10.8.r.2a MPID Version Date/Number

User Guidance	See Section D.8.r.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	None
Value Allowed	As per ISO IDMP.

Business Rule(s)	

D.10.8.r.2b Medicinal Product Identifier (MPID)

User Guidance	See Section D.8.r.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	As per ISO IDMP.
Value Allowed	As per ISO IDMP.
Business Rule(s)	
	Any given drug entry may have either MPID or PhPID, but NOT both.

D.10.8.r.3a PhPID Version Date/Number

User Guidance	See Section D.8.r.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	None
Value Allowed	As per ISO IDMP.
Business Rule(s)	

D.10.8.r.3b Pharmaceutical Product Identifier (PhPID)

User Guidance	See Section D.8.r.
Conformance	Optional Not allowed if D.10.8.r.2b is populated.
Data Type	As per ISO IDMP.
OID	As per ISO IDMP.
Value Allowed	As per ISO IDMP.
Business Rule(s)	
	Any given drug entry may have either MPID or PhPID, but NOT both.

D.10.8.r.4 Start Date

User Guidance	This data element captures the start date of relevant past drug history for the parent.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Minimum precision required is the year (i.e., “CCYY”). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.10.8.r.5 End Date

User Guidance	This data element captures the stop date of relevant past drug history for the parent.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Minimum precision required is the year (i.e., "CCYY"). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

D.10.8.r.6a MedDRA Version for Indication

User Guidance	This data element provides the MedDRA version for D.10.8.r.6b.
Conformance	Optional, but required if D.10.8.r.6b is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric and "."(dot)
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. For MedDRA version 15.1 value allowed is "15.1".

D.10.8.r.6b Indication (MedDRA code)

User Guidance	This data element captures the MedDRA LLT code for the indication of the medicinal product.
Conformance	Optional, but required if D.10.8.r.6a is populated.
Data Type	8N
OID	2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	

D.10.8.r.7a MedDRA Version for Reaction

User Guidance	This data element provides the MedDRA version for D.10.8.r.7b
Conformance	Optional, but required if D.10.8.r.7b is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric and "."(dot)
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. For MedDRA version 15.1 value allowed is "15.1".

D.10.8.r.7b Reactions (MedDRA code)

User Guidance	Medical judgment should be exercised in completing this data element. The information provided here describes previous experience of the parent with the drug described in D.10.8.r.
Conformance	Optional, but required if D.10.8.r.7a is populated.
Data Type	8N
OID	2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	

E.i REACTION(S)/EVENT(S) (REPEAT AS NECESSARY)

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.

	For technical reason, each reaction / event should be assigned an internal ID so that G.k.9.i.1 can refer to the reaction / event from the drug / event matrix.

	A separate block (i) should be used for each reaction / event term. For example, if two reactions are observed, the first reaction would be described in items E.1.1 through E.1.9, and the other reaction would be described in items E.2.1 through E.2.9.

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.1 Reaction / Event as Reported by the Primary Source

E.i.1.1a Reaction / Event as Reported by the Primary Source in Native Language

User Guidance	This data element captures the original reporter's words and / or short phrases used to describe the reaction/event. Text should be provided in the native language it was received, when it is received in a language *other* than English.
Conformance	Optional
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

E.i.1.1b Reaction / Event as Reported by the Primary Source Language

User Guidance	Provide the language used in E.i.1.1a by using an *International Standard, Codes for the representation of names of languages-- Part 2: alpha-3* code.
Conformance	Optional, but required if E.i.1.1a is populated.
Data Type	3A
OID	1.0.639.2
Value Allowed	ISO 639-2/RA, alpha-3
Business Rule(s)	

E.i.1.2 Reaction / Event as Reported by the Primary Source for Translation

User Guidance	This data element captures the original reporter's words and/or short phrases used to describe the reaction/event that should be provided in an English translation for international transmission.
Conformance	Optional
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

E.i.2.1a MedDRA Version for Reaction / Event

User Guidance	This data element provides the MedDRA version for E.i.2.1b.
Conformance	Required
Data Type	4AN
OID	None
Value Allowed	Numeric and “.”(dot)
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. For MedDRA version 15.1 value allowed is “15.1”.

E.i.2.1b Reaction / Event (MedDRA code)

User Guidance	This data element captures the MedDRA LLT most closely corresponding to the reaction/event as reported by the primary source. In the exceptional circumstance when a MedDRA term cannot be found, the sender should use clinical judgment to complete this item with the best MedDRA approximation (See MedDRA Term Selection: Points to Consider).
Conformance	Required
Data Type	8N
OID	2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	

E.i.3.1 Term Highlighted by the Reporter

User Guidance	A highlighted term is a reaction / event that the primary source indicated was a major concern or reason for reporting the case. If the information is not explicitly provided by the initial reporter the term should not be considered a highlighted term. This data element should be populated only if the medical concept conveyed in E.i.1 is consistent with the reason why the reporter contacted the sender. For example, this data element can be used to indicate the specific diagnosis that was identified by the reporter. Suppose the reporter specifies *flu-like syndrome* comprising of *fever*, *chills*, *sneezing*, *myalgia* and *headache*, then *flu-like syndrome* is the highlighted term. If only one event is cited in a case report, this one is by implication considered highlighted by the reporter. It is assumed that the event seriousness is provided by the reporter; otherwise, it is assessed by the sender.
Conformance	Optional
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.10
Value Allowed	1 = Yes, highlighted by the reporter, NOT serious 2 = No, not highlighted by the reporter, NOT serious 3 = Yes, highlighted by the reporter, SERIOUS 4 = No, not highlighted by the reporter, SERIOUS
Business Rule(s)	
	See E.i.3.2 for the 'seriousness' assessment of the highlighted term.

E.i.3.2 Seriousness Criteria at Event Level

The seriousness criteria of the reaction / event should be based on the definitions provided in the ICH E2A and E2D guidelines. More than one seriousness criteria can be chosen. If the event is not serious or there is no information regarding seriousness of the event then all of these data elements should be "NI". It is assumed that the event seriousness is provided by the reporter; otherwise, it is assessed by the sender.

In cases of foetal demise such as miscarriage, (where the ICSR should be prepared only for the parent), the seriousness criterion is "*Other medically important condition"*. Furthermore,

depending if the parent experienced complications, the seriousness criterion could also include "*life-threatening"* and / or "*hospitalisation"*.

E.i.3.2a Results in Death

User Guidance	See Section E.i.3.2.
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	

E.i.3.2b Life Threatening

User Guidance	See Section E.i.3.2.
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	

E.i.3.2c Caused / Prolonged Hospitalisation

User Guidance	See Section E.i.3.2.
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	

E.i.3.2d Disabling / Incapacitating

User Guidance	See Section E.i.3.2.
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	

E.i.3.2e Congenital Anomaly / Birth Defect

User Guidance	See Section E.i.3.2.
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	

E.i.3.2f Other Medically Important Condition

User Guidance	See Section E.i.3.2.
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	

E.i.4 Date of Start of Reaction / Event

User Guidance	This data element captures the date of the start of the reaction/event. When multiple terms are reported (e.g., diagnosis with signs and symptoms) and the reporter does not provide a specific onset date for *each* reaction / event, this data element should be populated with the start date of the first symptom.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Minimum precision required is the year (i.e., “CCYY”). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

E.i.5 Date of End of Reaction / Event

User Guidance	This data element captures the date the reaction / event is reported as *resolved / recovered* or *resolved / recoveredwithsequelae* (E.i.7). When multiple terms are reported (e.g., diagnosis with signs and symptoms) and the reporter does not provide a specific stop date for each reaction / event, this data element should be populated with the end date of the last symptom.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Minimum precision required is the year (i.e., "CCYY"). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

E.i.6a Duration of Reaction / Event (number)

User Guidance	This section will usually be computed from the start / end date and time of the reaction / event. However, there might be situations in which the precise duration of the reaction / event and date can be useful, such as for a reaction/event of short duration such as anaphylaxis or arrhythmia. In such a case, populate 1 data element for the date (start or end date) and this data element. This data element captures the value (quantity) for the duration of the reaction.
Conformance	Optional, but required if E.i.6b is populated.
Data Type	5N
OID	None
Value Allowed	Numeric
Business Rule(s)	

E.i.6b Duration of Reaction / Event (unit)

User Guidance	This data element captures the unit of time for the value recorded in E.i.6a.
Conformance	Optional, but required if E.i.6a is populated.
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.1.26
Value Allowed	Constrained UCUM codes
Business Rule(s)	

E.i.7 Outcome of Reaction / Event at the Time of Last Observation

User Guidance	This data element captures the latest outcome of the reaction / event at the time of the report. In case of irreversible congenital anomalies, the choice *not recovered / not resolved / ongoing* should be used. For other irreversible medical conditions, *recovered / resolved with sequelae* should be used. *Fatal* should be used when death is *possibly related* to the reaction / event. Considering the difficulty of deciding between "reaction / event caused death" and "reaction / event contributed significantly to death", both concepts are grouped in a single category. Where the death is unrelated to the reaction/event, according to both the reporter and the sender, "fatal" should NOT be selected here; nevertheless, death should be reported under Section D.9.
Conformance	Required
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.11
Value Allowed	1 = recovered/resolved 2 = recovering/resolving 3 = not recovered/not resolved/ongoing 4 = recovered/resolved with sequelae 5 = fatal 0 = unknown
Business Rule(s)	

E.i.8 Medical Confirmation by Healthcare Professional

User Guidance	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. If the healthcare professional also provides an assessment of causality (related or not to the suspect drug), that should be recorded in G.k.9.
Conformance	Optional
Data Type	Boolean
OID	None
Value Allowed	false true
Business Rule(s)	
	"False" means the event is not confirmed, it does not mean the event did not occur. If the event is reported by a healthcare professional, this is not transmitted.

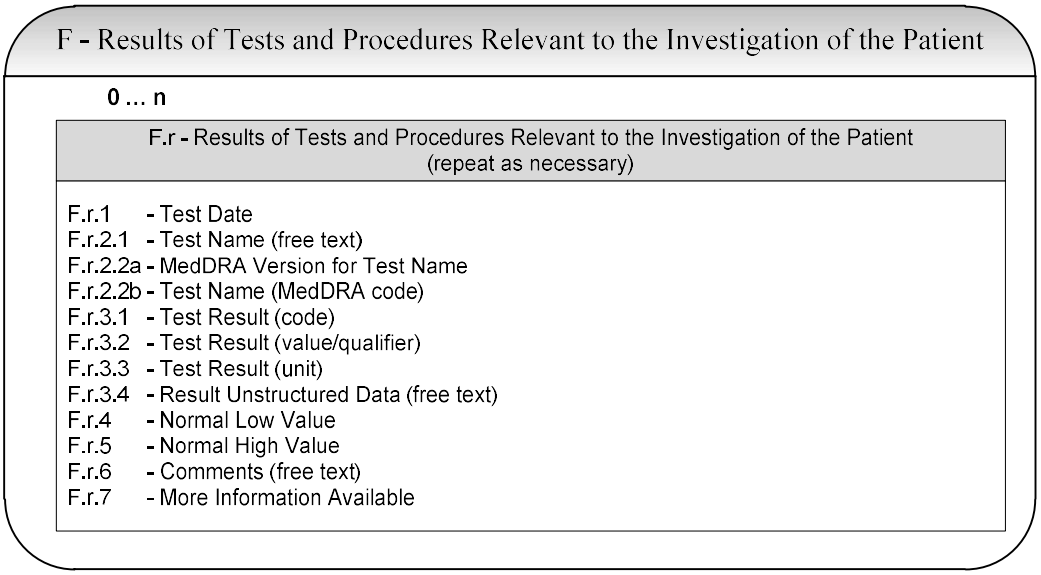
E.i.9 Identification of the Country Where the Reaction / Event Occurred

User Guidance	This data element captures the country where the reaction occurred. For example, a patient living in **Country A** experienced *headache* while travelling in **Country B**; this *headache* was suspected to be an adverse drug reaction and was reported by a health professional in **Country C**. The data element C.2.r.3 should be populated with **Country C**, and the data element E.i.9 should be populated with **Country B**.
Conformance	Optional
Data Type	2A
OID	1.0.3166.1.2.2
Value Allowed	ISO 3166-1 alpha-2, EU
Business Rule(s)	
	A two character country code will be used in all instances. The country code EU exists in the ISO 3166 country code list as an exceptional reservation code to support any application that needs to represent the name European Union.In this case, "EU" will be accepted as the country code.

F.r Results of Tests and Procedures Relevant to the Investigation of the Patient (repeat as necessary)

This section captures the tests and procedures performed to diagnose or confirm the reaction / event, including those tests done to investigate (exclude) a non-drug cause (e.g., serologic tests for infectious hepatitis in suspected drug-induced hepatitis). Both positive and negative results should be reported. While structured information is preferable, provisions are made to transmit the information as free text.

The designation of "r" in this section indicates that each item is repeatable and that it corresponds to the same "r" in all subsections. A separate block (r) should be used for each test / procedure. For example, if two tests are reported, the first test would be described in items F.1.1 through F.1.7, and the other test would be described in items F.2.1 through F.2.7.



F.r.1 Test Date

User Guidance	This data element captures the date of the test or procedure. Imprecise dates can be used.
Conformance	Optional, but required if F.r.2 is populated.
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information. nullFlavor = UNK
Business Rule(s)	
	Minimum precision required is the year (i.e., "CCYY"). The date specified cannot refer to a future date. If the test date is unknown, use nullFlavor =UNK. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

F.r.2 Test Name

F.r.2.1 Test Name (free text)

User Guidance	This data element captures a free text description of the test when an appropriate MedDRA code is unavailable.
Conformance	Optional, but required if F.r.1 is populated and F.r.2.2b is not populated.
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

F.r.2.2a MedDRA Version for Test Name

User Guidance	This data element provides the MedDRA version for F.r.2.2b.
Conformance	Optional, but required when F.r.2.2b is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric and “.”(dot)
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. For MedDRA version 15.1 value allowed is “15.1”.

F.r.2.2b Test Name (MedDRA code)

User Guidance	This data element captures the MedDRA LLT code for the test name.
Conformance	Optional, but required when F.r.1 is populated and F.r.2.1 is not populated.
Data Type	8N
OID	2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	

F.r.3 Test Result

A Test Result is required for each F block. When a numeric value cannot be used to describe the result, provisions are made to use a controlled vocabulary. If results and units cannot be split, F.r.3.4 should be used.

F.r.3.1 Test Result (code)

User Guidance	This data element allows a descriptive code to indicate the test result.
Conformance	Optional, but required if F.r.2 is populated, and neither F.r.3.2 nor F.r.3.4 is populated.
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.12
Value Allowed	1 = Positive 2 = Negative 3 = Borderline 4 = Inconclusive
Business Rule(s)	
	This data element can be used when a numeric value cannot describe the result.

F.r.3.2 Test Result (value / qualifier)

User Guidance	This data element captures the value (amount) for the test result. The supported qualifiers are “greater than”, “less than”, “greater than or equal to” and “less than or equal to”. See Appendix I (G) to the IG for XML examples of expression of qualifiers using nullFlavors. This data element is represented in HL7 IVL_PQ data type which is a composite data type with multiple attributes. ‘PINF’ and ‘NINF’ null flavors are used to express ‘Greater than’ and ‘Less than’ a specific value respectively.
Conformance	Optional, but required if F.r.2 is populated, and F.r.3.1 and F.r.3.4 is not populated.
Data Type	50N
OID	None
Value Allowed	Numeric nullFlavor: NINF, PINF
Business Rule(s)	
	If results and units cannot be split, F.r.3.4 should be used. Followings are examples for test results with exact value, greater or less than a specific value. Test Result = 10 (mg/dl): <value xsi:type="IVL_PQ"> Test Result < 10 (mg/dl): <value xsi:type="IVL_PQ"> <low nullFlavor="NINF"/> <high value="10" unit="mg/dl" inclusive="false"/></value> Test Result <= 10 (mg/dl): <value xsi:type="IVL_PQ"> <low nullFlavor="NINF"/> <high value="10" unit="mg/dl" inclusive="true"/></value> Test Result > 10 (mg/dl): <value xsi:type="IVL_PQ"> <low value="10" unit="mg/dl" inclusive="false"/> <high nullFlavor="PINF"/></value> Test Result >= 10 (mg/dl): <value xsi:type="IVL_PQ"> <low value="10" unit="mg/dl" inclusive="true"/> <high nullFlavor="PINF"/></value>

F.r.3.3 Test Result (unit)

User Guidance	This data element captures the unit for the test value. When a UCUM code is not suitable, or results (F.r.3.2) and units (F.r.3.3) cannot be split, F.r.3.4 should be used.
Conformance	Optional, but required if F.r.3.2 is populated.

Data Type	50AN
OID	2.16.840.1.113883.6.8
Value Allowed	UCUM
Business Rule(s)	
	Constrained UCUM is not provided for this unit. Select most appropriate unit from UCUM codes.

F.r.3.4 Result Unstructured Data (free text)

User Guidance	This data element is used when "results" and "units" cannot be split, often because a UCUM code is not available for the test unit. For example, for the test "protein excretion", the result could be recorded here as "125mg / 24 hours". Unstructured findings from tests and procedures such as CT, MRI, radiogram, etc. should also be provided as free text in field F.r.3.4.
Conformance	Optional, but required if F.r.2 is populated, and F.r.3 is not populated.
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rule(s)	

F.r.4 Normal Low Value

User Guidance	This data element captures the “lowest” value in the normal range for the test. This value is usually published by the laboratory providing the test results. The same units as used in F.r.3.3 are implied.
Conformance	Optional
Data Type	50AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	The value should be transmitted as two XML attributes: value and unit. Use only numeric data in “value” attribute and in the “unit” attribute provide the same unit as used F.r.3.3. The value will be transmitted as physical quantity (PQ) as separate amount and unit and following line indicates this value is normal low value: <value xsi:type="PQ" value="40" unit="mg/dl"/> <interpretationCode code="L" codeSystem="2.16.840.1.113883.5.83"/>

F.r.5 Normal High Value

User Guidance	This data element captures the “highest” value in the normal range for the test. This value is usually published by the laboratory providing the test results. The same units as used in F.r.3.3 are implied.
Conformance	Optional
Data Type	50AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	The value should be transmitted as two XML attributes: value and unit. Use only numeric data in “value” attribute and in the “unit” attribute provide the same unit as used F.r.3.3. The value will be transmitted as physical quantity (PQ) as separate amount and unit and following line indicates this value is normal high value : <valuexsi:type="PQ" value="80" unit="mg/dl"/> <interpretationCode code="H" codeSystem="2.16.840.1.113883.5.83"/>

F.r.6 Comments (free text)

User Guidance	This data element captures any relevant comments made by the reporter about the test result.
Conformance	Optional
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rule(s)	

F.r.7 More Information Available

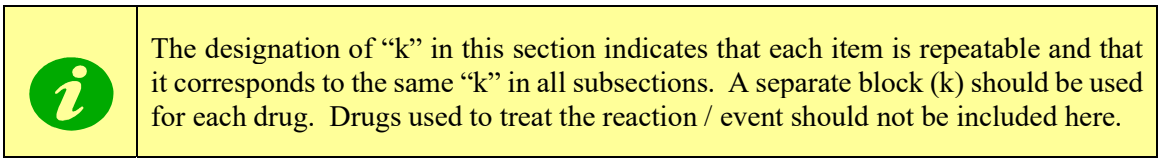
User Guidance	This data element indicates if more information is held by the sender about the test and test result. For example, “true” means that more documentation is available upon request e.g., ECG strips, chest X-ray. “False” means that no more documentation is available from the sender. If this data element is set to “true”, then C.1.6.1 should be set to “true”.
Conformance	Optional
Data Type	Boolean
OID	None
Value Allowed	false true
Business Rule(s)	

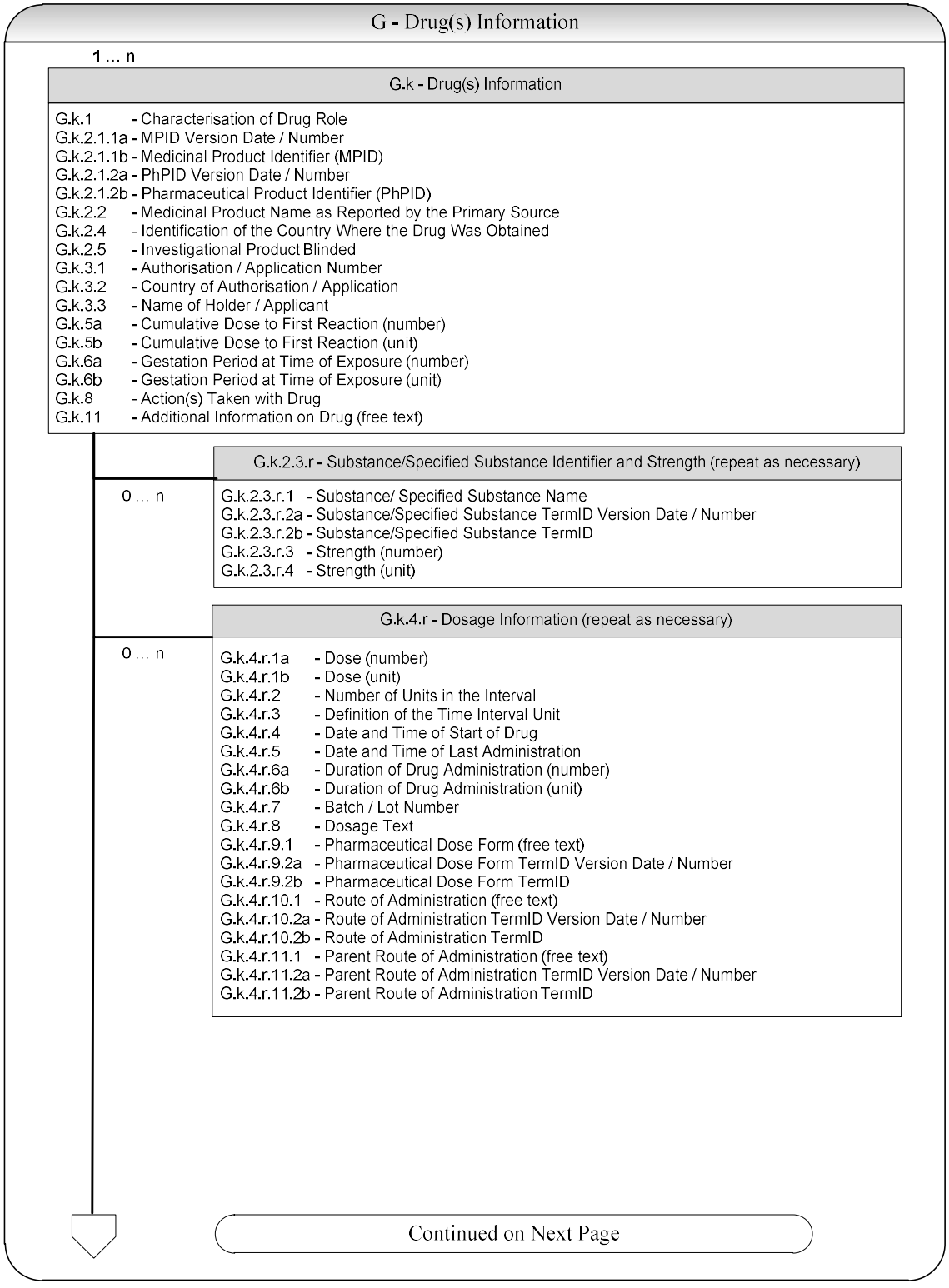
G.k DRUG(S) INFORMATION (REPEAT AS NECESSARY)

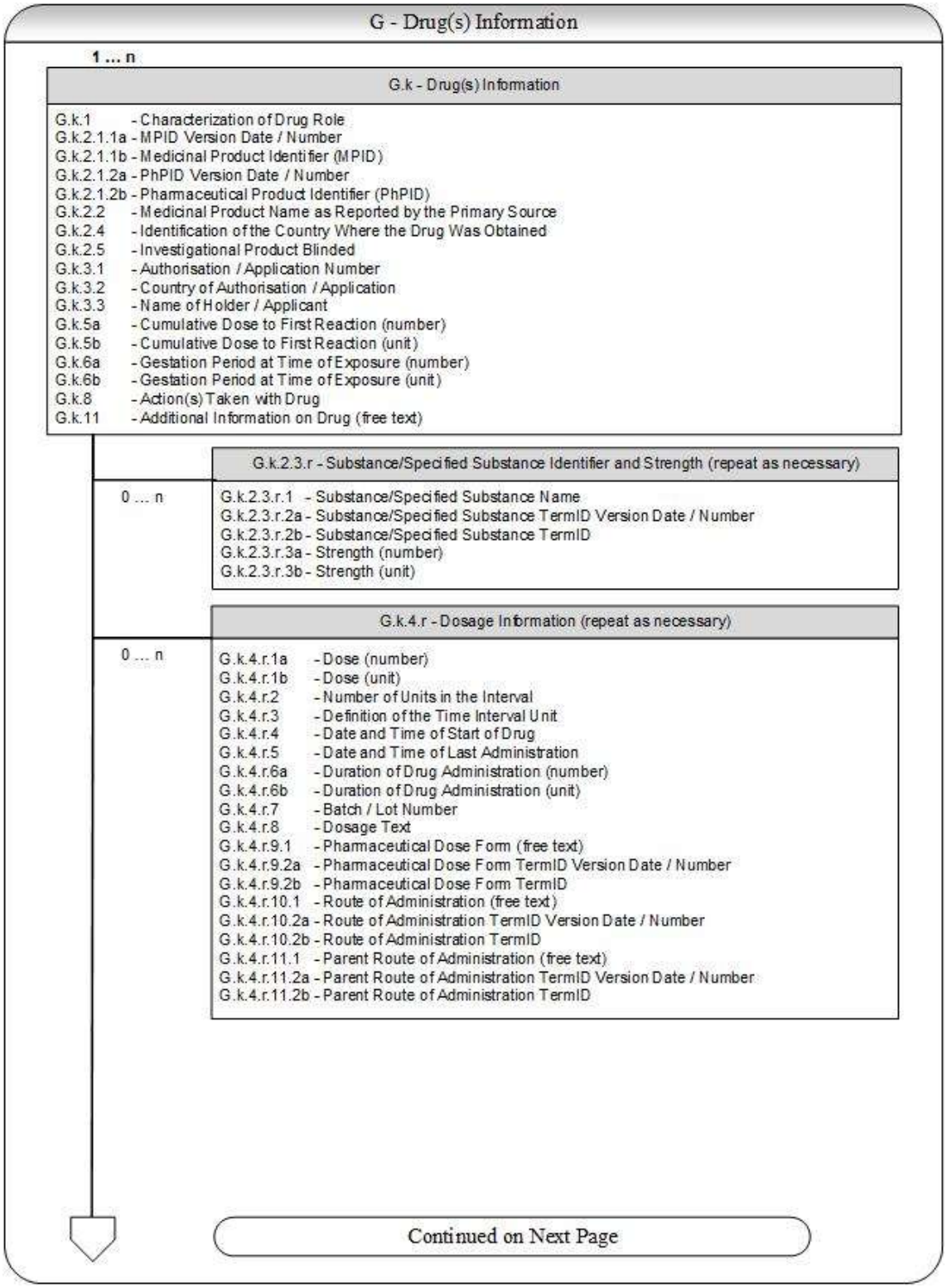
This section covers both suspect and concomitant medications (including biologics) including drugs suspected to have a type of interaction (e.g., drug, food, tobacco, etc). A minimum of one suspect medication needs to be provided for each valid ICSR. Medications used to treat the reaction/event should *not* be included here.

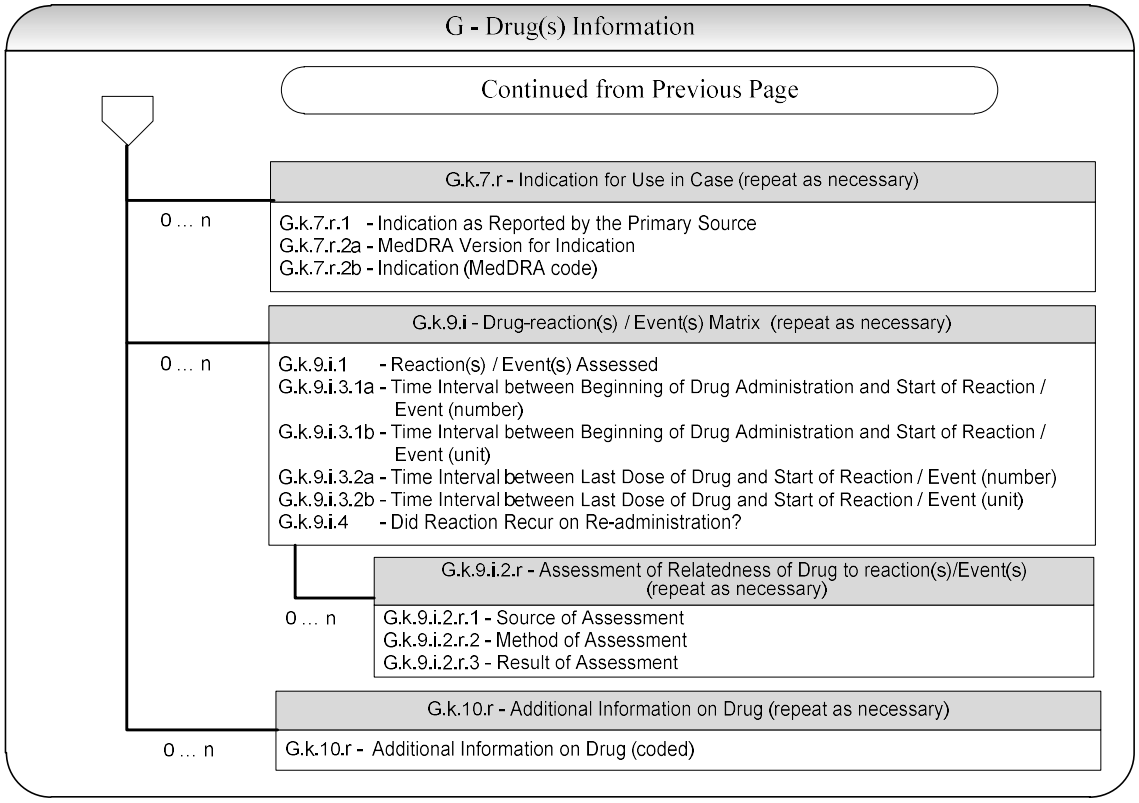
For each drug, the "Characterisation of the Drug Role" (G.k.1) is the one reported or implied by the primary reporter (e.g., the original source of the information). Suspect medications are those health products taken by the patient and suspected by the reporter to have contributed to the adverse reaction described in Section E. The suspect medication might have been stopped before the reaction is observed, for example, a single dose of an antibiotic could be suspected to cause diarrhoea one week later. However, concomitant medications are only those health products taken by the patient at the time the reaction is observed; other relevant medication history should be recorded in Section D.8.

As for the designation "i" in Section E above, the designation of "k" in this section indicates that each item is repeatable and that it corresponds to the same "k" in all subsections. A separate block (k) should be used for each health product. Within a block (k), subsections can also repeat using the designation "r", and within a subsection (r), further sub-subsections can repeat using the designation "i".




G - Drug(s) Information
1 ... n
G.k - Drug(s) Information
G.k.1 - Characterisation of Drug Role
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)
G.k.2.2 - Medicinal Product Name as Reported by the Primary Source
G.k.2.4 - Identification of the Country Where the Drug Was Obtained
G.k.2.5 - Investigational Product Blinded
G.k.3.1 - Authorisation / Application Number
G.k.3.2 - Country of Authorisation / Application
G.k.3.3 - Name of Holder / Applicant
G.k.5a - Cumulative Dose to First Reaction (number)
G.k.5b - Cumulative Dose to First Reaction (unit)
G.k.6a - Gestation Period at Time of Exposure (number)
G.k.6b - Gestation Period at Time of Exposure (unit)
G.k.8 - Action(s) Taken with Drug
G.k.11 - Additional Information on Drug (free text)
G.k.2.3.r - Substance/Specified Substance Identifier and Strength (repeat as necessary)
0 ... n
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
G.k.2.3.r.3 - Strength (number)
G.k.2.3.r.4 - Strength (unit)
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
Continued on Next Page


G - Drug(s) Information
1 ... n
G.k - Drug(s) Information
G.k.1 - Characterization of Drug Role
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)
G.k.2.2 - Medicinal Product Name as Reported by the Primary Source
G.k.2.4 - Identification of the Country Where the Drug Was Obtained
G.k.2.5 - Investigational Product Blinded
G.k.3.1 - Authorisation / Application Number
G.k.3.2 - Country of Authorisation / Application
G.k.3.3 - Name of Holder / Applicant
G.k.5a - Cumulative Dose to First Reaction (number)
G.k.5b - Cumulative Dose to First Reaction (unit)
G.k.6a - Gestation Period at Time of Exposure (number)
G.k.6b - Gestation Period at Time of Exposure (unit)
G.k.8 - Action(s) Taken with Drug
G.k.11 - Additional Information on Drug (free text)
G.k.2.3.r - Substance/Specified Substance Identifier and Strength (repeat as necessary)
0 ... n
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
G.k.2.3.r.3a - Strength (number)
G.k.2.3.r.3b - Strength (unit)
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
Continued on Next Page



G.k.1 Characterisation of Drug Role

User Guidance	This data element contains the characterisation 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 (See Section 3.3.1). If the reporter indicates a suspected interaction with other drug(s), "***interacting"*** should be selected for all suspected interacting drug(s). If an interaction is suspected with food or other non-drug compounds, "***interacting"*** should be selected for the suspect drug. For evaluation purposes, all interacting drugs are considered to be suspect drugs. The type of interaction (e.g., drug interaction, food interaction, alcohol interaction, etc.), should be captured with the appropriate MedDRA LLT(s) in **Section E.i** Reaction(s) / Event(s) along with any event(s) resulting from the suspected interaction. "***Drug not administered"*** can be used in two circumstances: **In clinical trial**: if the adverse event occurred after the informed consent was signed but prior to the administration of the study drug (e.g., during the screening period or the washout procedure), the adverse event should in general be reported as per the trial procedure. In that case, only sections G.k.1, G.k.2 and G.k.8 are to be filled out for that Section G. The information on the suspect cause of the event should be provided in the narrative H.1. In addition, comments can be provided by the reporter in H.2 and by the sender in the H.4.

	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 (including the fact that it was not administered), as well as the information on the dispensed drug as the 'suspect' drug. The medication error should be captured with the appropriate MedDRA LLT code in Section E.i Reaction(s) / Event(s).
Conformance	Required
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.13
Value Allowed	1 = Suspect 2 = Concomitant 3 = Interacting 4 = Drug Not Administered
Business Rule(s)	
	Each ICSR must contain at least one "Suspect", "Interacting" or "Drug Not Administered".

	Suspect medications are those health products taken by the patient and suspected by the reporter to have contributed to the adverse reaction described in Section E. Concomitant medications are only those health products taken by the patient *at the time* the reaction is observed; other relevant medication history should be recorded in Section D.8.

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, ISO IDMP should be used. When available, the most precise structured information should be provided when identifying medicinal products and redundant information does not have to be repeated. For example, if a MPID is provided in G.k.2.1.1, there is no need to provide a PhPID in G.k.2.1.2. Likewise, if a PhPID is provided, there is no need to provide information for Substance.

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.

The product name used by the reporter should always be provided.

G.k.2.1 Medicinal Product Unique Identifier / Pharmaceutical Product Unique Identifier

G.k.2.1.1a MPID Version Date / Number

User Guidance	This data element provides the version date for G.k.2.1.1b.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	None
Value Allowed	As per ISO IDMP.
Business Rule(s)	

G.k.2.1.1b Medicinal Product Identifier (MPID)

User Guidance	This data element captures MPID. If an MPID for the reported medicinal product is not available, this data element should be left blank.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	As per ISO IDMP.
Value Allowed	As per ISO IDMP.
Business Rule(s)	

	When a MPID (G.k.2.1.1) is provided, the remainder of Section G.k.2.1 and G.k.2.3.r (G.k.2.3.r.1 through G.k.2.3.r.3) should be blank.

G.k.2.1.2a PhPID Version Date/Number

User Guidance	This data element providesthe version date for G.k.2.1.2b.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	None
Value Allowed	As per ISO IDMP.
Business Rule(s)	

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

User Guidance	This data element captures PhPID. If a PhPID for the reported medicinal product is not available, this data element should be left blank.
Conformance	Optional Not allowed if G.k.2.1.1 is provided.
Data Type	As per ISO IDMP.
OID	As per ISO IDMP.
Value Allowed	As per ISO IDMP.
Business Rule(s)	
	Any given drug entry may have either MPID or PhPID, but NOT both.



When a MPID (G.k.2.1.1) is not available but a PhPID (G.k.2.1.2) is provided, G.k.2.3.r (G.k.2.3.r.1 through G.k.2.3.r.3) should be blank.

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

User Guidance	This data element captures the name of the medicinal product as used by the reporter. It is recognized that a single product can have different proprietary names in different countries, even when it is produced by a single manufacturer.
Conformance	Required
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

G.k.2.3.r Substance / Specified Substance Identifier and Strength (repeat as necessary)

If either of MPID or PhPID is not available, each active ingredient should be specified individually by repeating this section. For each active ingredient, ISO IDMP *substance / specified substance TermID* should be provided, if available. If the substance / specified substance TermID is not available, the INN or the active ingredient name or the drug identification code should be provided.

G.k.2.3.r.1 Substance / Specified Substance Name

User Guidance	If a 'Substance Name TermID' (G.k.2.3.r.2b) is not available, provide a text description of the substance. A medical device can be described here.
Conformance	Optional
Data Type	250 AN
OID	None
Value Allowed	Free text
Business Rule(s)	

G.k.2.3.r.2a Substance / Specified Substance TermID Version Date / Number

User Guidance	This data element provides the version date for the Substance Name TermID.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	None
Value Allowed	As per ISO IDMP.
Business Rule(s)	

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

User Guidance	If both MPID (G.k.2.1.1) and PhPID (G.k.2.1.2) are unavailable, use the most appropriate substance identifier. If an identifier is not available, this data element will be left blank.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	As per ISO IDMP.
Value Allowed	As per ISO IDMP.
Business Rule(s)	

G.k.2.3.r.3a Strength (number)

User Guidance	If PhPID (G.k.2.1.2) is unavailable, this data element provides the lower numerator of the strength for the substance or if not a range, the numerator of the strength when known.
Conformance	Optional
Data Type	10N
OID	None
Value Allowed	Numeric
Business Rule(s)	

G.k.2.3.r.3b Strength (unit)

User Guidance	This data element captures the unit for G.k.2.3.r.3a.
Conformance	Optional, but required if G.k.2.3.r.3a is populated.
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.1.25
Value Allowed	Constrained UCUM codes
Business Rule(s)	

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

User Guidance	This data element captures the country where the medicinal was obtained.
Conformance	Optional
Data Type	2A
OID	1.0.3166.1.2.2
Value Allowed	ISO 3166-1 alpha-2, EU
Business Rule(s)	
	A two character country code will be used in all instances. The country code EU exists in the ISO 3166 country code list as an exceptional reservation code to support any application that needs to represent the name European Union.In this case, “EU” will be accepted as the country code.

	Technically, data type of G.k.2.4 is defined as string instead of code by HL7. To ensure data quality, this IG requires use of ISO country code instead of free text.

G.k.2.5 Investigational Product Blinded

User Guidance	This data element is applicable only to ICSRs from clinical trials. The ICH E2A guideline recommends that the case safety reports with *blinded* therapy should *not* be reported. However, if it is important to exchange a blinded case safety report during a clinical trial, this data element should be used as follows: until the investigational product is un-blinded, the status "blinded" should be indicated by using "true" in this data element. When this data element is "true", Section G.k.2 **Drug Identification** should be populated with the characteristics of the investigational product. When more than one investigational product is potentially suspect, each suspect product should be represented in separate G.k blocks. After un-blinding, if appropriate, "placebo" should be reported in G.k.2.3.r as a suspect drug.
Conformance	Optional
Data Type	Boolean
OID	None
Value Allowed	true
Business Rule(s)	
	The value for this data element should be set to "true" for ICSRs from clinical trials when the product status is still blinded at the time the ICSR is created. Otherwise, this data element should not be transmitted.

G.k.3 Holder and Authorisation / Application Number of Drug

If ISO IDMP MPID is not available for the reported medicinal product, the name of the holder should be provided along with the authorisation or application number in the country where the drug was obtained when the case report is sent to that country. Pharmaceutical companies should provide this information for their own suspect drug(s).

G.k.3.1 Authorisation / Application Number

User Guidance	If MPID (G.k.2.1.1) is unavailable, this data element captures the Authorisation or Application number of the medicinal product for the country where it was obtained when the case report is sent to that country. Pharmaceutical companies should provide this information at least for their own suspect drug(s).
Conformance	Optional
Data Type	35 AN
OID	2.16.840.1.113883.3.989.2.1.3.4
Value Allowed	Free text
Business Rule(s)	
	The following notation will be used to represent G.k.3.1: <id extension="authorisation / application number" root="2.16.840.1.113883.3.989.2.1.3.4"/> The root indicates the namespace of G.k.3.1, the actual authorisation / application number is populated at id extension.

G.k.3.2 Country of Authorisation / Application

User Guidance	If MPID (G.k.2.1.1) is unavailable, this data element captures the country where the drug was authorised when the case report is sent to that country if known.
Conformance	Optional, but required if G.k.3.1 is provided.
Data Type	2A
OID	1.0.3166.1.2.2
Value Allowed	ISO 3166-1 alpha-2, EU
Business Rule(s)	
	A two character country code will be used in all instances. The country code EU exists in the ISO 3166 country code list as an exceptional reservation code to support any application that needs to represent the name European Union. In this case, "EU" will be accepted as the country code.

G.k.3.3 Name of Holder / Applicant

User Guidance	This data element captures the name of the licence holder as indicated on the package.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text
Business Rule(s)	

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. For example, 5 mg (in one dose) every other day, subsections G.k.4.r.1 through G.k.4.r.3 would be 5, mg, 2, day, respectively. In the same way, 50mg daily would be 50, mg, 1, day, respectively.

For multiple dosages within a given interval, a fraction of that interval is given. For example, 5mg four times in one day (QID), subsections G.k.4.r.1 through G.k.4.r.3 would be 5, mg, 0.25, day, respectively.

For fixed dose combination drugs dose unit (G.k.4.r.1b) should be provided as arbitrary unit {DF} instead of mg.

In the case of a parent-child / foetus report, the dosage section applies to the known parental dose. For example, if the mother took the drug(s) suspected of causing adverse reaction(s) in a nursing infant, then the dosage information (G.k.4.r.1 to G.k.4.r.11.2) relates to how the mother took the medication(s). If the mother is the source of the suspect drug(s) then the dosage information reflects how the mother ingested or was administered the drug(s). If a father is the source of the suspect drug(s) then the additional information on drug (G.k.10) is provided. The case narrative (H.1) should describe the entire case, including the father's information.

For a dosage regimen that involves more than one dosage form, and where provision of structured dosage information is not possible, the information should be provided as text in Section G.k.4.r.8.

Note: More dosing examples are provided in Appendix I (G)

G.k.4.r.1a Dose (number)

User Guidance	This data element captures the value (number) of each administered dose.
Conformance	Optional
Data Type	8N
OID	None
Value Allowed	Numeric
Business Rule(s)	

G.k.4.r.1b Dose (unit)

User Guidance	This data element captures the unit for the dose value in G.k.4.r.1a.
Conformance	Optional, but required if G.k.4.r.1a is populated.
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.1.25
Value Allowed	Constrained UCUM codes: {DF}
Business Rule(s)	
	UCUM allows using non-unit expression for symbols not in UCUM. In this case, {DF} can be used in XML message.

G.k.4.r.2 Number of Units in the Interval

User Guidance	This data element captures the value (amount) for the time interval between each administered dose (G.k.4.r.1a and G.k.4.r.1b). If *either* G.k.4.r.2 or G.k.4.r.3 is unknown, both should be left blank unless the definition of the time interval unit is "*cyclical*", "*asnecessary*", or "*total*".
Conformance	Optional
Data Type	4N
OID	None
Value Allowed	Numeric
Business Rule(s)	

G.k.4.r.3 Definition of the Time Interval Unit

User Guidance	This data element captures the UCUM code that best describes the unit for the dosing time interval (G.k.4.r.2). When a specific time interval for drug administration is not known, but is confirmed that the drug is used cyclically or as necessary, then 'cyclical' or 'asnecessary' can be used in this data element. When the total amount of a drug is provided without any particular dose and dosing interval (e.g., in the case of an overdose), the quantity and unit (G.k.4.r.1a and G.k.4.r.1b) is provided along with 'Total' in this data element (G.k.4.r.2 is left blank).

Conformance	Optional, but required if G.k.4.r.2 is populated.
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.1.26
Value Allowed	Constrained UCUM codes: {cyclical}, {asnecessary}, {total}
Business Rule(s)	
	UCUM allows using non-unit expression for symbols not in UCUM. In this case, {cyclical}, {asnecessary}, and {total} can be used in XML message.

G.k.4.r.4 Date and Time of Start of Drug

User Guidance	This data element captures the date and time when drug administration started.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Minimum precision required is the year (i.e., "CCYY"). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

G.k.4.r.5 Date and Time of Last Administration

User Guidance	This data element captures the date and time when drug administration ended. For ongoing drug administration after the onset of the reaction / event, this item should be blank and the "Action(s) Taken with Drug" (G.k.8) should be used. If drug administration is stopped but the date is unknown, apply the appropriate nullFlavor to G.k.4.r.5.
Conformance	Optional
Data Type	Date / Time
OID	None
Value Allowed	nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Minimum precision required is the year (i.e., "CCYY"). The date specified cannot refer to a future date. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

G.k.4.r.6a Duration of Drug Administration (number)

User Guidance	This section will usually be computed from the start / end date and time of the administration. However, there might be situations in which the precise duration of the drug administration can be useful, such as minutes or hours. Also, this item should be used in addition to dates if exact dates of drug administration are not available at the time of the report, but there is information concerning the duration of drug administration. In such a case, populate 1 data element for the date (start or end date) and this Section. The information requested is the overall duration of drug administration and covers intermittent administration. This data element captures the value (quantity) for the duration of the administration.
Conformance	Optional, but required if G.k.4.r.6b is populated.
Data Type	5N
OID	None
Value Allowed	Numeric
Business Rule(s)	

G.k.4.r.6b Duration of Drug Administration (unit)

User Guidance	This data element captures the unit for the "Duration of Drug Administration" (G.k.4.r.6a).
Conformance	Optional, but required if G.k.4.r.6a is populated.
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.1.26
Value Allowed	Constrained UCUM codes
Business Rule(s)	

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

User Guidance	This data element captures the batch or lot number for the medicinal product. This information is particularly important for vaccines and biologics. The most specific information available should be provided. For expiration date and other related information, see the Additional Information on Drug (G.k.11).
Conformance	Optional
Data Type	35AN
OID	None
Value Allowed	Free text
Business Rule(s)	

G.k.4.r.8 Dosage Text

User Guidance	This data element captures free text information when structured dosage information is not possible, or to provide more detail on structured dosage data elements. There is no need to duplicate information provided in the structured dosage data elements.
Conformance	Optional
Data Type	2000AN

OID	None
Value Allowed	Free text
Business Rule(s)	

G.k.4.r.9 Pharmaceutical Dose Form

G.k.4.r.9.1 Pharmaceutical Dose Form (free text)

User Guidance	This data element captures a free text description of the pharmaceutical dose form when the "Pharmaceutical Dose Form TermID" (G.k.4.r.9.2b) is not available.
Conformance	Optional
Data Type	60 AN
OID	None
Value Allowed	Free text nullFlavor: ASKU, NASK, UNK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

G.k.4.r.9.2a Pharmaceutical Dose Form TermID Version Date/Number

User Guidance	This data element provides the version date for the Pharmaceutical Dose Form TermID.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	None
Value Allowed	As per ISO IDMP.
Business Rule(s)	

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

User Guidance	If PhPID (G.k.2.1.2) is unavailable, the pharmaceutical dose form should be provided as a ISO IDMP TermID using the *Pharmaceutical Dose Form* controlled vocabulary. If the Pharmaceutical Dose Form TermID is not available, free text in G.k.4.r.9.1 should be used.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	As per ISO IDMP.
Value Allowed	As per ISO IDMP.
Business Rule(s)	

G.k.4.r.10 Route of Administration

G.k.4.r.10.1 Route of Administration (free text)

User Guidance	This data element captures a free text description of the route of administration when the "Route of Administration TermID" (G.k.4.r.10.2b) is not available. An appropriate nullFlavor can be used if the source has not provided or does not know the information.
Conformance	Optional
Data Type	60 AN
OID	None
Value Allowed	Free text nullFlavor: ASKU, NASK, UNK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

G.k.4.r.10.2a Route of Administration TermID Version Date / Number

User Guidance	This data element provides the version date for the Route of Administration TermID.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	None
Value Allowed	As per ISO IDMP.
Business Rule(s)	
	Until ISO IDMP TermID is available, use version number in the ICH E2B(R3) code list 14.

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

User Guidance	Route of administration should be provided as TermID using *Route of administration* controlled vocabulary. Until ISO IDMP TermID is available, use the existing code list attached in Appendix I (F). No other identifiers should be used in this data element. 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. The parent's route of administration should be provided in G.k.4.r.11.
Conformance	Optional
Data Type	As per ISO IDMP. Until ISO IDMP TermID is available, this is 3N.
OID	As per ISO IDMP. Until ISO IDMP TermID is available, use 2.16.840.1.113883.3.989.2.1.1.14.
Value Allowed	As per ISO IDMP. Until ISO IDMP TermID is available, use code list in Appendix I (F).
Business Rule(s)	

G.k.4.r.11 Parent Route of Administration (in case of a parent child / foetus report)

G.k.4.r.11.1 Parent Route of Administration (free text)

User Guidance	This data element captures a free text description of the route of administration when the "Parent Route of Administration TermID" (G.k.4.r.11.2b) is not available. An appropriate nullFlavor can be used if the source has not provided or does not know the information.
Conformance	Optional
Data Type	60 AN
OID	None
Value Allowed	Free text nullFlavor: ASKU, NASK, UNK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

G.k.4.r.11.2a Parent Route of Administration TermID Version Date / Number

User Guidance	This data element provides the version date for the Route of Administration TermID.
Conformance	Optional
Data Type	As per ISO IDMP.
OID	None
Value Allowed	As per ISO IDMP.
Business Rule(s)	

G.k.4.r.11.2b Parent Route of Administration TermID

User Guidance	This data element captures the known route of administration of the drug as taken by the parent for the dosage described in G.k.4.r.1 to G.k.4.r.3. The parent's route of administration should be provided as TermID using *Route of administration* controlled vocabulary. Until ISO IDMP TermID is available, use the existing code list attached in Appendix I (F). No other identifiers should be used in this data element.
Conformance	Optional
Data Type	As per ISO IDMP. Until ISO IDMP TermID is available, this is 3N.
OID	As per ISO IDMP. Until ISO IDMP TermID is available, use 2.16.840.1.113883.3.989.2.1.1.14.
Value Allowed	As per ISO IDMP. Until ISO IDMP TermID is available, use code list in Appendix I (F).
Business Rule(s)	

G.k.5a Cumulative Dose to First Reaction (number)

User Guidance	This data element captures the value (amount) cumulative dose administered until the onset of the *first* sign, symptom or reaction / event.
Conformance	Optional, but required if G.k.5b is populated.
Data Type	10N
OID	None
Value Allowed	Numeric
Business Rule(s)	

G.k.5b Cumulative Dose to First Reaction (unit)

User Guidance	This data element captures the unit for the value in G.k.5a.
Conformance	Optional, but required if G.k.5a is populated.
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.1.25
Value Allowed	Constrained UCUM codes: {DF}
Business Rule(s)	
	UCUM allows using non-unit expression for symbols not in UCUM. In this case, {DF} can be used in XML message.

G.k.6a Gestation Period at Time of Exposure (number)

User Guidance	This data element captures the number for the gestational age at the time of the earliest exposure. A clinical judgment should be used to choose the most appropriate value / unit.
Conformance	Optional, but required if G.k.6b is populated.
Data Type	3N
OID	None
Value Allowed	Numeric
Business Rule(s)	
	The gestational age is expressed in terms of days, weeks, months or trimester (G.k.6b).

G.k.6b Gestation Period at Time of Exposure (unit)

User Guidance	This data element captures the unit for the value in G.k.6a. Although the mother's drug exposure has started prior to her pregnancy, this data element is appropriate to capture the earliest exposure during pregnancy. This data element should be populated on the child / foetus report and / or mother report. A clinical judgment should be used to choose the most appropriate unit.
Conformance	Optional, but required if G.k.6a is populated.
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.1.26
Value Allowed	UCUM codes for Month (mo), Week (wk), Day (d) and {Trimester}
Business Rule(s)	
	Units commonly used in clinical practice but not defined in UCUM can be transmitted using curly braces like e.g., {trimester}.

G.k.7.r Indication for Use in Case (repeat as necessary)

G.k.7.r.1 Indication as Reported by the Primary Source

User Guidance	This data element captures the original reporter's words and / or short phrases used to describe the indication for drug use in an English translation for international transmission. NullFlavors may be used if the source has not provided or does not know the information, respectively.
Conformance	Optional
Data Type	250AN
OID	None
Value Allowed	Free text nullFlavor: ASKU, NASK, UNK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information. Please use nullFlavor with original text attribute in XML instance (See Appendix I (D) the Reference Instance).

G.k.7.r.2a MedDRA Version for Indication

User Guidance	This data element provides the MedDRA version for G.k.7.r.2b
Conformance	Optional, but required if G.k.7.r.2b is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric and “.”(dot)
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. For MedDRA version 15.1 value allowed is “15.1”.

G.k.7.r.2b Indication (MedDRA code)

User Guidance	This data element captures the MedDRA LLT code for the indication of the medicinal product.
Conformance	Optional, but required if G.k.7.r.2a is provided.
Data Type	8N
OID	2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	
	If nullFlavor is used in G.k.7.r.1, select an appropriate MedDRA term to reflect that the indication is not available.

G.k.8 Action(s) Taken with Drug

User Guidance	This data element captures the action taken with the drug as a result of the reaction(s) / event(s). The value "1"(Drug withdrawn), taken together with the "Outcome of Reaction /Event at the Time of Last Observation" (E.i.7), describe the dechallenge. "***Not applicable***" should be used in circumstances such as when the patient has died or the treatment had been completed prior to reaction(s) / event(s) or the "Characterisation of Drug Role" (G.k.1) is "Drug Not Administered". When 'Not applicable' is used, details should be captured in Section H.
Conformance	Optional
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.15
Value Allowed	Actions taken codes: 1 = Drug withdrawn 2 = Dose reduced 3 = Dose increased 4 = Dose not changed 0 = Unknown 9 = Not applicable
Business Rule(s)	

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. For the purpose of reporting, there is an implied suspicion of causality for spontaneous reports. It is recognised that information concerning the relatedness, especially for spontaneous reports, is often subjective and might not be available.

The following example illustrates the functionality contained in this section.

- Assume the patient has had three adverse events: Event1, Event2, and Event3
- The reporter provided assessment of causality for events Event1 and Event2, but not for Event3. The reporter's assessment of causality is based on overall impression, which the sender codes as 'global introspection'.
- The sender provided two methods of causality assessment, one with an algorithm (coded algorithm) and the other a Bayesian analysis (coded Bardi).
- From the above there are 2 sets of data for the reporter (2_events X 1_method of assessment) and 6 sets for the sender (3_events X 2_methods of assessment) for a total 8 sets of data.

The appropriate item with the 'relatedness' information is G.k.9.i.2.r.x (where x equals the 3 sub data elements 1-3). Please note the sub data elements 1-3 are repeatable. For subsection G.k.9.i.1, a technical reference to the reaction / event in E.i should be used. Subsections G.k.9.i.2.r.1, G.k.9.i.2.r.2 and G.k.9.i.2.r.3 do not call for a standardised methodology or vocabulary.

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



If an event is spontaneously reported to a company about a patient who took that company's drug, and the relationship is unstated, it implies a suspected causal relationship to the drug. However, data elements G.k.9.i.1 through G.k.9.i.2.r.3 should be left blank unless otherwise required by local regulation.

The company's causality assessment can be captured in data elements G.k.9.i.1 through G.k.9.i.2.r.3. Additionally, the *Sender's Comments* in Section H.4 can be used to further elaborate sender's position or assessment.

Local regulatory requirements regarding expedited and periodic reporting determine whether inclusion of sponsor assessments is necessary.

G.k.9.i.1 Reaction(s) / Event(s) Assessed

User Guidance	This data element captures a *technical reference* within the message that is used to identify which *reaction / event* in Section E.i is being assessed. This is not a user entered element.
Conformance	Optional
Data Type	N/A
OID	None
Value Allowed	N/A
Business Rule(s)	
	This is not a user entered element.

G.k.9.i.2.r Assessment of Relatedness of Drug to Reaction(s) / Event(s) (repeat as necessary)

G.k.9.i.2.r.1 Source of Assessment

User Guidance	This data element indicates the source of the assessment provided in G.k.9.i.2.r.3.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text
Business Rule(s)	

G.k.9.i.2.r.2 Method of Assessment

User Guidance	This data element indicates the method of the assessment provided in G.k.9.i.2.r.3. For example global introspection, algorithm, Bayesian calculation, etc.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text
Business Rule(s)	

G.k.9.i.2.r.3 Result of Assessment

User Guidance	This data element capturesthe result of the assessment for relatedness. The ‘value’ will depend on the method used for the assessment.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text
Business Rule(s)	

G.k.9.i.3.1a Time Interval between Beginning of Drug Administration and Start of Reaction / Event (number)

User Guidance	This data element captures the value (amount) for the interval of time between the *start* of drug administration and the onset of the reaction. Even when other dates are provided, this data element is useful also to be transmitted for circumstances where, for example the interval is very short minutes, such as in anaphylaxis, or in which only imprecise dates are known but more information concerning the interval is known. If the sender wants to provide time intervals as well as dates, then the date of the first day of administration should be counted as Day 1 of the interval.
Conformance	Optional, but required if G.k.9.i.3.1b is populated.
Data Type	5N
OID	None
Value Allowed	Numeric
Business Rule(s)	

G.k.9.i.3.1b Time Interval between Beginning of Drug Administration and Start of Reaction / Event (unit)

User Guidance	This data element captures the unit for the value in G.k.9.i.3.1a.
Conformance	Optional, but required if G.k.9.i.3.1a is populated.
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.1.26
Value Allowed	Constrained UCUM codes
Business Rule(s)	

G.k.9.i.3.2a Time Interval between Last Dose of Drug and Start of Reaction / Event (number)

User Guidance	This data element captures the value (amount) for the interval of time between the *end* of drug administration and the onset of the reaction. Even when other dates are provided, this data element is useful also to be transmitted for circumstances where, for e.g., the interval is very short minutes, such as in anaphylaxis, or in which only imprecise dates are known but more information concerning the interval is known. If the sender wants to provide time intervals as well as dates, then the date of the last day of administration should be counted as Day 1 of the interval.
Conformance	Optional, but required if G.k.9.i.3.2b is populated.
Data Type	5N
OID	None
Value Allowed	Numeric
Business Rule(s)	

G.k.9.i.3.2b Time Interval between Last Dose of Drug and Start of Reaction / Event (unit)

User Guidance	This data element capturesthe unit for the value in G.k.9.i.3.2a.
Conformance	Optional, but required if G.k.9.i.3.2a is populated.
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.1.26
Value Allowed	Constrained UCUM codes
Business Rule(s)	

G.k.9.i.4 Did Reaction Recur on Re-administration?

User Guidance	This data element indicates both if the patient was rechallenged with the drug *and* the known outcome. This data element should not be coded if it was *not reported* whether or not a rechallenge was done.
Conformance	Optional
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.16
Value Allowed	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)
Business Rule(s)	
	If the sender does not know whether a rechallenge was performed, this data element should not be transmitted.

G.k.10.r Additional Information on Drug (coded) (repeat as necessary)

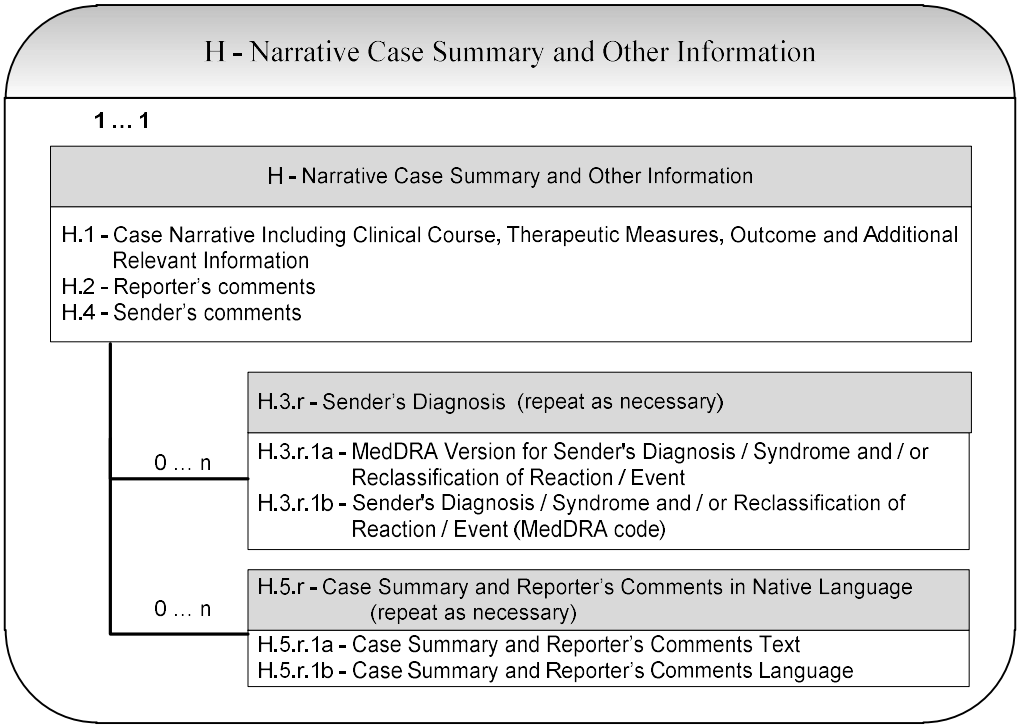
User Guidance	This data element capturesany additional information pertinent to the case that is not covered by the sections above. For example, cases where the suspect drug was taken by the father, this should be indicated in this data element as '3' (*Drug taken by the father*). If the additional information cannot be described by G.k.10.r, then use the data element G.k.11.
Conformance	Optional
Data Type	2N
OID	2.16.840.1.113883.3.989.2.1.1.17
Value Allowed	1 = Counterfeit 2 = Overdose 3 = Drug taken by the father 4 = Drug taken beyond expiry date 5 = Batch and lot tested and found within specifications 6 = Batch and lot tested and found not within specifications 7 = Medication error 8 = Misuse 9 = Abuse 10 = Occupational exposure 11 = Off label use
Business Rule(s)	

G.k.11 Additional Information on Drug (free text)

User Guidance	This data element captures any additional drug information in free text format not described in G.k.10.r. For example, *expiry date* for the lot number described in G.k.4.r.7 would be captured in this data element.
Conformance	Optional
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	If provided, this element needs to be separated and independent from any value selected in the code list for G.k.10.r.

H NARRATIVE CASE SUMMARY AND FURTHER INFORMATION

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



H.1 Case Narrative Including Clinical Course, Therapeutic Measures, Outcome and Additional Relevant Information

User Guidance	This data element captures a focused, factual and clear description of the case, including the words or short phrases used by the reporter.
Conformance	Required
Data Type	100000AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	Each ICSR must include a narrative. This data element should not be confused with Reporter's or Sender's comments.

H.2 Reporter's Comments

User Guidance	This data element captures the reporter's comments on the diagnosis, causality assessment or other issues considered relevant.
Conformance	Optional
Data Type	20000AN
OID	None
Value Allowed	Free text
Business Rule(s)	

H.3.r Sender's Diagnosis (repeat as necessary)

H.3.r.1a MedDRA Version for Sender's Diagnosis / Syndrome and / or Reclassification of Reaction / Event

User Guidance	This data element provides the MedDRA version for H.3.r.1b.
Conformance	Optional, but required if H.3.r.1b is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric and “.”(dot)
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. For MedDRA version 15.1 value allowed is “15.1”.

H.3.r.1b Sender's Diagnosis / Syndrome and / or Reclassification of Reaction / Event (MedDRA code)

User Guidance	This data element provides the sender with an opportunity to combine signs and symptoms that were reported into a succinct diagnosis. Supporting rationale for the term selection is included in Section H.4.A MedDRA LLT code should be used.
Conformance	Optional, but required if H.3.r.1a is populated.
Data Type	8N
OID	2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	

H.4 Sender's Comments

User Guidance	This data element captures the sender's assessment of the case and can be used to describe disagreement with, and / or alternatives to the diagnoses given by the reporter(s). Also, in case of linkage of multiple ICSRs using C.1.10.r, the reason should be provided in these comments.
Conformance	Optional
Data Type	20000AN
OID	None
Value Allowed	Free text
Business Rule(s)	

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.

H.5.r.1a Case Summary and Reporter's Comments Text

User Guidance	See Section H.5.r.
Conformance	Optional
Data Type	100000AN
OID	None
Value Allowed	Free text
Business Rule(s)	

H.5.r.1b Case Summary and Reporter's Comments Language

User Guidance	Provide the language used in H.5.r.1a by using an *International Standard, Codes for the representation of names of languages-- Part 2: alpha-3* code.
Conformance	Required if H.5.r.1a is populated.
Data Type	3A
OID	1.0.639.2
Value Allowed	ISO 639-2/RA, alpha-3
Business Rule(s)	

3.5 DOCUMENT ATTACHMENTS

In order to provide supplemental information, the sender of an ICSR might need to attach documents to the ICSR. Attachments can be presented in-line within the ICSR message itself; however, a reference to a document URL is not permitted. In-line data is transmitted as part of the encapsulated data value in the ICSR message.

3.5.1 User Guidance

When the sender holds a clinical document other than a literature article provided from a primary source (e.g., autopsy reports, ECG strips, chest X-ray, or photographs, etc), then C.1.6.1 should be set to "true" and a description of that document is required in C.1.6.1.r.1. Furthermore, an electronic file of that document can be attached in C.1.6.1.r.2.

When a literature article is sent as an attachment, the literature citation in Vancouver style is captured in C.4.r.1 *and* the electronic file of the document (e.g., journal article) is attached in C.4.r.2, rather than in C.1.6.1.r.2. (Please refer to Section 3.4 for detailed specifications for each data element.)

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. Although several file formats of documents (e.g., PDF, jpeg, tiff, and DICOM) are *technically* permissible as attachments, each region will determine the file types and the file size that can be processed.

When an ICSR contains attachments following the previous report, field 'Report Nullification/Amendment' (C.1.11.1) should be set to "2=amendment" if medical information captured in E2B(R3) data elements is the *same* as that of the previous report (see the guidance for C.1.11.1). Otherwise, the ICSR, along with its attachments, should be transmitted as a follow-up report.

3.5.2 Technical specification

Embed attachments into the structure of the ICSR XML message. Providing a hyperlink to the document stored separately is not acceptable.

Each attachment has up to 3 properties, and the appropriate value for each property should be provided in either C.1.6.1.r.2 or C.4.r.2:

i) **Media Type**: Identifies the type of the encapsulated data and identifies a method to interpret or render the data. This property indicates the data type standardised by RFC 2046 (http://www.ietf.org/rfc/rfc2046.txt), (e.g., application/PDF, image/jpeg, application/DICOM). The default value for media Type is text/plain.
ii) **Representation**: Presents the type of the encapsulated data. Use TXT for text data or B64 for binary data encoded by Base 64.
iii) **Compression**: Indicates whether the data is compressed, and what compression algorithm was used (e.g., value DF means the deflate algorithm was used).

3.5.3 Examples of XML instances

When an ICH ICSR message has 2 documents as attachment, one is a PDF file and the other is a compressed JPEG file, these attachments are encoded in XML instance.

```
<reference typeCode=”REFR”>
    <document classCode=”DOC” moodCode=”EVN”>
        <code code=”documentsHeldBySender”
codesystem=”2.16.840.1.113883.3.989.2.1.1.27”/>
        <title>C.1.6.1.r.1</title>
        <text mediaType='application/pdf'  representation='B64'>
        omSJUEdmde9j44zmMiromSJUEdmde9j44zmMirdMDSsWdIJdksIJR3373jeu836edjz
        MMIjdMDSsWdIJdksIJR3373jeu83MNYD83jmMdomSJUEdmde9j44zmMir..MNYD
        83jmMdomSJUEdmde9j44zmMir6edjzMMIjdMDSsWdIJdksIJR3373jeu834zmMir6ed
        jzMMIjdMDSsWdIJdksIJR3373jeu83==
        </text>
    </document>
</reference>
<reference typeCode=”REFR”>
    <document classCode=”DOC” moodCode=”EVN”>
        <code code=”documentsHeldBySender”
codesystem=”2.16.840.1.113883.3.989.2.1.1.27”/>
        <title>C.1.6.1.r.1</title>
        <text mediaType='image/jpeg' representation='B64' compression="DF">
        omSJUEdmde9j44zmMiromSJUEdmde9j44zmMirdMDSsWdIJdksIJR3373jeu836edjz
        MMIjdMDSsWdIJdksIJR3373jeu83MNYD83jmMdomSJUEdmde9j44zmMir..MNYD
        83jmMdomSJUEdmde9j44zmMir6edjzMMIjdMDSsWdIJdksIJR3373jeu834zmMir6ed
        jzMMIjdMDSsWdIJdksIJR3373jeu83==
        </text>
    </document>
</reference>
```

4.0 THE ICSR ACKNOWLEDGEMENT TRANSACTION

An acknowledgment transaction will be sent after receipt of every ICH ICSR from known trading partners (information received from unauthorized or unknown trading partners is not acknowledged). The acknowledgement message includes a standard ICH ICSR header, an acknowledgment for the message, and a repeating details section that provides information about the processing of the original message, e.g., successful parsing or problems that prevented parsing/accepting the message.

It is important to note that the **ICH ICSR Acknowledgement** is structured as the response to a *batch message*, and that it contains information both for the batch and for individual messages (reports) within that batch.

4.1 Acknowledgement Message in HL7

Within HL7 messaging, this functionality is managed using the Transmission Infrastructure.

For the purposes of this IG, it will be assumed that all transactions are batched, and that all responses will refer to the original batch wrapper, as well as to the message. The root message types needed are MCCI_IN200101UV and MCCI_MT200101UV; the stub is MCCI_MT000200UV.



For the purposes of this IG, it will be assumed that all transactions are batched, and that all responses will refer to the original batch wrapper, as well as to each message in that batch.

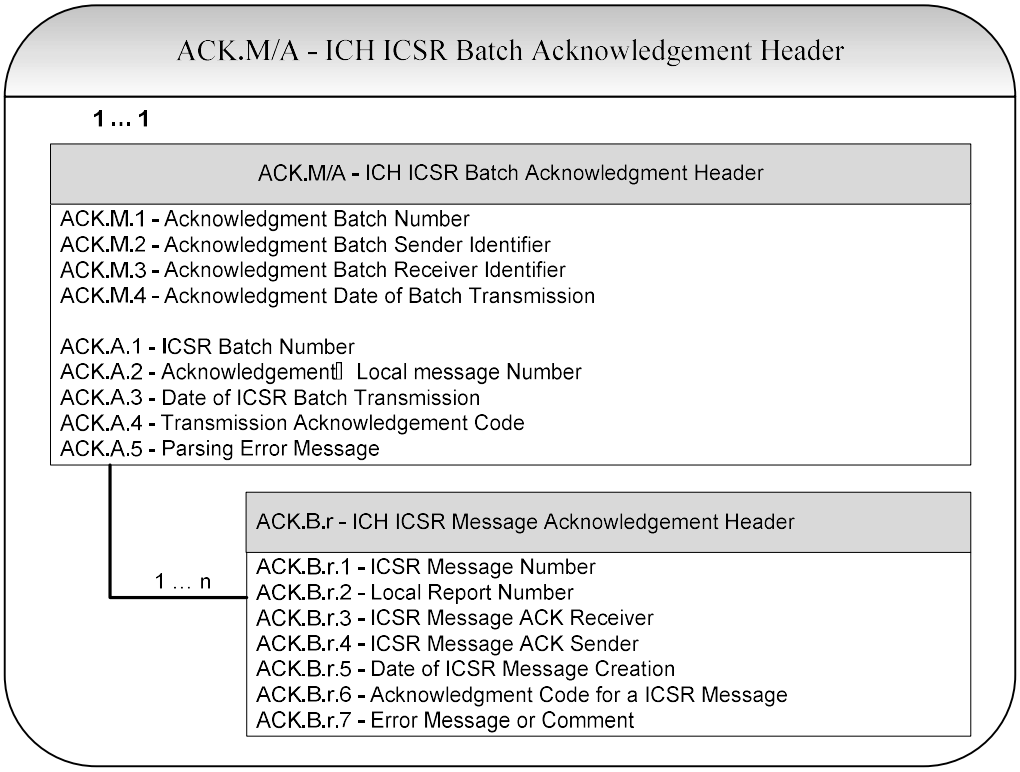
4.2 ICH ICSR Acknowledgement Message

The Acknowledgement header contains core transactional information related to the receipt of the batch transmission. The data elements used for the **ICH ICSR Acknowledgement** are described below.

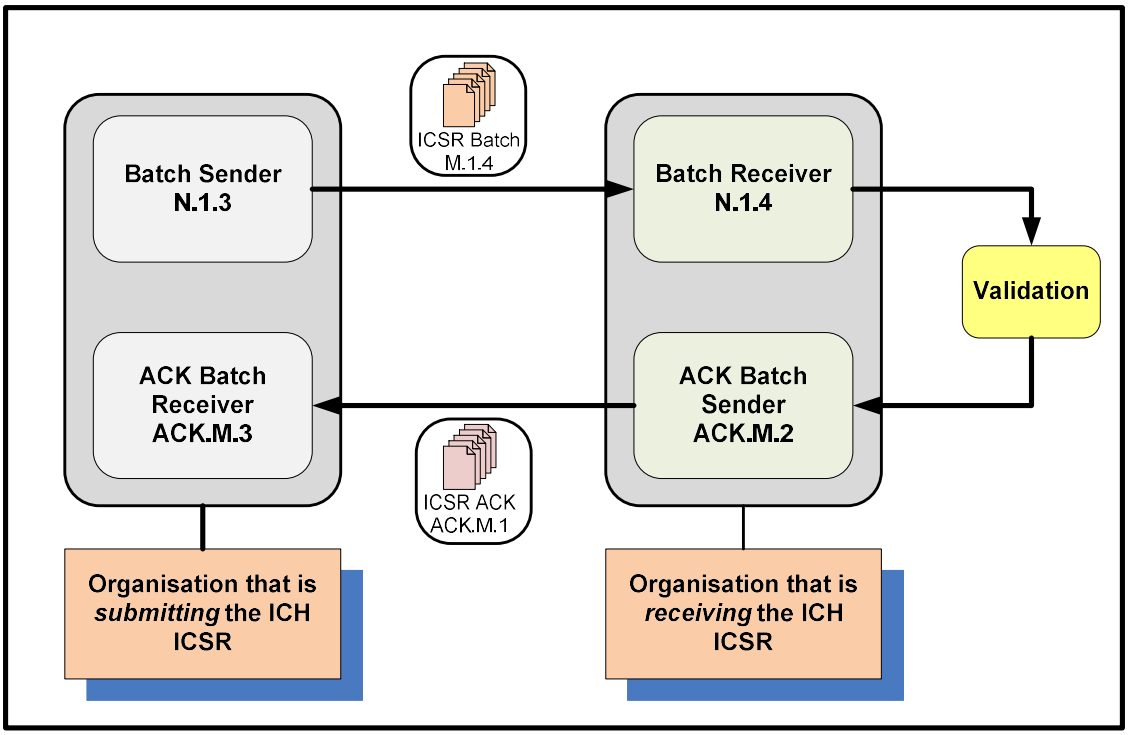
Data elements beginning with ACK.M contain technical information required for Acknowledgement message.

Data elements beginning with ACK.A contain technical information relating to batch received. This A section provides information to identify the *batch* being acknowledged as well as providing summary data on receipt and parsing. In particular, the information provided is for the entire batch rather than for any specific ICSR message in that batch.

Data elements beginning with ACK.B contain information relating to each ICSR message within the received batch. This B section contains information related to each ICSR message within a batch, including any errors detected within the message.



These header elements are used to organise and identify the acknowledgement transaction. The ACK header elements relate to the *Message Header* elements in received ICSR messages. The diagram below illustrates the submission and acknowledgement transaction at the batch message level.



ACK.M / AICH ICSR BATCH ACKNOWLEDGEMENT

ACK.M.1 Acknowledgement Batch Number

User Guidance	This data element captures a unique tracking number assigned to a particular ICH ICSR Acknowledgement batch file transmitted by the sender. This number is unique to the sender.
Conformance	Required
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	

ACK.M.2 Acknowledgement Batch Sender Identifier

User Guidance	This data element identifies the sender of the ICH ICSR Acknowledgement batch file (creator of ICH ICSR Acknowledgement batch file).
Conformance	Required
Data Type	60AN
OID	2.16.840.1.113883.3.989.2.1.3.17
Value Allowed	Free text
Business Rule(s)	
	This should be the same identifier as N.1.4. The following notation will be used to represent ACK.M.2:

	<id extension="acknowledgement sender identifier" root="2.16.840.1.113883.3.989.2.1.3.17"/> The root indicates the namespace of ACK.M.2, the actual batch sender identifier is populated at id extension. The sender identifier should be agreed between trading partners.

ACK.M.3 Acknowledgement Batch Receiver Identifier

User Guidance	This data element identifies the intended recipient of the transmission of ICH ICSR Acknowledgement batch file.
Conformance	Required
Data Type	60AN
OID	2.16.840.1.113883.3.989.2.1.3.18
Value Allowed	Free text
Business Rule(s)	
	This should be the same identifier as N.1.3. The following notation will be used to represent ACK.M.3: <id extension="acknowledgement receiver identifier" root="2.16.840.1.113883.3.989.2.1.3.18"/> The root indicates the namespace of ACK.M.3, the actual batch receiver identifier is populated at id extension. The sender identifier should be agreed between trading partners.

ACK.M.4 Acknowledgement Date of Batch Transmission

User Guidance	This data element captures the date on which the ICH ICSR Acknowledgement batch file was transmitted.
Conformance	Required
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information.
Business Rule(s)	
	Minimum precision required is date and time to the second. The date specified cannot refer to a future date; the time zone may have to be specified. (i.e., “CCYYMMDDhhmmss[+/-ZZzz]”)

ACK.A.1 ICSR Batch Number

User Guidance	This data element identifies the transaction (that is the batch) that is being acknowledged. It is a unique tracking number that was assigned to the ICH ICSR batch file by its sender. This ICSR batch number is unique to the sender of the ICH ICSR batch (i.e., the organisation that submitted the ICH ICSR).
Conformance	Required
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	This should be the same number as N.1.2 of the batch being acknowledged.

ACK.A.2 Acknowledgement Local Message Number

User Guidance	This data element captures a value assigned to the ICH ICSR Batch Acknowledgement by the organisation sending the acknowledgement (i.e., the organisation that received the ICH ICSR).
Conformance	Optional
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	

ACK.A.3 Date of ICSR Batch Transmission

User Guidance	This data element captures the date on which the ICSR batch being acknowledged was originally sent.
Conformance	Required
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information
Business Rule(s)	
	This should be the same date as N.1.5.

ACK.A.4 Transmission Acknowledgement Code

User Guidance	This data element captures a code to inform the organisation that submitted the ICH ICSR batch whether to (i) take no further action, (ii) review the remainder of the acknowledgement to determine which ICSR message(s) need further action, or (iii) re-send the entire transaction.
Conformance	Required
Data Type	2A
OID	None
Value Allowed	**AA** – *Application Acknowledgement Accept* (message successfully processed, no further action) **AE** – *Application Acknowledgment Error* (error detected, error response has additional detail, some ICSR message(s) need further action) **AR** – *Application Acknowledgment Reject* (parsing error, no data extracted, re-send the entire transaction)
Business Rule(s)	

ACK.A.5 Batch Validation Error

User Guidance	This data element provides a description of the error(s)detected in the ICH ICSR batch XML. This data element contains an explanation for the code triggered in ACK.A.4.
Conformance	Optional
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

ACK.B ICH ICSR MESSAGE ACKNOWLEDGEMENT

ACK.B.r.1 ICSR Message Number

User Guidance	This data element captures the number assigned to each ICH ICSR message (each message within a batch) by the organisation that submitted the ICH ICSR.
Conformance	Required
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	This is the same as N.2.r.1 and C.1.1 (Sender's (case) Safety Report Unique Identifier).

ACK.B.r.2 Local Report Number

User Guidance	This data element captures the number assigned to the ICH ICSR message by the organisation that received the ICH ICSR.
Conformance	Optional
Data Type	100AN
OID	None

Value Allowed	Free text
Business Rule(s)	

ACK.B.r.3 ICSR Message ACK Receiver

User Guidance	This data element identifies the organisation that submitted the ICH ICSR message (creator of ICH ICSR message).
Conformance	Required
Data Type	60AN
OID	2.16.840.1.113883.3.989.2.1.3.16
Value Allowed	Free text
Business Rule(s)	
	This should be the same identifier as N.2.r.2. The following notation will be used to represent ACK.B.r.3: <id extension="ack receiver identifier" root="2.16.840.1.113883.3.989.2.1.3.16"/> The root indicates the namespace of ACK.B.r.3, the actual message receiver identifier is populated at id extension. The ACK receiver identifier should be agreed between trading partners.

ACK.B.r.4 ICSR Message ACK Sender

User Guidance	This data element identifies the organisation that received the ICH ICSR message.
Conformance	Required
Data Type	60AN
OID	2.16.840.1.113883.3.989.2.1.3.15
Value Allowed	Free text
Business Rule(s)	
	This should be the same identifier as N.2.r.3. The following notation will be used to represent ACK.B.r.4: <id extension="ack sender identifier" root="2.16.840.1.113883.3.989.2.1.3.15"/> The root indicates the namespace of ACK.B.r.4, the actual message sender identifier is populated at id extension. The ACK sender identifier should be agreed between trading partners.

ACK.B.r.5 Date of ICSR Message Creation

User Guidance	This data element captures the date the ICSR message was created.
Conformance	Required
Data Type	Date / Time
OID	None
Value Allowed	See Appendix II for further information.
Business Rule(s)	
	This should be the same as N.2.r.4 and C.1.2 (Date of Creation).

ACK.B.r.6 Acknowledgement Code for a ICSR Message

User Guidance	This data element captures a code to inform the organisation that submitted the ICH ICSR message whether to (i) ICSR message successfully loaded, or (ii) the ICSR message contains fatal error that prevents the ICSR from being loaded.
Conformance	Required
Data Type	2A
OID	None
Value Allowed	**CA** – *Commit Accept* (the ICSR message successfully loaded) **CR** – *Commit Reject*(the ICSR message contains fatal error that prevents the ICSR from being loaded)
Business Rule(s)	

ACK.B.r.7 Error / Warning Message or Comment

User Guidance	This data element provides a description of the error(s) detected in the ICH ICSR message. This data element contains an explanation for the code triggered in ACK.B.r.6, including *non-fatal* warning messages when ACK.B.r.6 is "CA".
Conformance	Optional
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

APPENDICES

The following appendices contain specifications related to various components referenced throughout this document. These appendices provide the necessary details to facilitate the preparation of a valid ICH ICSR message or an ICSR Acknowledgment message for electronic submission.

APPENDIX I – PREPARING AND SENDING ICH ICSRS:

Appendix I (A) – ICH ICSR SCHEMAs

1. List of schemas for ICH ICSR messages and ICSR Acknowledgement messages

The necessary schemas for creating or exchanging ICH ICSR messages and ICH Acknowledgement messages are listed as schema file names which can be identified from Appendix I (C) schema files. These schemas are included in a published standard package named ISO/HL7 27953-2 (published on 21 November 2011). HL7 has developed each schema as an individual file, and used XML "include" statements to link these files. All schema files with user guidance are listed by categorisation.

	Major Category	Sub-Category	Schema File Name
a.	**Core Schemas:** *A common schemas underlying HL7 messages*	-	infrastructureRoot datatypes-base datatypes voc
b.	**Send Batch Interaction:** *A schema set specific to ICSR messages*	ICSR Batch Interaction: *Batch wrapper schemas for single or multiple ICSR messages*	MCCI_IN200100UV01 MCCI_MT200100UV
		ICSR Single Interaction: *Schemas for individual ICSR message*	PORR_IN049016UV MCCI_MT000100UV01 MCAI_MT700201UV01 PORR_MT049016UV PORR_MT049023UV
		ICSR Common Product Model CMET: *Schemas for medicinal products*	POCP_MT010200UV POCP_MT020200 POCP_MT030100UV POCP_MT030200UV POCP_MT040100UV POCP_MT050100UV POCP_MT081100UV
c.	**Send Response Batch Interaction:** *A schema set for Acknowledgement messages*	Acknowledgement Batch Interaction: *Batch wrapper schemas for Acknowledgement messages*	MCCI_IN200101UV01 MCCI_MT200101UV
		Acknowledgement Single Interaction:	MCCI_IN000002UV01 MCCI_MT000200UV01

		Schemas for each Acknowledgement message	

2. User Guidance for each ICH ICSR schemas

a. Core Schemas

infrastructureRoot

User Guidance	Infrastructure Root Class locates at the top layer of HL7 Class structure and defines necessary properties which are applied to all elements in messages for transmission. This schema, derived from Infrastructure Root Class, defines attributes commonly used in complex type where attributes or child elements are defined. *infrastructureRoot* schema is referenced from complex type.

datatypes-base

User Guidance	The HL7 datatypes, which are used within the definition of all model elements, are defined within the two schemas, *datatypes-base*, and *datatypes*. *Datatypes-base* schema defines data types for both complex type (e.g., ED, CD) and simple type (e.g., ST, CS). HL7 data types are categorised into "Basic data type" and "Generic data type". This schema defines Basic data type and part of Generic data type. Basic data type is a combination of Generic data types and such components are included in this schema.

datatypes

User Guidance	The HL7 datatypes, which are used within the definition of all model elements, are defined within the two schemas, *datatypes-base* and *datatypes*. *Datatypes* defines "Generic data type" which is used by setting a parameter in definition (e.g., A Generic data type IVL_<T> becomes IVL_<TS> or IVL_<PQ> with parameters at <T>).

voc

User Guidance	The schema includes the vocabulary items that are defined by HL7 for use by all Implementers (at the "universal" level). It includes the vocabulary domains that have been defined through RIM harmonisation, and the value sets that are defined by HL7.For the most part, these apply to HL7 structural attributes, and to data types.

Note: Only **NarrativeBlock** schema in core schema set is not used for ICH ICSR messages and ICSR Acknowledgement message.

b. Send Batch Interaction

ICSR Batch Interaction

MCCI_IN200100UV01

User Guidance	*"Sends a Batch, which groups 0 or more Messages for communication purposes" (ISO/HL7 27953-2).* For ICH ICSR messages, this schema defines root element.

MCCI_ MT200100UV

User Guidance	*"The Batch class functions in similar way to the Message class in an individual V3 message" (ISO/HL7 27953-2).* For ICH ICSR messages, this schema defines all of data elements in N.1 section.

ICSR Single Interaction

PORR_IN049016UV

User Guidance	This schema is corresponding to individual ICSR messages in a Batch message. For ICH ICSR messages, this schema defines individual reports including initial, follow-up and nullification in a batch message, while HL7 provides separated schemas for each report.

MCCI_MT000100UV01

User Guidance	*"The 'HL7 Transmission wrapper' includes information needed by a sending application or message handling service to package and route the V3 Composite Message to the designated receiving application(s) and/or message handling service(s)" (ISO/HL7 27953-2).* For ICSR messages, this schema defines most of data elements in N.2 section.

MCAI_MT700201UV01

User Guidance	*"The 'Trigger Event Control Act' contains administrative information related to the 'controlled act' which is being communicated as a messaging interaction" (ISO/HL7 27953-2).* It specifies the intermediate wrapper structure in the HL7 version 3 composite message payload specification that is used for notification and request for action type message interactions. For ICH ICSR messages, this schema defines the Date of Creation (C.1.2).

PORR_MT049016UV

User Guidance	*"The Human Pharmaceuticals Base Model RMIM is designed to support a report about an investigation into an adverse event(s) or reaction(s) suffered by a person that experienced an intervention (substance administration or procedure) within a therapeutic context. The suspect event may or may not have a causal relationship with the intervention and the model supports events suffered by associated persons* e.g., *mother/child or siblings" (ISO/HL7 27953-2).*

PORR_MT049023UV

User Guidance	*"The A_HumanPharmaceuticalsPRRI RMIM captures information about the acts that describe how a product was used by an investigative subject. The information includes use of a product (substance administration and device procedures) and any associated clinical or laboratory information directly related to the product's use at a particular point in time,* e.g. *related to an adverse event, or as part of a subject's medical history. The model also supports other patient care or healthcare-related processes such as actions taken to mitigate or reduce harm" (ISO/HL7 27953-2).*

ICSR Common Product Model CMET

POCP_MT010200UV

User Guidance	This schema is derived from "E_ProductKind CMET" which supports specified drug information. For ICH ICSR messages, this schema defines drug information such as identifiers (e.g., Medicinal Product Identifier (MPID) (G.k.2.1.1b) and Pharmaceutical Product Identifier (PhPID) (G.k.2.1.2b)) and the Pharmaceutical Dose Form (G.k.4.r.9).

POCP_MT020200UV

User Guidance	This schema is derived from "R_ProductReportable CMET" which supports information of drugs in reports and drugs for administration. For ICH ICSR messages, this schema defines the Batch / Lot Number (G.k.4.r.7).

POCP_MT030100UV

User Guidance	This schema is derived from "R_ProductRelatedAssignedEntity CMET": *"A combination of a person and/or organisation involved in the product life cycle in some way (*e.g. *creation and review of a product labeling document, performing a testing activity)" (ISO/HL7 27953-2).* For ICH ICSR messages, this schema defines the Identification of the Country Where the Drug Was Obtained (G.k.2.4).

POCP_MT030200UV

User Guidance	This schema is derived from "E_ProductEstablishment CMET": *"Any organisation that plays a role in the product life-cycle in any way" (ISO/HL7 27953-2).* For ICH ICSR messages, this schema defines the Name of Holder / Applicant (G.k.3.3).

POCP_MT040100UV

User Guidance	This schema is derived from "A_ProductEvent CMET" which supports information on drug manufacturing, transportation, and control with referencing to "R_ProductRelatedAssigned Entity CMET". For ICH ICSR messages, the Identification of the Country Where the Drug Was Obtained (G.k.2.4) is mapped to "R_ProductRelatedAssigned Entity CMET" and thus defined by this schema.

POCP_MT050100UV

User Guidance	This schema is derived from "A_ProductInformation CMET" which supports information on approval of new drug marketing and relevant documents. For ICH ICSR messages, this schema defines Authorisation / Application Number (G.k.3.1).

POCP_MT081100UV

User Guidance	This schema is derived from "E_SubstanceClinical CMET" which supports drug ingredients. For ICH ICSR messages, this schema defines the Substance / Specified Substance Identifier and Strength (G.k.2.3.r).

c. Send Response Batch Interaction

<u>Acknowledgement Batch Interaction</u>

MCCI_IN200101UV01

User Guidance	*"Send a Batch, which groups 0 or more Application level Messages into a Batch for communication purposes; sent as a response to either a Batch, or as a response to a Message which explicitly requested a Batched response" (ISO/HL7 27953-2).* For Acknowledgement messages, this schema defines root element. The acknowledgement specialises that of the Transmission by adding structures to identify the message being acknowledged, and to allow details about the acknowledgement to be added. This is especially important for reject messages.

MCCI_MT200101UV

User Guidance	A Response Batch can be used for (1) batches of accept acknowledgements, (2) batches of application responses. The only difference between this R-MIM (MCCI_RM200101UV) and the Batch R-MIM (MCCI_RM200100UV) for ICSR messages is the fact that the former contains a mandatory Acknowledgement class. For Acknowledgement messages, this schema defines ACK.M and ACK.A sections.

Acknowledgement Single Interaction

MCCI_IN000002UV01

User Guidance	*"Accept Acknowledgement by Sender to the Receiver. This message would not contain a domain payload " (ISO/HL7 27953-2).* For Acknowledgement messages, this schema defines ACK.B section.

MCCI_MT000200UV01

User Guidance	*"Accept Acknowledgement by Sender to the Receiver. This message would not contain a domain payload " (ISO/HL7 27953-2).* For Acknowledgement messages, this schema defines ACK.B section.

Appendix I (B) – Backwards & Forwards Compatibility

The document of Backwards & Forwards Compatibility is provided separately from this IG.

Appendix I (C) – Schema files

The set of schema files included in the published standard named ISO/HL7 27953-2 is provided separately from this IG.

Appendix I (D) – Reference Instances for ICH ICSR message and ICSR Acknowledgement message

XML files of Reference Instances for both the ICH ICSR and ICSR Acknowledgements messages are provided separately from this IG.

Appendix I (E) – Example Instances of report cases

XML files of Example Instances are provided separately from this IG.

Appendix I (F) – ICH E2B code lists

Lists of ICH E2B codes in XML format are provided separately from this IG.

Appendix I (G) – Technical Information

The document of Technical Information is provided separately from this IG.

Appendix I (H) – SGML & XML conversion

The conversion style sheet is informative materials and provided separately from this IG.

APPENDIX II – DATE / TIME

ICH has elected to utilise the HL7 Standard for datatypes to specify numeric representations of date and time. The time notation is the de facto standard in almost all countries while the date notation is increasingly popular. HL7 Standard for datatypes notation is the commonly recommended format for representing date and time as human-readable strings in communication protocols and file formats.

This notation has several important advantages when used in electronic files or messages as compared to traditional date and time notations. Since it orders the units from most significant to least significant, there are benefits with regard to flexibility, sorting, and for comparison after truncation.

Appendix II (A) Date / Time

The international standard date / time notation is **CCYYMMDDhhmmss**where

i) **CCYY** is the century and year in the usual Gregorian calendar,
ii) **MM** is the month of the year between 01 (January) and 12 (December),
iii) **DD** is the day of the month between 01 and 31,
iv) **hh** is the number of complete hours that have passed since midnight (00-24),
v) **mm** is the number of complete minutes that have passed since the start of the hour (00-59), and
vi) **ss** is the number of complete seconds since the start of the minute (00-59).

For example, the fourth day of February, 1995 is written as **19950204.**

If only the month is of interest, then **CCYYMM** can be used.

Example: **199502**

If only the year is of interest, then just **CCYY** is acceptable.

Example: **1995**

The time (hhmmss) one second before midnight is written as **235959**.

The precision can be reduced by omitting the seconds or both the seconds and minutes.

Example: **2359**, or just **23**

It is also possible to add fractions of a second after a decimal dot (.).

Example: **235959.9942** is 5.8ms before midnight.

As every day both "start" *and* "end" with midnight, the two notations **00:00** and **24:00** are available. This means that the following two notations refer to exactly the same point in time:

199502042400=**199502050000**.**"**0000" is usually the preferred notation for midnight and not "2400".

If a date and a time are displayed on the same line, then always write the date in front of the time.

Example: **19951231235959** is December 31, 1995 at 1 second before midnight.

Appendix II (B) Time Zone

The syntax is 'CCYYMMDDHHMMSS.UUUU[+|-ZZzz]' where digits can be omitted from the right side to express less precision.

Note: The Z stands for the 'zero meridian', which goes through Greenwich in London. Coordinated Universal Time (UTC) was called Greenwich Mean Time (GMT, also known as "Zulu Time") prior to 1972; however, GMT should no longer be used.

The strings **+ZZzz**, or **+ZZ** can be added to the time to indicate that the used local time zone is ZZ hours and zz minutes ahead of UTC. For time zones west of the zero meridian, which are behind UTC, the notation **–ZZzz**, or **–ZZ** is used instead.

If the date / time is provided as UTC, the time would be expressed with a zero offset.

Example: CCYYMMDDHHMM+0 or CCYYMMDDHH+0
Note: This may need to be taken into consideration during data migration/conversion from E2B(R2) source data

When transmitting across the time zone, use this indicator to ensure no confusion about future dates.

Example: 200509211242-08 is 12:42 pm (in the time zone that is 8 hours before UTC) on September 21, 2005.

Appendix II (C) ISO 8601 Compliant XML Examples

April 7, 2000
```
<effectiveTime value="20000407"/>
```

12:42 pm (in a time zone 8 hours before UTC) on September 21, 2005.
```
<effectiveTime value="200509211242-08"/>
```

Sometime in the year 2000
<effectiveTime value="2000"/>

November 5, 1994, 8:15:30 am, *US Eastern Standard Time*:
19941105081530-0500 (local time with offset)

To further illustrate date and time: June 1, 2009, at 3:31:15:05:5 pm *Pacific Time Zone:*

- to the millisecond: **200906011531105.5-0800**
- to the second: **20090601231105**
- to the minute: **200906012331**
- to the hour: **2009060123**
- to the day: **20090601**
- to the month: **200906**
- to the year: **2009**

APPENDIX III - ABBREVIATIONS AND GLOSSARY OF TERMS

Appendix III (A) ABBREVIATIONS

Abbreviations	Definition
A	Alpha
ADR	Adverse Drug Reaction
AE	Adverse Event
AN	Alphanumeric
APEC	Asia-Pacific Economic Cooperation
CDISC	Clinical Data Interchange Standards Consortium
CE	Coded with Equivalents*
CEN	Comité Européen de Normalisation (European Committee for Standardisation, a federation of 28 national standards bodies that are also ISO member bodies)
CIOMS	Council for International Organisations of Medical Sciences
CMET	Common Message Element Type
CS	Coded Simple Value
DSTU	Draft Standard for Trial Use
DTD	Document Type Definition
ECG	Electrocardiogram
ED	Encapsulated Data*
EDI	Electronic Data Interchange
EDIFACT	Electronic Data Interchange for Administration, Commerce and Transport
EEA	European Economic Area
EMA	European Medicines Agency
EFPIA	European Federation of Pharmaceutical Industries and Associations
EFTA	European Free Trade Association
ESTRI	Electronic Standards for the Transmission of Regulatory Information
EU	European Union

Abbreviations	Definition
FDA	United States Food and Drug Administration
HL7	Health Level 7
HMD	Hierarchical Message Description
ICH	International Conference of Harmonisation
ICSR	Individual Case Safety Report
IDMP	Identifier for Medicinal Products – inclusive of all controlled vocabularies (See Section 3.2.1.1)
IFPMA	International Federation of Pharmaceutical Manufacturers Associations
ISO	International Organisation for Standardisation
ISO 27953	Reference number for working document prepared by ISO Technical Committee TC215 on Health informatics jointly with HL7 and CEN
JIC	Joint Initiative Council
JPMA	Japan Pharmaceutical Manufacturers Association
LLT	Lower Level Term
MAH	Market Authorisation Holders
MedDRA	Medical Dictionary for Regulatory Activities
MHLW	Japan Ministry of Health and Welfare
MPID	Medicinal Product Identifier
MSSO	Maintenance and Support Services Organization
N	Numeric
OID	Object Identifier
PANDRH	Pan American Network on Drug Regulatory Harmonization
PhPID	Pharmaceutical Product Identifier
PhRMA	Pharmaceutical Research and Manufacturers of America
PMDA	Japan Pharmaceuticals and Medical Devices Agency
RHI	Regional Harmonisation initiatives
RIM	Reference Information Model
RMIM	Refined Message Information Model
RQ	Ratio Quantity
SADC	South African Development Community
SDO	Standards Development Organisation
SGML	Standard Generalised Markup Language. An ISO standard for describing structured information in a platform independent manner
ST	Character String*
TS	Point in Time*
UCUM	UCUM (Unified Code for Units of Measure)
UTC	Coordinated Universal Time
W3C	World Wide Web Consortium
WHO	World Health Organisation
XML	eXtensible Markup Language

* These acronyms and definitions pertain to HL7.

Appendix III (B) GLOSSARY of TERMS

This section identifies the vocabulary sets referenced within the message, including both those vocabularies already defined and those which are still under development.

In addition, there are many different terms used to describe basic concepts in healthcare available from various national and international organisations. For the purposes of this document, the following terms and definitions apply to facilitate conformance and interoperability for regulatory reporting of adverse events for human pharmaceuticals.

Term	Definition
Adverse Event	Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product (see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting). [ICH E6(R1)]
Acknowledgement Message (ICSRACK)	The acknowledgement message is an EDI Message with the information on the result of the acknowledgement of receipt procedure to acknowledge the receipt of one safety message and the safety report(s) contained in the safety file. [EMA]
Adverse Drug Reaction (ADR)	In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) cannot be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase 'responses to a medicinal product' means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, e.g., the relationship cannot be ruled out. Regarding marketed medicinal products: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function (See the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting). [ICH E6(R1)]
Case	An observation requiring investigation, and includes problems that might or might not involve individual or groups of investigative subjects. [HL7 Patient Safety]

Term	Definition
Counterfeit Medicine	A medicine which is deliberately and fraudulently mislabelled with respect to identity and / or source. Counterfeiting can apply to both branded and generic products and counterfeit products can include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging. [WHO][13]
Drug	(See Medicinal Product)
Electronic Data Interchange (EDI)	A technology for exchanging structured information for the purpose of conducting business transactions. [ICH M2]
EDI Message	An EDI Message consists of a set of segments, structured using an agreed standard, prepared in a computer readable format and capable of being automatically and unambiguously processed. [EMA]
Healthcare Professional	Person entrusted with the direct or indirect provision of defined healthcare services to a subject of care or a population of subjects of care. [ENV 1613:1995] [ISO 21574-7] EXAMPLE Qualified medical practitioner, pharmacist, nurse, social worker, radiographer, medical secretary or clerk
Individual Case Safety Report	The complete information provided by a reporter at a certain point in time to describe an event or incident of interest. The report can include information about a case involving one subject or a group of subjects. [27953 Human Pharmaceutical Reporting]
Marketing Authorisation Holder	An organisation, usually a biopharmaceutical firm, that holds a valid marketing authorisation for a medicinal product delivered by the Health Authority of a country.
Medical Dictionary for Regulatory Activities	Medical Dictionary for Regulatory Activities (MedDRA) terminology for adverse event reporting used globally by the biopharmaceutical industry and regulators to promote consistent reporting and data analysis.
Medicinal Product	Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; Any substance or combination of substances which might be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis. [ISO 11615] Any substance or combination of substances which might be administered to human beings or animals for treating or preventing disease, with the view to making medical diagnosis or to restore, correct or modify physiological functions. [ENV 13607] [Directive 65/65/EEC, modified]

[13] World Health Organisation International Medical Products Anti-Counterfeiting Task Force (IMPACT)http://www.who.int/impact/FinalBrochureWHA2008a.pdf

Term	Definition
Non-proprietary Drug (generic) Name	Drug name that is not protected by a trademark, usually descriptive of its chemical structure; sometimes called a public name. International Non-proprietary Names (INN) allocated by WHO, identify pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognised and is public property. A non-proprietary name is also known as a generic name. In the US, most generic drug names are assigned by the US Adopted Name Council (USAN).
Pharmacovigilance	The science of activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. [(2) WHO; 2002;]
Product	A thing or things produced by labour or effort for a specific use and marketed to satisfy a need or want. [HL7 Patient Safety]
Regional Pharmacovigilance Centre	A governmentally recognised centre (or integrated system) within a country with the clinical and scientific expertise to collect, collate, analyze and give advice on all information related to drug safety.
Regulatory Agency or Regulatory Authorities	Geopolitical entities have established agencies/authorities responsible for regulating products used in health care. The agencies are collectively referred to as regulatory agencies.
Reference Information Model (RIM)	The HL7 information model from which all other information models, e.g., RMIMS, and messages are derived.
Refined Message Information Model (RMIM)	An information structure that represents the requirements for a set of messages.
Reporter	The primary source of the information, e.g., a person who initially reports the facts provided in the ICSR. This should be distinguished from the sender of the message, though the reporter could also be a sender. [ICH E2B(R2)]
Safety Message	A safety message is an EDI message including the information provided for one/more Individual Case Safety Reports contained in one safety file exchanged between one sender and one receiver in one message transaction. [EMA]
Sender	The person or entity creating the message for transmission. Although the reporter and sender may be the same person, the function of the sender should not be confused with that of the reporter. [ICH E2B(R2)]
Serious Adverse Reaction or Serious Adverse Drug Reaction	Any untoward medical occurrence that at any dose: - results in death, - is life-threatening, - requires inpatient hospitalization or prolongation of existing hospitalization, - results in persistent or significant disability / incapacity, or - is a congenital anomaly/birth defect (See the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting). [ICH E6(R1)]

Term	Definition
Sponsor	An individual, company, institution, or organization which takes responsibility for the initiation, management, and / or financing of a clinical trial. [ICH E6(R1) & E2F]
Spontaneous Reporting	An unsolicited communication to a company, regulatory authority or other organisation that describes an adverse drug reaction in a patient given one or more medicinal products and which does not derive from a study or any organized data collection scheme. [ICH E2C(R1)]
Standard	A technical specification which addresses a business requirement, has been implemented in viable commercial products, and, to the extent practical, complies with recognised standards organisations such as ISO.
Use Case	A description of a system's behaviour as it responds to a request that originates from outside of that system. [Objectory AB]