INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH E2B(R3) Expert Working Group

Electronic Transmission of Individual Case Safety Reports (ICSRs)
Implementation Guide
Data Elements and Message Specification

Version 3.01, Revision June 16, 2011

Depending on the progress of M5 this paper may subsequently change

TABLE OF CONTENTS

NOTE: The numbering in the Table of Contents is linked to the current numbering of the elements and sections in this Step 2 document for consultation. This will be renumbered and the Table of Contents will reflect the new numbering and structure after the public consultation period.

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I. INTRODUCTION / EXECUTIVE SUMMARY

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

The ICH E2B(R3) message standard is built upon the Health Level 7 (HL7) ICSR Release 3 standard (or HL7 ICSR R3). The HL7 ICSR R3 standard is a particular message based on the HL7 Version 3 messaging standard (or HL7 V3), a broader platform for health care information transfer. Please see section 2.2 for an explanation of HL7 versions.

Conceptually, an ICSR is a report of information describing adverse event(s) / reaction(s) experienced by an individual patient; the event(s)/reaction(s) can be related to the administration of one or more medicinal products at a particular point in time. [1] The ICSR can also be used for exchange of other information, such as medication error(s) that do not involve adverse events(s)/reaction(s). The information for the report is provided by a primary source, although, depending on regional requirements, new information, or for practical or logistical issues, a given ICSR can be updated or retransmitted by either the initial sender or a 3rd party.

The ICH requirements for implementation of the ICSR focuses on medicinal products and therapeutic biologics for human use, although regional applications of the ICSR can include a wider scope, such as for Pharmacovigilance 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 guide is intended to support the implementation of software tools for creating, editing, sending and receiving electronic ICSR messages. It is not intended as a guide to pharmacovigilance practices nor is it intended to explain the underlying scientific or medical issues that support the collation, categorisation or analysis of safety information. It is also not intended to explain the rationale that underlies the content requirements for safety reporting – the regulatory requirements and harmonised practices that determine what elements are required or optional and what types of information must fill those elements.

This is a technical implementation guide. It is meant to be consulted by system developers, IT professionals, system implementors and system users who need to understand the requirements for constructing and using valid electronic messages to transmit ICSRs. It provides a pathway to support the development of forms and user interfaces and the determination of pick lists in tools. It provides the technical requirements to design style sheets, data transformations and coding of exported messages. It should not be interpreted as a guidance or recommendation for any particular database technology or software platform, other than the requirement to generate valid XML code according to the standard outlined in this Implementation Guide.

- *Business context for the implementation of the ICSR standard*
  - *Short summary of the business problem this standard addresses*
  - *References the relevant EWG documentation*
- *Short summary of how this standard will be used in practical, day to day applications*

[1] The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)

- *This is how used by ICH.*

II. OPEN ISSUES

(This section will be removed in a future version of this document)
This section will identify known, outstanding issues with the Draft Implementation Guide. During the public consultation period, we will be taking feedback from readers on

- *Changes required to better inform the reader*
- *Suggestions on how the document can be better organised*

Open Issues include:

- *Section 3.2.4 addresses the different transactions relevant for ICSR messaging. These transactions are discussed within the HL7 ballot material under the heading of "Interactions."*

- *NUMBERING: The current element numbers in this guide contain gaps and do not reflect a uniform or consistent approach. These numbers are a by-product of the E2B(M) guideline and the iterative development process for this version. THESE NUMBERS ARE NOT FINAL. The elements in the ICH ICSR message will be renumbered upon completion of the public consultation period and changed to an appropriate, comprehensible numbering scheme that reflects the final structure and version of the message.*

1.0 PURPOSE

The business objective of this implementation guide is to standardise the definition of all data elements for transmission of all types of ICSRs, regardless of source and destination. This guide includes data elements for ICSRs for both pre- and post-authorisation periods and covers both adverse drug reaction and adverse event reports. The technical objective of this guide is to assist reporters and recipients (including pharmaceutical companies, regulatory authorities and non-commercial sponsors) in implementing systems and constructing transmittable ICSR messages. In addition, the ICSR representation should use an international standard that is platform, application and vendor independent.

1.1 SCOPE

The format and content of ICSRs that is described in this guideline includes a large number of data elements, allowing an almost identical reporting of medical content to any regulatory authority or other business partner; therefore requests for inclusion of additional local data should not be necessary and should be avoided as much as possible. This format can also be used for other types of case reports but without adverse events or adverse reactions such as medicinal product administration during pregnancy, overdose, medication error, or potential lack of efficacy. However this format is not intended for cases in the integrated safety summary of a marketing authorisation application dossier. The scope of this implementation guide 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, and regulations, ICSRs can be transmitted, for example;

- 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
- From authorities to the World Health Organisation (WHO) Collaborating Center for International Drug Monitoring.

The transmission of ICSRs 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 an electronic format 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 the definition for common data elements and standard transmission procedures that are provided in this document.

Over the last ten years, exchange of individual case reports has increasingly shifted from paper-based to electronic reports and electronic transmission of case safety information is an essential component of global pharmacovigilance. ICH released a consensus electronic standard for ICSRs in 1997 and this standard has undergone multiple 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 regulatory jurisdictions and is accepted in all. This document describes the electronic message used to transmit the information required for ICSR exchange utilising the International Organisation for Standardisation (ISO) ICSR standard, prEN ISO 27953 (ICSR Part 2).

Prior to the message standard described in this ICH guide, ICH electronic messaging standards were developed by the ICH M2 EWG for Electronic Standards for the Transmission of Regulatory Information (ESTRI). Development of the standard that is the subject of this implementation guide represents an ICH process change, as the messaging standard was developed through a partnership with external Standards Development Organisations (SDOs). Specifically, this message was developed through a collaborative relationship between ICH and the Joint Initiative Council (JIC), a partnership of the ISO, HL7, the European Committee for Standardisation (CEN), the Clinical Data Interchange Standards Consortium (CDISC), and the International Health Terminology Standards Development Organisation (IHTSDO).

1.3 APPLICATION

The ICH E2B (R3) message standard was built using the HL7 ICSR Release 3 standard (or HL7 ICSR R3 standard), which is intended for a broader use and can be applied to regions and business cases beyond the narrow intended use as ICH E2B(R3). The HL7 ICSR R3 standard is a particular message based on the HL7 version 3 messaging standard (or HL7 V3), a broader platform for health care information transfer. See section 2.2 for an explanation of HL7 versions.

This document contains information on implementation and use of the ICH sub-set of the HL7 ICSR R3 standard that serves as the foundation for the ISO ICSR standard. ICH implementation applies to the safety reporting requirements for medicinal products in the three main ICH regions (Japan, the European Union (EU), and the United States US) and in those regions that are ICH Observers or are working with ICH through the auspices of the Global Cooperation Group (GCG). ICH implementation was derived from the ISO Draft International Standard (DIS) which was excerpted from the HL7 ICSR R3 message to support electronic messaging for the ICH E2B(R3) data elements. Therefore, elements of the HL7 ICSR R3 standard which solely relate to use cases outside the remit of ICH will not be addressed within this ICH implementation guide.

Further information about ICH, its EWGs and standards, and supporting documentation, beyond that contained in Section 2 of this document, is available from the ICH website: http://www.ich.org More detailed information on technical standards from the ICH M2 EWG, including testing and

implementation, can be found at the ESTRI website: http://www.ich.org/products/electronic-standards.html.

2.0 BACKGROUND

2.1 GENERAL BACKGROUND AND HISTORY

2.1.1 The ICH and Its Partners

The ICH was organised to provide a consensus forum for tripartite harmonisation initiatives to be developed with input from both regulatory and pharmaceutical industry representatives. The primary ICH focus is harmonisation of technical requirements for the registration of pharmaceutical products among three regions: Japan, the EU, and the US. The six ICH Parties are the European Commission for the EU, the European Federation of Pharmaceutical Industries' Associations (EFPIA), the Ministry of Health, Labor, and Welfare, Japan (MHLW), the Japan Pharmaceutical Manufacturers Association (JPMA), the US Food and Drug Administration (FDA), and the Pharmaceutical Research and Manufacturers of America (PhRMA). The International Federation of Pharmaceutical Manufacturers Associations (IFPMA) serves as ICH Secretariat.

The ICH Steering Committee includes representatives from each of the ICH Parties; the Secretariat, and Observers from WHO, Health Canada – Health Products and Food Branch, and the European Free Trade Area also participate.

In addition to the above, ICH supports a Global Cooperation Group (GCG), which has representatives from the six ICH Parties, three Observers, and Secretariat, representatives from other Regional Harmonisation Initiatives (RHIs) for pharmaceutical regulation, namely the Asia-Pacific Economic Cooperation (APEC), the Association of Southeast Asian Nations (ASEAN), the Gulf Cooperation Countries (GCC), the Pan American Network on Drug Regulatory Harmonization (PANDRH) and the South African Development Community (SADC). It is hoped that this Implementation Guide will be of use to the regions represented through the GCG, should they optionally implement the ICH E2B(R3) ICSR for medicinal products.

2.1.2 Historical Perspective

The first ICH E2B guideline, Data Elements for Transmission of Individual Case Safety Reports, was endorsed on July 17, 1997, was modified in November 2000, and was then issued in February 2001 as the ICH Step 4 E2B(M) guideline. The Step 4 E2B(M) guideline was renamed as the E2B(R2) guideline in May 2005, without any change in business requirements. The ICH M2 EWG prepared the Electronic Transmission of Individual Case Safety Reports Message Specification guideline in 2001 to standardise the data elements for the electronic transmission of ICSRs by identifying and defining the essential elements for an ICSR, regardless of source or destination. This included case safety reports for both pre- and post- authorisation periods and covered both adverse drug reaction and adverse event reports.

2.1.3 The Process of Revision

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 to continually enhance electronic transmission of safety reports in a format that can be generated and processed automatically by a transactional database. This need has led to periodic revision of the initial 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 agreement regarding common data elements and on the syntactical definition of the electronic message. Hence the adoption of a standardised electronic message across regions, regulatory agencies, and other participants is of paramount importance. In 2006, the decision was made that the ICH would pursue a new model for the development of the ICH M2 messaging standard to support the third revision of E2B. This Implementation Guide describes the messaging standard that will implement the E2B(R3) message developed through this new process.

As mentioned in Section 1.2, above, prior to 2007 ICH routinely developed its own electronic standards and guidance, and developed the supporting electronic messaging standards itself. However, ICH broadened outreach for standards development and is now aligned with SDOs to develop messaging standards. ISO, HL7, CEN, CDISC, and IHTSDO, with their respective technical committees (TCs) and their stakeholders for health informatics Standardisation have collectively identified a need and opportunity to collaborate, coordinate, and cooperate in delivering global, implementable electronic standards. A decision has been taken by the ICH Steering Committee to work together to better support harmonisation and implementation of standards.

The SDOs noted above have formed a Joint Initiative to partner with organisations such as the ICH to support the creation of broad, global electronic health information standards that can be integrated into the broader healthcare environment. Governance of the Joint Initiative is via a Joint Initiative Council (JIC), which has representation from member SDOs. The approach is to identify common scope and purpose, to align development, and to agree on content, thus, leading to a single best standard for each problem, and full mutual recognition and endorsement of standards by participating SDOs. For ICH, the need to work with SDOs to leverage resources for electronic standards development and avoid overlapping, counter-productive, or counter-acting standards is critical to achieve and maintain its own harmonisation goals.

2.2 THE FRAMEWORK FOR ICH ICSR E2B (R3)

The decision by ICH to progress new revisions to the message specification for E2B through collaboration with this Joint Initiative has necessitated certain changes to the technical approach compared with that of the prior ICH ICSR Document Type Definition (DTD).

After the ICH's original proposal to ISO for the ICSR (when E2B(R3) was accepted as an ISO activity), the prEN ISO 27953 standard was advanced through the Joint Initiative on SDO Global Health Informatics Standardisation. The Joint Initiative was formed to enable common health informatics standards by addressing and resolving issues of gaps, overlaps, and counter-productive Standardisation efforts through an agreed upon decision process for international Standardisation needs.

The ICSR was approved 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 ICH message specification for E2B(R3) is based on a "constrained" set of schemas derived from the prEN ISO 27953 standard (ISO ICSR Part 2). The project team for prEN ISO 27953 created a "*framework for international data exchange and information sharing by providing a common set of data elements and a messaging format for transmission of ICSRs for adverse drug reactions (ADR), adverse events (AE) including infections and incidents that can occur upon the administration of one or more human pharmaceutical products to a patient, regardless of source and destination.*" The prEN ISO 27953 consolidated content and messaging requirements 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 HL7 Version 2 (V2) messaging standard has been broadly implemented across segments of the healthcare environment in over 20 countries. The HL7 V3 messaging standard, which supersedes HL7 V2, 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.[2]

HL7 V3 was developed to address the complex requirements of health information technology. 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 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.[2]

2.3 REPRESENTATION OF THE ELECTRONIC ICSR

2.3.1 Why Standardisation and Electronic ICSR Exchange Are Needed

The primary reason for ICSR message harmonisation is to protect patient safety and thus, to promote the public health. Many organisations need to exchange ICSRs across stakeholder communities during clinical trials and to monitor health products for continued safety once they are authorised for marketing. Electronic reporting speeds the transfer of information that can lead to actionable knowledge that will improve patient safety. Electronic reporting also makes safety data readily available for further processing, visibility and analysis. These advantages allow regulators, MAHs, healthcare professionals (HCPs) and consumers to make better informed decisions regarding the use of health products.

Harmonisation is required; otherwise, a multiplicity of message and/or content standards across regions and regulatory jurisdictions would result in diseconomies of scale and increase the burden for mandatory reporters. A lack of harmonisation might lead to difficulties 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.

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

In November 1996, the ICH M2 EWG produced a DTD of the message for the electronic transmission of ICSRs: the ICH_ICSR.DTD.

[2] Available from the HL7 Website, along with other materials, at http:///www.hl7.org or http://www.hl7.org.uk/marketing/publications.asp

At the following meeting of the ICH M2 EWG in March 1997, the six ICH parties agreed on the relational data model to be used for the definition of an electronic message, which was based on the ICH E2B document Step 2/3, Version 5.

Once the ICH E2B document was adopted as a Step 4 guideline in July 1997, the ICH M2 EWG finalised the relational model and the message definition. The first official release of the ICH_ICSR.DTD was agreed in October 1997 in Washington, DC. The maintenance EWG for E2B was established in October 1999. This group was charged with improving definitions and descriptions in both the E2B Step 4 guideline and the ICSR specification since both are referenced in the creation of an ICSR message. New releases of the ICH message and specifications were completed in November 2000 and released in February 2001.

Subsequent to the publication of the E2B(M) guideline, ICH formed an E2B(M) Implementation Working Group (IWG) to facilitate implementation of the guideline by the ICH Parties through a Q&A document. Within the "Electronic Transmission of Individual Case Safety Reports Message Specification (ICH ICSR DTD Version 2.1), Final Version 2.3" published in February of 2001 (http://estri.ich.org/icsr/index.htm), detailed instructions for preparing an SGML file are available. The guidance within this document provides the means to accomplish the electronic exchange of ICSRs – between sponsors / MAHs (including co-sponsors, Clinical Research Organisations, etc.), between sponsors and health authorities, and between health authorities globally. The guidance also enables adverse event/reaction data to be populated and extracted from clinical safety databases including Spontaneous Reporting System databases.

At that time, prior work on standardisation of an electronic message by HL7 and EDIFACT (Electronic Data Interchange for Administration, Commerce and Transport) was considered, but the ICH selected SGML (Standard Generalised Markup Language, ISO 8879:1986) as the preferred alternative because SGML was the de facto standard for the interchange of information. It also supported the multi-lingual character sets needed across ICH regions.

In spite of this fact, the SGML-based 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.

2.3.2.1 Markup Languages[3]

First published in 1988, Standard Generalised Markup Language (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 require information to be available for extended periods of time (archived). It is powerful but complex. It serves as a basis for Extensible Markup Language (XML) which is simpler than SGML yet maintains the most useful parts of SGML.

SGML requires that structured documents reference a Document Type Definition (DTD) to be valid. The DTD is the tool used to create and describe the expected SGML or XML. Simply stated, 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 called 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 called invalid.

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

The DTD specifies the required structure and format of a particular document. But 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, but also the ability to have more flexibility in well-formed data.

In general, DTDs work better for documents or text-intensive information. XML schema work best for data-intensive information[4]. 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[5].

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[6]. 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[7].

2.3.2.2 Advantages to Electronic Submissions

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 (data or text) electronically across platforms. XML is used for encapsulating information to pass it between two computing systems, which might otherwise be unable to communicate. It provides a common envelope for inter-process communication (messaging). It is backed by an international standard and will, therefore, remain accessible[8].

The ICH ICSR has enhanced 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, and facilitate the transfer of information to organisations who need them;
- Enables incoming messages to be automatically processed and routed;
- Facilitates aggregation of safety data for analysis; and
- Allows resources to be redirected away from data entry activities to more analytical activities.

3.0 ESSENTIAL COMPONENTS

Developing software specifications to support business requirements, such as those specified in the E2B(R3) requirements, needs an approach where the functional and procedural requirements are well understood and reflected accurately in the electronic message. The electronic message must contain

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

[5] "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

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

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

[8] 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/

not only 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 Implementation Guide lists the exact E2B(R3) data elements and essential components required to develop usable and exchangeable ICH ICSR messages.

ICH ICSR RELATIONAL DIAGRAMS

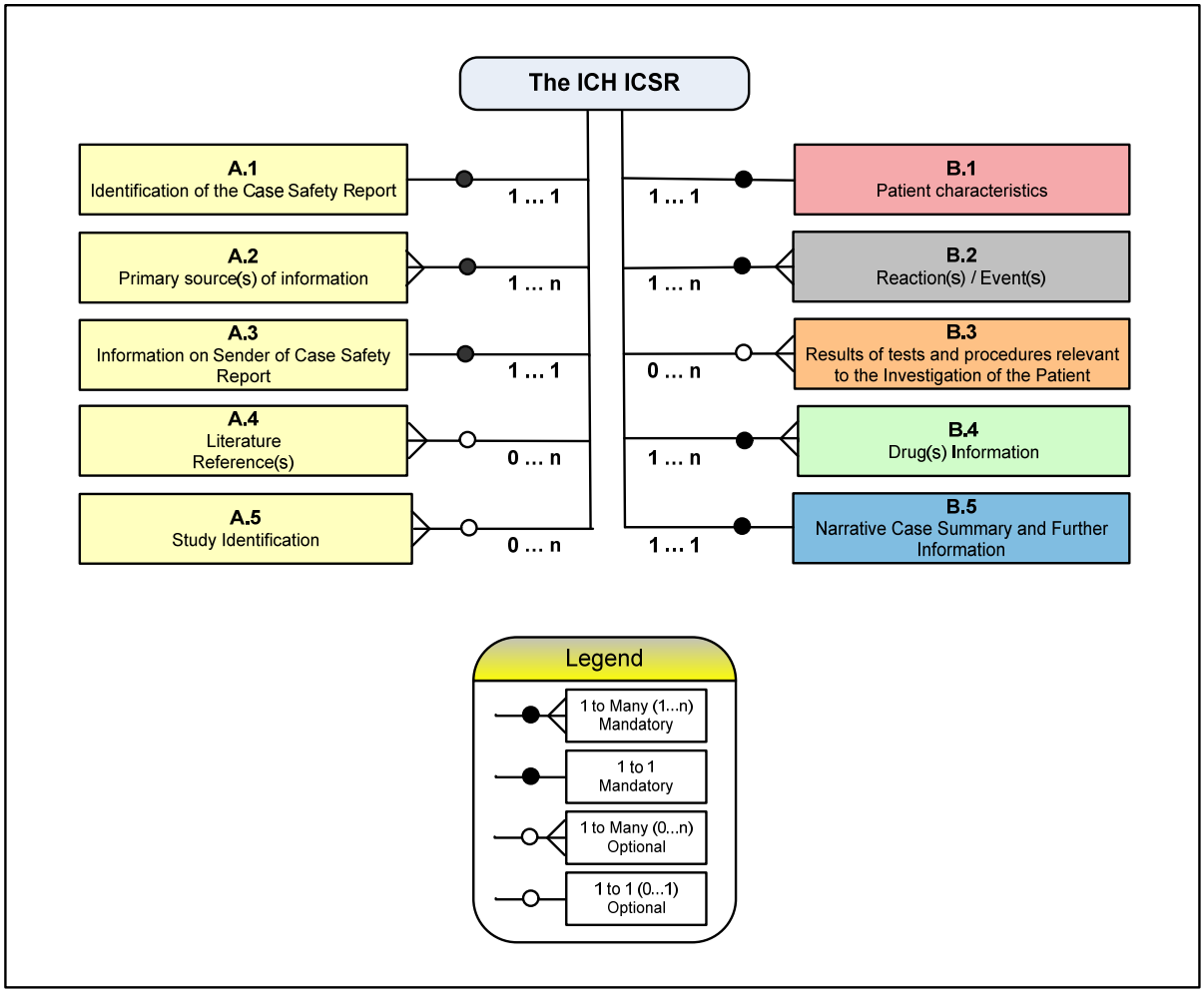
Figure 1 illustrates the relationship between the main sections defined in E2B(R3) for the ICH ICSR message and XML descriptors. Each box in the diagram represents a related section of the E2B(R3) data element structure, and all the data elements in that block are listed in the attribute list (Section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

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

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

Figure 1 below illustrates the structure of an ICSR message. Figure 2: Diagram of ICH ICSR Elements: Concept Areas , in section 3.4.7b provides the next level of detail and is 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



3.1 ICH ICSR SCHEMA

This section discusses the schemas used for ICH ICSR messaging. This section includes the exchange of ICSRs as single files and as batched ICSRs, including acknowledgement of receipt. The reader should note that HL7 has developed each schema as an individual file, and used XML "include" statements to link these files.

All of schema files for ICH use are categorised and summarised in the following table. User guidance is available for each schema file in 3.2.1, 3.2.2, and 3.2.3.

	Major Category	Sub-Category	Schema File Name
1.	**Core Schemas:** A common schema set, lie under all of HL7 messages.		infrastructureRoot datatypes-base datatypes voc (narrativeblock)
2.	**Send Batch Interaction:** A schema set for ICSR messages	ICSR Batch Interaction: Batch wrapper schemas for single or multiple ICSR messages	MCCI_IN200100UV01 MCCI_MT200100UV
		ICSR Single Interaction: Schemas for each ICSR message	PORR_IN049016UV01 (PORR_IN049017UV01) (PORR_IN049018UV01) MCCI_MT000100UV01

			MCAI_MT700201UV01 PORR_MT049016UV PORR_MT049023UV POCP_MT010200UV POCP_MT010200UV POCP_MT030100UV POCP_MT030200UV POCP_MT040100UV POCP_MT050100UV POCP_MT081100UV
3.	**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: Schemas for each Acknowledgement message	MCCI_IN000002UV01 MCCI_MT000200UV01

3.1.1 Core Schemas

The core schemas are those used for all HL7 messages. Because the ICH ICSR is built upon HL7 V3, these schemas are also the underlying basis for the ICH ICSR. These are briefly discussed; however, Implementors normally will not access these schemas directly. This collection of schemas is grouped within the folder "coreschemas", which is parallel to the folder "multicacheschemas" within HL7 publications. This should be considered when schemas are moved since it affects the form of "include" statements.

3.1.1.1 InfrastructureRoot

User Guidance	The schema defines properties that are valid for all elements across all HL7 schemas. This includes elements derived from R-MIM[9] classes, as well as RMIM attributes. The elements, realmCode, typeId, and templateId are used when an HL7 specification is specialised. They are not called upon within this Implementation Guide

3.1.1.2 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 includes the definitions of the "atomic" datatypes Boolean and String, which are used as building blocks for the more complex ones.

[9] Refined Message Information Model. Refer to Appendix VII - Abbreviations for this and other HL7 messaging terminology abbreviations.

676 **3.1.1.3 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* includes the definitions of the "compound" datatypes such as periodic intervals which are created using base types within their definition.

677 **3.1.1.4 Voc**

User Guidance	The schema includes the vocabulary items that are defined by HL7 for use by all Implementors (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.

678 **3.1.1.5 Narrative Block**

User Guidance	The schema is used for structured documents, and is relevant within the Clinical Document Architecture. Though this is included in the ICH ICSR schema file set, this schema file is not used for ICH ICSR message.

679 **3.1.2 Send Batch Interaction**

680 **3.1.2.1 Send Batch Interaction**

681 Wrapper schemas, such as Send Batch Interaction, are used to validate common elements in all
682 transactions. The HL7 Transmission wrapper is required for all V3 messages. It contains a large
683 number of optional fields so the message overhead will vary from one context to another. Like the
684 core schemas, these are shared across HL7 implementations.

685 ***3.1.2.1.1 Interaction (MCCI_IN200100UV01)***

User Guidance	The schema for an interaction makes it possible to identify the trigger event for the message, as well as indicating payload schema.

686 ***3.1.2.1.2 Transmission (MCCI_ MT200100UV)***

User Guidance	The HL7 documentation notes: "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). The structure is used to identify the sender and receiver of the message as well as carrying basic transactional information." All ICSR messages contain content from the transmission wrapper. When an acknowledgement is sent, the acknowledgement content for an individual message is contained within the transmission wrapper.

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688 **3.1.2.2 ICSR Single Interaction**

689 ***3.1.2.2.1 ICSR Interaction***

690 ***3.1.2.2.1.1 ICSR Create (PORR_IN049016UV)***

User Guidance	This schema is the only one to be used for ICH ICSR interactions created to report or transmit, as well as for follow up, amendment and nullification The schema for an interaction makes it possible to identify the trigger event for the message, as well as indicating the wrappers and primary payload schema.

691 ***3.1.2.2.1.2 ICSR Amendment (PORR_IN049017UV)***

User Guidance	This schema is used for ICSR single interactions which ammend values in previously created ICSR message. The schema for an interaction makes it possible to identify the trigger event for the message, as well as indicating the wrappers and primary payload schema. Though this schema file is included in the ICH ICSR schema file set, it is not used for ICH ICSR message.

692 ***3.1.2.2.1.3 ICSR Nullification (PORR_IN049018UV)***

User Guidance	This schema is used for ICSR single interactions which nullify previously created ICSR message. The schema for an interaction makes it possible to identify the trigger event for the message, as well as indicating the wrappers and primary payload schema. Though this schema file is included in the ICH ICSR schema file set, it is not used for ICH ICSR message.

693 ***3.1.2.2.2 Transmission (MCCI_MT000100UV01)***

User Guidance	The HL7 documentation notes: “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). The structure is used to identify the sender and receiver of the message as well as carrying basic transactional information.” All ICSR messages contain content from the transmission wrapper. When an acknowledgement is sent, the acknowledgement content for an individual message is contained within the transmission wrapper.

694 ***3.1.2.2.3 Control Act (MCAI_MT700201UV01)***

User Guidance	The HL7 documentation notes: “The ‘Trigger Event Control Act’ contains administrative information related to the "controlled act" which is being communicated as a messaging interaction. A Trigger Event Control Act describes the 'action' that is happening to the subject of the message (the payload). The Trigger Event Control Act contains details about the trigger event for the message such as who, when, where and why.”

	Since ICSR messaging simply addresses notifications related to actions that have already taken place, and the relevant information is carried in the body of the report (message payload), the contents of this model are not used.

3.1.2.2.4 ICSR Payload

The message schemas contain the content of the ICSR. These schemas have been re-generated for the ICH-based implementation to include only those elements needed for implementations using data defined within the ICH ICSR requirements.

3.1.2.2.4.1 ICSR Base (PORR_MT049016UV)

User Guidance	The ICSR Base model contains information about the reporting of the adverse event / reaction or product problem, the investigative subject, and the event(s) / reaction. It also provides the entry point for information on suspect, interacting, and concomitant substance administrations and related products.

3.1.2.2.4.2 Product Reporting Related Information (PORR_MT049023UV)

User Guidance	The Product Reporting Related Information model captures information about characteristic of the subject such as age group, weight ,height, and substance administrations related to the adverse event / reaction. Historical data on the investigative subject and on related parties are captured as well. It also provides the entry point for information on suspect, interacting, and concomitant products (typically, for ICH, pharmaceutical products).

3.1.2.2.4.3 Common Product Model

POCP_MT010200UV
POCP_MT010200UV
POCP_MT030100UV
POCP_MT030200UV
POCP_MT040100UV
POCP_MT050100UV
POCP_MT081100UV

User Guidance	The common product model provides information on medicinal products that were administered to the investigative subject or to a related person, e.g. parent.

3.1.3 Send Response Batch Interaction

3.1.3.1 Acknowledgement Batch Interaction

3.1.3.1.1 Interaction (MCCI_IN200101UV01)

User Guidance	The HL7 Documentation notes:

	"Describes general message control acknowledgement structure for communication level acknowledgements. This RMIM contains a mandatory Acknowledgement class to convey the link between the Accept Acknowledgement and the message being acknowledged." 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.

713 ***3.1.3.1.2 Transmission (MCCI_MT200101UV)***

User Guidance	The HL7 Documentation notes: "There are instances when it is convenient to transfer a batch of HL7 interactions …. Such a batch could be sent online using a common file transfer protocol, or offline via tape or diskette. Although a batch will usually consist of a single type of interaction, there is nothing in the definition that restricts a batch to only one interaction type. It should be noted that the "unit of work" of HL7 is the interaction, not the batch. Thus some interactions contained within the batch can be successfully processed, while others are not."

714 **3.1.3.2 Acknowledgement Single Interaction**

715 ***3.1.3.2.1 Interaction (MCCI_IN000002UV01)***

User Guidance	The acknowledgement can be used for any HL7 message.

716 ***3.1.3.2.2 Transmission (MCCI_MT000200UV01)***

User Guidance	The acknowledgement can be used for any HL7 message.

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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 of mass or time or country codes. Others are specific to the medical sector, such as MedDRA. Still others are specific code lists created by ICH. This section will address these code sets, terminologies and vocabularies. Specific guidance will be found in section 3.4 in the instruction for the individual elements.

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 idendified by the OID 2.16.840.1.113883.6.163 which also represents the branch "joint-iso-itu-t.country.us.organization.hl7.external-code-system.MedDRA."

An organization can obtain OID by requesting an identifier from a registrar, and if it desires, an organisation may in turn become a registrat and subsequently child OIDs to its internal objects. ICH is implementing OIDs to identify code systems used in ICSR message exchange. The combination of code and OID (code system) provides unique identifier to the code and its definition.

Currently, ICH is in the process of obtaining ICH OID and establishing a methodology to assign child OIDs within ICH. Therefore the OIDs required for the coded data element are not available at this time. To expedite the progress to Step 3 public consultation, temporary OIDs in the form of "ich-dataelement-oid" are used in this document. The temporary OIDs will be replaced with the actual ICH assigned OID at later time. ICH OIDs and code lists will be available on the ICH website at this later date.

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 Expert Working Groups M5 and M2, ISO is currently developing 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. These also include controlled identifiers to enable cross-border identification of the pharmaceutical products and mapping to the component medicinal products and substances.

The ICH M5 guideline is under development and will be available after this Implementation Guide is published. ISO IDMP standards are the basis of ICH M5 guideline, these include:

- prEN ISO 11238 Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated information on substances
- prEN 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
- prEN ISO 11240 Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of units of measurement

- prEN ISO 11595: Health informatics — Pharmacovigilance – Data elements and structures for the reporting of laboratory results and clinical observations
- prEN ISO 11615 Health Informatics – Identification of medicinal products – Data elements and structures for the unique identification and exchange of regulated medicinal product information
- prEN 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 these vocabularies are listed in detail in Section 3.4 of this document. In these data elements, all terms and identifiers (codes) as described in the M5 Implementation Guide should be used; where M5 terms and/or identifiers are not available the Implementation Guide also provides instructions for alternate means to code the information.

Note: Until the M5 controlled vocabularies are available, tentative rules are applied to the data elements. . For instance, controlled vocabularies for route of administration are available in Appendix VI of this Implementation Guide and the appropriate code should be used if available in free text fields in an ICSR. The other terms and identifiers (codes) will be provided by each region until the M5 controlled vocabularies are implemented.

Element id	Element Name	OID Name	OID Reference[10]
B.1.8.r.a1	Medicinal Product Identifier (MPID)	**ISO 11615**	***MPID***
B.1.8.r.a3	Pharmaceutical Product Identifier (PhPID)	**ISO 11616**	***PhPID***
B.1.10.8.r.a1	Medicinal Product Identifier (MPID)	**ISO 11615**	***MPID***
B.1.10.8.r.a3	Pharmaceutical Product Identifier (PhPID)	**ISO 11616**	***PhPID***
B.4.k.2.1.1a	Medicinal Product Identifier (MPID)	**ISO 11615**	***MPID***
B.4.k.2.1.2a	Pharmaceutical Product Identifier (PhPID)	**ISO 11616**	***PhPID***
B.4.k.2.3.r.2a	Substance/Specified Substance TermID	**ISO 11238**	***IDMP Substance***
B.4.k.4.r.11.2a	Pharmaceutical Dose Form TermID	**ISO 11239**	***IDMP Dosage Forms & Routes of Admin***
B.4.k.4..12.2a	Route of Administration TermID	**ISO 11239**	***IDMP Dosage Forms & Routes of Admin***
B.4.k.4.13.2a	Parent Route of Administration TermID	**ISO 11239**	***IDMP Dosage Forms & Routes of Admin***

3.2.1.2 MedDRA - the Medical Dictionary for Regulatory Activities[11]

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.

[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 the webpage.

MedDRA was developed by the International Conference on Harmonisation (ICH) and is owned by the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) acting as trustee for the ICH steering committee.

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 medical information relating to reactions, events and medical history. The following elements require MedDRA coding. Please note that only one version of MedDRA can be used in a single ICSR.

Element id	Element Name	OID Name	OID Reference
B.1.7.1.r.a.2	Structured Medical History Information (disease / surgical procedure / etc.)	MedDRA	***2.16.840.1.113883.6.163***
B.1.8.r.f.2	Indication	MedDRA	***2.16.840.1.113883.6.163***
B.1.8.r.g.2	Reaction	MedDRA	***2.16.840.1.113883.6.163***
B.1.8.4.b1	Reported Causes(s) of Death (MedDRA code)	MedDRA	***2.16.840.1.113883.6.163***
B.1.9.4.r.b1	Autopsy-determined Causes(s) of Death (MedDRA code)	MedDRA	***2.16.840.1.113883.6.163***
B.1.10.7.1.r.a.2	Structured Information (disease / surgical procedure / etc.)	MedDRA	***2.16.840.1.113883.6.163***
B.1.10.8.r.f.2	Indication	MedDRA	***2.16.840.1.113883.6.163***
B.1.10.8.r.g.2	Reactions (if any and known)	MedDRA	***2.16.840.1.113883.6.163***
B.2.i.1.b	Reactions / Event in MedDRA Terminology	MedDRA	***2.16.840.1.113883.6.163***
B.3.r.c2	Test Name (MedDRA code)	MedDRA	***2.16.840.1.113883.6.163***
B.4.k.7.r.2a	Indication in MedDRA Terminology (LLT code)	MedDRA	***2.16.840.1.113883.6.163***
B.5.3.r.2	Sender's Diagnosis / Syndrome and / or Reclassification of Reaction / Event	MedDRA	***2.16.840.1.113883.6.163***

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

This section contains a table of Code Sets and OIDs relevant to this Implementation Guide specifically created for ICH requirements. These code sets are maintained by or for ICH.

Element id	Element Name	ICH Placeholder OID
M.1.1	Type of Messages in Batch	***ich-type-of-message-in-batch-oid***
M.1.5	Batch Sender Identifier	***ich-batch-sender-identifier-oid***
M.1.6	Batch Receiver Identifier	***ich-batch-receiver-identifier-oid***
M.2.r.5	Message Sender Identifier	***ich-message-sender-identifier-oid***
M.2.r.6	Message Receiver Identifier	***ich-message-receiver-identifier-oid***
A.1.0.1	Sender's (case) Safety Report Unique Identifier	***ich-senders-safety-report-identifier-oid***
A.1.4	Type of Report	***ich-type-of-report-oid***
A.1.10.1	Worldwide Unique Case Identification number	***ich-worldwide-case-identifier-oid***
A.1.10.2	First Sender of this Case	***ich-first-sender-of-this–case-oid***
A.1.13	Report Nullification / Amendment	***ich-report-nullification-amendment-oid***
A.2.r.1.4	Qualification	***ich-qualification-oid***
A.3.1	Sender Type	***ich-sender-type-oid***
A.5.4	Study Type Where Reaction(s) / Event(s) Were Observed	***ich-study-type-oid***
B.1.1.1a	Patient Medical Record Number(s) and the Source(s) of the Record Number (GP Medical Record Number)	***ich-gp-medical-record-number-oid***
B.1.1.1b	Patient Medical Record Number(s) and the Source(s) of the Record Number (Specialist Record Number)	***ich-specialist-medical-record-number-oid***
B.1.1.1c	Patient Medical Record Number(s) and Source(s) of the Record Number (Hospital Record Number)	***ich-hospital-medical-record-number-oid***
B.1.1.1d	Patient Medical Record Number(s) and Source(s) of the Record Number (Investigation Number)	***ich-investigation-medical-record-number-oid***
B.1.2.3	Patient Age Group (as per reporter)	***ich-patient-age-group-oid***
B.2.i.2.1	Term Highlighted by the Reporter	***ich-term-highlighted-oid***
B.2.i.6	Outcome of Reaction / Event at the Time of Last Observation	***ich-outcome-of-reaction-event-oid***
B.3.r.d1	Test Result (Code)	***ich-test-result-code-oid***
B.4.k.1	Characterisation of Drug Role	***ich-characterisation-of-drug-role-oid***
B.4.k.4.r.12.2a	Route of Administration TermID	***ich-route-of-administration-oid***
B.4.k.4.r.13.2a	Parent Route of Administration TermID	***ich-route-of-administration-oid***
B.4.k.8	Action(s) Taken with Drug	***ich-action-taken-with-drug-oid***
B.4.k.9.i.4	Did Reaction Recur on Re-Administration?	***ich-recur-on-readministration-oid***
B.4.k.10.r	Coded Drug Information	***ich-addional-info-on-drug-code-oid***

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Element id	Element Name	ICH Placeholder OID
ACK.M.2	Acknowledgement Batch Sender Identifier	***ich-ack-batch-sender-identifier-oid***
ACK.M.3	Acknowledgement Batch Receiver Identifier	***ich-ack-batch-receiver-identifier-oid***
ACK.B.r.3	ICSR Message ACK Receiver	***ich-ack-receiver-identifier-oid***
ACK.B.r.4	ICSR Message ACK Sender	***ich-ack-sender-identifier-oid***

Observation Codes	ICH Placeholder OID
Observation Codes in ICSR message	***ich-observation-code-oid***
Observation Codes in ACK message	***ich-ack-observation-code-oid***

3.2.3 International Standard Code Sets

This section contains information on Code Sets and OIDs relevant to this Guidance 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

- 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://www.regenstrief.org/medinformatics/ucum/downloads

Element id	Element Name	Coding Scheme Name	OID Reference
A.2.r.1.3	Reporter's Country Code	ISO 3166 Part 1 (alpha-2)	***1.0.3166.1.2.2***
A.3.4e	Sender's Country Code	ISO 3166 Part 1 (alpha-2)	***1.0.3166.1.2.2***
A.5.1.r.2	Registration Country	ISO 3166 Part 1 (alpha-2)	***1.0.3166.1.2.2***
B.1.10.2.2b	Age of Parent (age unit)	UCUM	***2.16.840.1.113883.6.8***
B.1.10.6	Sex of Parent	ISO 5218	***1.0.5218***
B.1.5	Sex	ISO 5218	***1.0.5218***
B.2.i.5b	Duration of Reaction / Event (Duration Unit)	UCUM	***2.16.840.1.113883.6.8***
B.2.i.8	Identification of the Country Where the Reaction / Event Occurred	ISO 3166 Part 1 (alpha-2)	***1.0.3166.1.2.2***
B.3.r.e	Unit	UCUM	***2.16.840.1.113883.6.8***
B.4.k.2.3.r.4	Strenght Unit	UCUM	***2.16.840.1.113883.6.8***
B.4.k.2.4	Identification of the Country Where the Drug was Obtained	ISO 3166 Part 1 (alpha-2)	***1.0.3166.1.2.2***
B.4.k.3.2	Country of Authorisation / Application	ISO 3166 Part 1 (alpha-2)	***1.0.3166.1.2.2***
B.4.k.4.r.8b	Duration of the Drug Administration (Unit)	UCUM	***2.16.840.1.113883.6.8***
B.4.k.4r.2	Dose (unit)	UCUM	***2.16.840.1.113883.6.8***
B.4.k.5.2	Cumulative Dose to First Reaction (unit)	UCUM	***2.16.840.1.113883.6.8***
B.4.k.9.i.3.1b	Time Interval between Beginning of Drug Administration and Start of Reaction / Event (unit)	UCUM	***2.16.840.1.113883.6.8***
B.4.k.9.i.3.2b	Time Interval between Last Dose of Drug and Start of Reaction / Event (unit)	UCUM	***2.16.840.1.113883.6.8***

There is one exception not included in the table above. The element A.1.0.1, Sender's (case) Safety Report Unique Identifier and A.1.10.1, Worldwide Unique Case Identification Number, are not listed as they are not directly coded using ISO 3166 Part 1. It is in fact a constructed identifier unique to the message. However it does reference the ISO Country Code system as the identifier is constructed by the sender and includes a two-letter country code.

3.2.3.1 Use of ISO 3166 Country Codes

Multiple fields within the ICSR identify countries, either in relation to the drug, the event, the sender or the reporter. Country codes were first published by ISO in 1997 (ISO 3166-1). ISO defined three sets of country codes as follows:

- ISO 3166-1 alpha-2: a two-letter country code (used most prominently for the Internet)
- ISO 3166-1 alpha-3: a three-letter country code
- ISO 3166-1 numeric: a three-digit country code

Using France as an example:

- {iso(1) standard(0) country-codes(3166) part1(1) edition2(2) numeric(1) 250}
- {iso(1) standard(0) country-codes(3166) part1(1) edition2(2) alpha-2(2) fra (250)}
- {iso(1) standard(0) country-codes(3166) part1(1) edition2(2) alpha-3(3) fra (250)}
- Using dot notation, these three examples would be denoted respectively as:
  - 1.0.3166.1.2.1.250
  - 1.0.3166.1.2.2.250

- 1.0.3166.1.2.3.250

E2B(R3) use the first set listed above, ISO 3166-1 alpha-2, in the data elements which capture country codes.

3.3 ICH E2B(R3) SPECIFICATIONS FOR THE TRANSMISSION OF ICSRS

The E2B(R3) requirements specify a detailed breakdown of the data elements for the 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 might exist at the regional level

	Information boxes like this one have been inserted throughout this Implementation Guide to emphasise key points and concepts. Pay particular attention to the information in these boxes.

	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 fulfill 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, field B.1.1 can still be populated and user guidance for this field 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 most instances, a substantial 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 data elements. However, in certain cases it is important to understand if a field 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.

However, in addition to the minimum information required for an ICSR report (see 3.4.1 above) certain specific administrative information should be provided to properly process the report:

- The sender's (case) safety report unique identifier (A.1.0.1);
- The type of report (A.1.4);
- The date of the most recent information (A.1.7);
- Whether this case fulfils the local criteria for an expedited report (A.1.9);
- The worldwide unique case identification number (A.1.10.1);
- The country of the primary source (A.2.r.1.3) or, if not available to the sender, the country where the reaction/event occurred (B.2.i.8).
- The sender identifier (A.3.2);
- When type of report="Study," the study type in which the reaction(s) / event(s) were observed (A.5.4)

3.3.3 General Principles

While complete information is desirable, a minimum set of information is 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.

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), MedDRA (medical history, indication, and reaction / event), UCUM [13](units of measurement), and ICH M5 (see 3.3.1 for details) . Please refer to each standard for further information.

Although the exchange of other unstructured data, such as published articles, full clinical records and/or images is outside the scope of this guideline, the technical solution to transmit attachments is provided in Section 3.5.

3.3.4 Retransmission of cases

Based on the reporting obligations and business arrangements in pharmacovigilance, ICSRs are re-transmitted between different senders and receivers. During this re-transmission process, medical information on the case should not be omitted or changed if no new information on the case is available to the re-transmitting sender.

There are certain exceptions and the following fields might be updated:

- Sender's (case) safety report unique identifier - A.1.0.1;
- Date of creation - A.1.3;
- Date report was first received from source - A.1.6, for initial reports;
- Date of the most recent information for this case - A.1.7;
- Are Additional Documents Available? - A.1.8.1;
- Does this case fulfill the local criteria for an expedited report? - A.1.9;
- Information on sender of case safety report - A.3;
- Seriousness criteria at event level - B.2.i.2.2;

[13] UCUM (Unified code for Units of Measure) URL: http://unitofmeasure.org/

- More Information Available - B.3.r.4;
- Relatedness of drug to reaction(s)/event(s) - B.4.k.9.r.2, repeat B.4.k.9.r.2.r.1 through B.4.k.9.r.2.r.3 as necessary;
- Sender's diagnosis/syndrome and/or reclassification of reaction/event - B.5.3;
- Sender's comments - B.5.4; or
- English translation of the free text fields in the ICSRs.

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

When there are multiple ICSRs there could be situations in which more than one ICSR shares the Worldwide Unique Case Identification Number (A.1.10.1) due to sequential updates to information in the case, or more than one ICSR shares the same Date of Most Recent Information (A.1.7). For these situations A.1.3 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
  - A.1 - Identification of the case safety report;
  - A.2 - Primary source(s) of information;
  - A.3 - Information on sender of case safety report;
  - A.4 - Literature reference(s); and
  - A.5 - Study identification.
- Section B
  - B.1 - Patient characteristics;
  - B.2 - Reaction(s)/event(s);
  - B.3 - Results of tests and procedures relevant to the investigation of the patient;
  - B.4 - Drug(s) information; and
  - B.5 - Narrative case summary and further information.

In addition to the letters “i” and “k” indicating iterations of the event (B.2.i) or the drug (B.4.k), the letter “r” was used to indicate that the field or the section is repeatable.

It is recognised that some data element numbers of this guideline do not match those of E2B (R2) guideline and some numbers are missing. The latter will be fixed in the final document to be released as ICH Step 4 in the Implementation Guide.

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; however, dates and times can be represented with a greater or lesser degree of precision. This date format makes it possible to provide data to the appropriate precision.

Refer to Appendix II in this Implementation Guide and/or the HL7 Version 3 data type specifications for more detail

For E2B(R3), minimum requirements for the level of date precision for each date field are specified in Section 3.4.

	A single format (CCYYMMDDHHMMSS.UUUU[+|-ZZzz]) is used to represent dates and times throughout this Implementation Guide. This format allows for information down to seconds to be exchanged; however, dates and times can be represented with varying degree of precision, e.g. to the year, to the month, to the day, to the hour, to the minute, to the second. Minimum requirements for the level of precision for each date field are specified in Section 3.4. Unless otherwise specified for the date field, the default level of precision is to the day (CCYYMMDD). In those cases where this level of precision is not known, as much information as available should be provided. Refer to Appendix II in this Implementation Guide and/or the HL7 Version 3 data type specifications for more detail on the time and date format.

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- All free text fields (with the exception of the B.2.i.0.a Reaction by Primary Source in Native Language and B.5.5 Narrative in Native Language) are to be provided in English for international transmission.
- Metric units only should be used
- For ICSR reporting, MedDRA is commonly used in EU, US, and Japan as well as other countries/regions that are ICH Observers (e.g. Canada and Switzerland). The MedDRA LLT most closely corresponding to the event/reaction as reported by the primary source is recommended for all medical terminology. When there is not an exact match to MedDRA Lowest Level Term (LLT), the LLT most closely corresponding to the term as reported by the primary source should be given. The selection of MedDRA terms should be made according to the most current *MedDRA™ Term Selection: Points to Consider* document (available on the ICH website). Furthermore, requests can be made to the MSSO – *MedDRA maintenance organisation* to add the missing terminology. In certain instances, provisions have been made for transmission of free text items, including a full text case summary narrative. Text fields 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 advice on describing syndromes, please refer to the latest edition of the ICH document "MedDRA Term Selection: Points to Consider" as published at http://www.ich.org. At the time of this writing, advice is provided in sections on "Diagnosis reported with signs and symptoms" and "Provisional diagnoses."

	For all data elements that reflect a MedDRA coded value, the same MedDRA version should be used for all data fields in a single ICSR. However, 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 fields that require controlled vocabulary, such as A.1.1 Identification of the Country - 2A, to accommodate the ISO3166 code. The string fields 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 field 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/. For example, when the XML special characters >, < and & occur in text, fields they should always be replaced by > < and & respectively; or
  - N=numeric: String field 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 will be represented by:
    - "***false***" which can also equate to "no";
    - "***true***" which can also equate to "yes";
    - "null flavor" which can have different meanings in different scenarios. HL7 refers to these as "null flavors." (See below)

  There is one exception to this rule for the purposes of this Implementation Guide in data element "B.4.k.2.0 Investigational Product Status" where "true"=blinded.

- Particular 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 (in our case essentially a blank field). 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. Not all nullFlavors are valid for all data types (for example PINF and NINF).

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.
OTH	Other	The actual value is not an element in the value domain of a variable. (e.g. concept not provided by required code system).

Code	Name	Definition
UNK	Unknown	A proper value is applicable, but not known.
NA	Not Applicable	No proper value is applicable in this context (e.g. last menstrual period for a male).
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.
NAV	Temporarily Unavailable	Information is not available at this time but it is expected that it will be available later.
TRC	Trace	The content is greater than zero, but too small to be quantified
NP	Not Present	Value is not present in a message. This is only defined in messages, never in application data! All values not present in the message should be replaced by the applicable default, or no-information (NI) as the default of all defaults.

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The concept of a "nullFlavor" might be new to implementors who were not previously familiar with HL7 messaging. The following sample demonstrates how nullFlavor can be used to code values for ICH:

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

```
<component typeCode="COMP">
        <adverseEventAssessment classCode="INVSTG" moodCode="EVN">
          <subject1 typeCode="SBJ">
            <primaryRole classCode="INVSBJ">
              <player1 classCode="PSN" determinerCode="INSTANCE">
                <name nullFlavor="MSK"/>
                <!-- B.1.1:  Patient (name or initials) -->
                <administrativeGenderCode code="B.1.5" codeSystem="TBD"/>
                <!-- B.1.5 Sex [1] Male [2]Femail -->
                <birthTime value="20090101"/>
                <!-- B.1.2.1: Date of Birth -->
                <deceasedTime value="20090101"/>
                <!-- B.1.9.1: Date of Death -->
```

Example2. "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"/>
            <!-- B.1.10.1:  Parent Indentification -->
            <administrativeGenderCode code="B.1.10.6" codeSystem="TBD"/>
            <!-- B.1.10.6: Sex of Parent [1]Male [2]Female-->
            <birthTime value="20090101"/>
            <!-- B.1.10.2.1: Date of Birth of Parent -->
          </associatedPerson>
```

3.3.7 Details of ICH E2B(R3) Data Elements

All of the E2B(R3) data elements are listed in each table in section 3.4 to provide respective specifications determined by E2B(R3). The tables should be used to verify the accuracy and compliance of data entered when preparing an ICSR XML data file. The E2B(R3) data element table contains:

- The data element number;
  - For the purpose of this implementation guide, data elements for the Acknowledgement message will be preceded by the letters ACK (e.g. ACK.M.1). For example;
    - Data element M.1.4 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.
- A title;
- A description documented as "User Guidance" that provides information to ICSR users so they can populate safety information correctly into E2B (R3) data fields;
- "Conformance" indicates if the data element is required or optional as determined by the ICSR user and by the schema. Technically required data elements must be filled in or errors will result when parsing the message. A list of required elements is provided in Section 4.1;
- The "Data Type" and field length - each data element will use a number to denote the width of a field followed by A for alpha, N for numeric, or AN for alphanumeric;
- An Object Identifier ("OID") if appropriate;
- "Value Allowed" which indicates possible values for this field; and
- "Business Rule(s)" that might pertain to the data element.

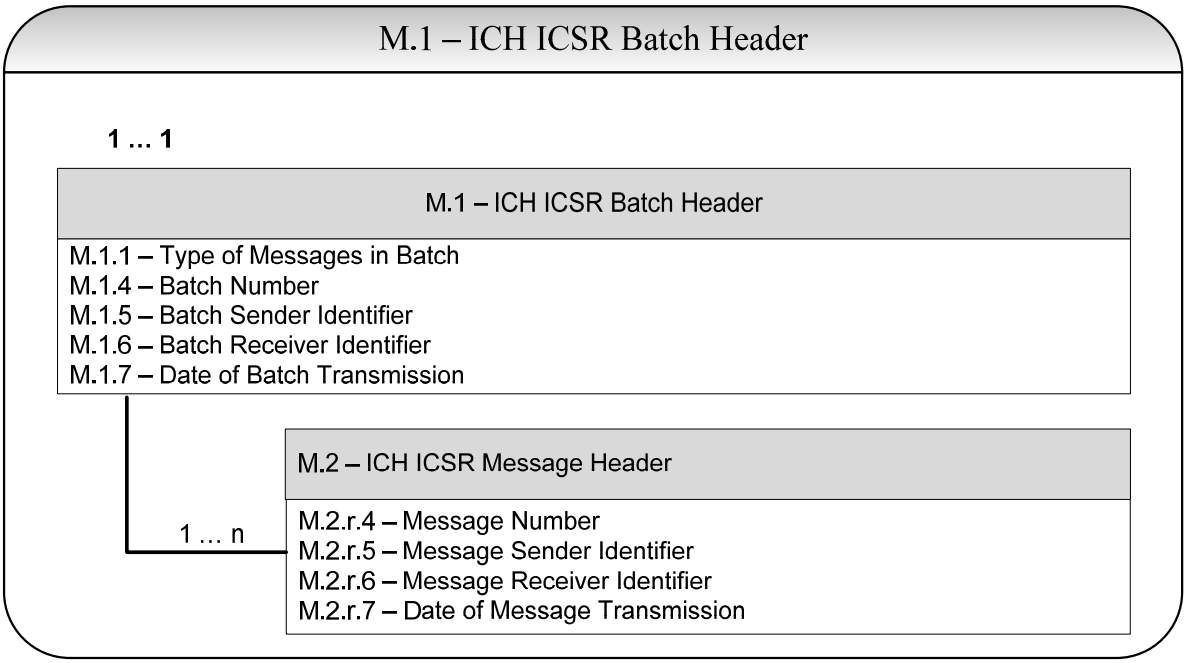
The ICH E2B(R3) data element tables in section 3.3.7 should be used to verify the accuracy and compliance of data entered when preparing an ICSR XML data file.

To help manage, route, identify, and track ICH ICSR messages in the three ICH regions, and to help automate electronic submissions of ICSRs, the following elements constitute the message header section. The reference instance of these elements is presented in Appendix V – Examples and Sample messages.

3.4 ICH E2B(R3) DATA ELEMENTS

M.1 ICH ICSR Transmission Identification (Batch Wrapper)

This section assumes the establishment of an EDI trading partnership agreement that will help define the message number, sender ID, receiver ID, and message date.



M.1.1 Type of Messages in Batch

User Guidance	The message type contains information on the type of information being transmitted. One ICH ICSR batch can contain one or more safety reports (ICSRs). However, one ICH ICSR batch should contain only one type of safety report. When creating an ICH ICSR message, the value of this field should be populated with one of the following five values for Message Type:
Conformance	Required
Data Type	11A
OID	ich-type-of-message-in-batch-oid
Value Allowed	Common ICH code: ichicsr Regional codes: ichicsr = "ICSRs expedited post-marketing report" cticsr = "ICSRs expedited report from interventional clinical trials" psuricsr = "ICSRs non-expedited post-marketing report" backlogicsr = "ICSR not reported in E2B format in the past" dsuricsr = "ICSRs non-expedited report during interventional clinical trials"
Business Rule(s)	
	One ICH ICSR message can contain one or more ICSRs. However, one ICH ICSR message should contain only one type of ICSR.

Note: There is a known gap between the numbers of the previous and next data elements.

1098 **M.1.4 Batch Number**

User Guidance	Sender defined message number (Wrapper number unique to the sender): The message number is a unique tracking number assigned to a specific ICH ICSR batch file transmitted by the sender. This batch number is unique to the sender.
Conformance	Required
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	The following notation will be used to represent M.1.4: <id extension=”batch number" root="sender-identifier-value"/> The root will be the content of the element M.1.5, the actual identifier (name) of the sender as agreed with the trading partner.

1099 **M.1.5 Batch Sender Identifier**

User Guidance	This field identifies the sender of the ICSR reports (creator of ICH ICSR batch file), e.g. company name or regulatory authority
Conformance	Required
Data Type	60AN
OID	ich-batch-sender-identifier-oid
Value Allowed	Free text
Business Rule(s)	
	The following notation will be used to represent M.1.5: <id extension="sender identifier" root="ich-batch-sender-identifier-oid"/> The sender identifier should be agreed between trading partners.

1100 **M.1.6 Batch Receiver Identifier**

User Guidance	This field identifies the intended recipient of the transmission of ICSR batch file
Conformance	Required
Data Type	60AN
OID	ich-batch-receiver-identifier-oid
Value Allowed	Free text
Business Rule(s)	
	The following notation will be used to represent M.1.6: <id extension="receiver identifier" root="ich-batch-receiver-identifier-oid"/> The receiver identifier should be agreed between trading partners.

1101 **M.1.7 Date of Batch Transmission**

User Guidance	The batch date is the date on which the ICH ICSR batch file was transmitted.
Conformance	Required

Data Type	Date
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"). The date specified cannot refer to a future date. The date should be local time at point of transmission of ICSR message.

1102 **M.2 ICH ICSR Message Header (Message Wrapper)**

1103 **M.2.r.4 Message Identifier**

User Guidance	Sender defined message identifer (Wrapper identifier unique to the sender): The message identifier is a unique tracking identifier assigned to a specific ICH ICSR message transmitted by the sender. This message identifier is unique to the sender.
Conformance	Required
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	The value is the same as A.1.0.1. Therefore the notation would be: <id extension="message identifier" root="ich-senders-safety-report-identifier-oid"/>

1104 **M.2.r.5 Message Sender Identifier**

User Guidance	This field identifies the sender of the ICSR reports (creator of ICH ICSR message), e.g. company name or regulatory authority
Conformance	Required
Data Type	60AN
OID	ich-message-sender-identifier-oid
Value Allowed	Free text
Business Rule(s)	
	The following notation will be used to represent M.2.r.5: <id extension="message sender identifier" root="ich-message-sender-identifier-oid"/> The sender identifier should be agreed between trading partners.

1105 **M.2.r.6 Message Receiver Identifier**

User Guidance	This field identifies the intended recipient of the transmission of ICSR message.
Conformance	Required
Data Type	60AN
OID	ich-message-receiver-identifier-oid
Value Allowed	Free text
Business Rule(s)	
	The following notation will be used to represent M.2.r.6: <id extension="message receiver identifier" root="ich-message-receiver-identifier-oid"/> The receiver identifier should be agreed between trading partners.

1106 **M.2.r.7 Date of Message Creation**

User Guidance	The message date is the date on which the ICH ICSR message was created.
Conformance	Required
Data Type	Date
OID	None
Value Allowed	See Appendix II for further information.
Business Rule(s)	
	The value must be the same as A.1.3. The full precision of date and time must be recorded down to the second (i.e. CCYYMMDDhhmmss). The date specified cannot refer to a future date. The date should be local time at point of transmission of ICSR message.

1107

ICH ICSR Concept Area Diagram

This diagram illustrates relationships between groups of ICH ICSR elements, and the organization of those elements into repeatable structures.

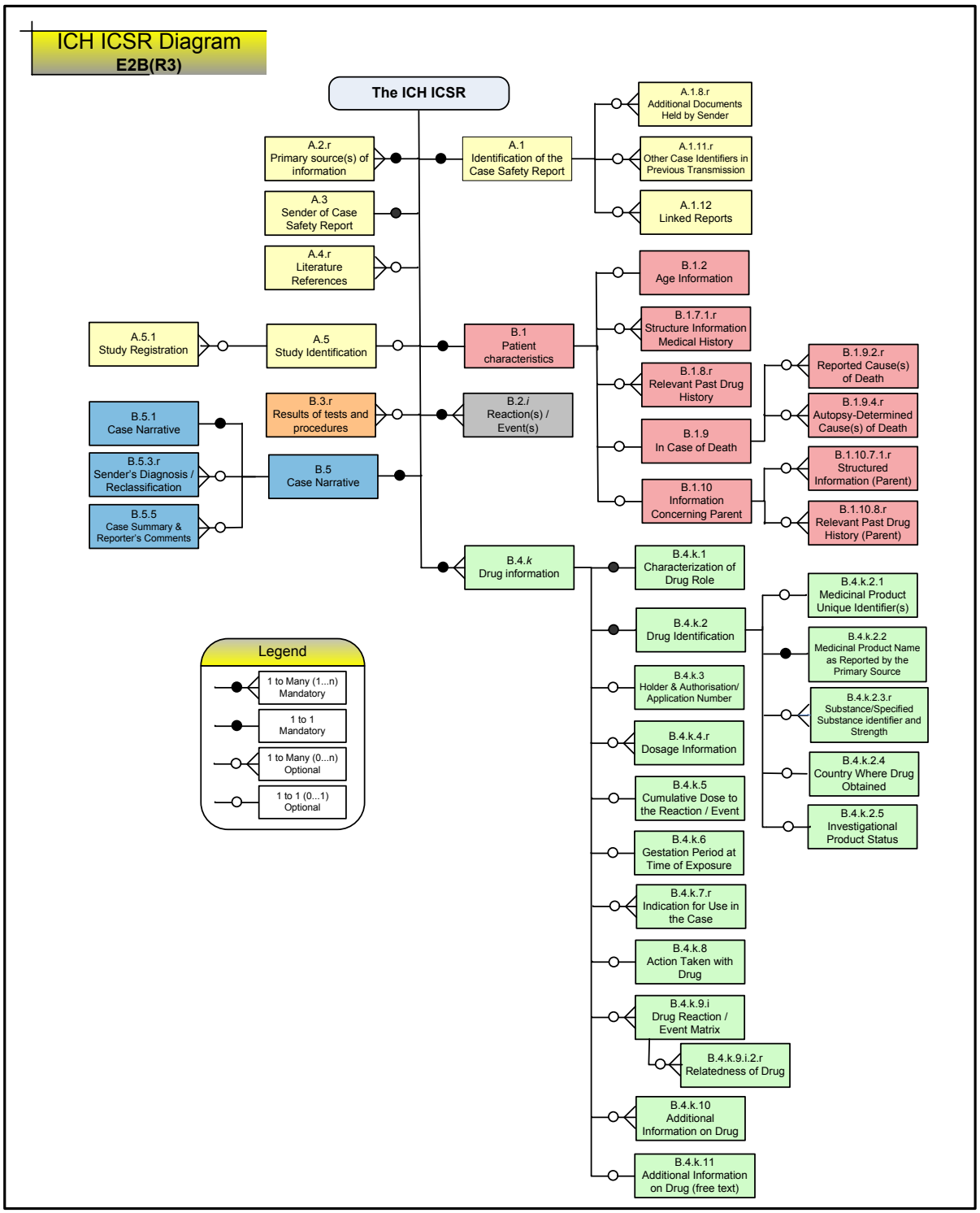
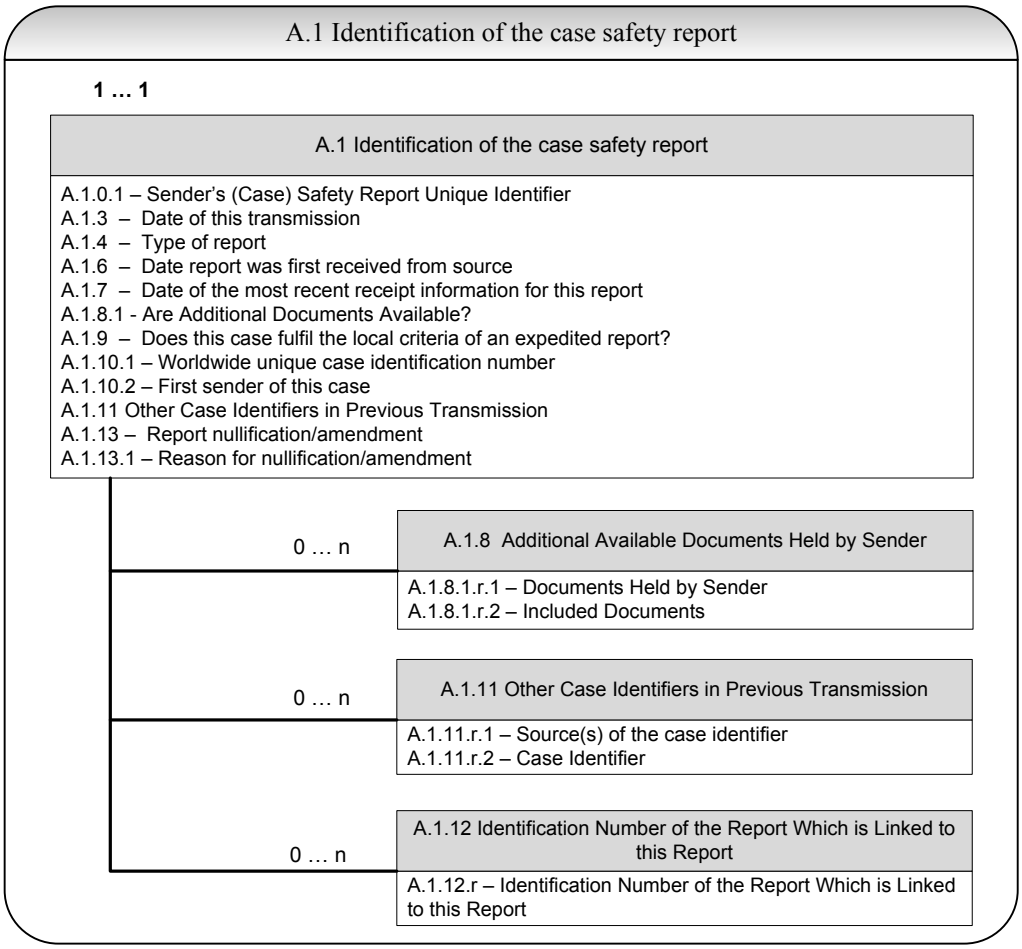


Figure 2: Diagram of ICH ICSR Elements: Concept Areas

A.1 IDENTIFICATION OF THE CASE SAFETY REPORT

This section corresponds to the root of the case safety report, which can repeat within a given Message file. It should be noted that an ICSR Message file must contain at least one case safety report, and therefore, there must be at least one "subject" element within "controlActProcess".



A.1.0.1 Sender's (case) Safety Report Unique Identifier

User Guidance	This identifier should remain constant in subsequent transmissions of the case by the *same* sender. Retransmitters should replace this value with their own unique identifier. The value should be a concatenation of "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 (A.2.r.1.5). In exceptional circumstances where the country of primary source is unknown, the country where the reaction occurred (B.2.i.8) should be used to indicate the country code. The company or regulator name is an internationally unique abbreviation or code for the sender's organisation. The report number is the organisation's international case number. Each component is separated from the other by a hyphen. For example, a report transmitted by a company to a regulatory authority concerning a case from France would populate A.1.0.1 with "FR-companyname-12345" where 12345 is a company's unique case report number. In the case of an organisational change, (e.g. a merger between companies or a name change), follow-up reports should be identified in A.1.0.1 by the identifier of the newly named organisation. However, the worldwide unique case identifier number (A.1.10.1) used in previous transmissions of the case should remain the same (see the user guidance for A.1.10).
Conformance	Required
Data Type	100AN
OID	ich-senders-safety-report-identifier-oid
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. An ISO country code does not exist for the "EU". In this case, "EU" will be accepted as the country code. Both the Sender's (case) Safety Report Unique Identifier (A.1.0.1) and the Worldwide Unique Case Identification (A.1.10.1) data elements are mapped to the repeatable XML attribute <id> in the "investigationEvent" entity in the HL7 ICSR model. (See the Reference Instance) The HL7 model uses two values - "ich-senders-safety-report-identifier-oid" and "ich-worldwide-case-identifier-oid" in the root portion of the investigationEvent.id to distinguish A.1.0.1 and A.1.10.1 The following notation will be used to represent A.1.0.1: <id extension="country code-company name-sequence no" root="ich-senders-safety-report-identifier-oid"/> And the following for A.1.10.1: <id extension="country code-company name-sequence no" root="ich-worldwide-case-identifier-oid"/>

Note: There is a known gap between the numbers of the previous and next data elements.

A.1.3 Date of Creation

User Guidance	By having the function of a timestamp, this field also represents the equivalent of a version number for the ICSR. Every safety report (ICSR) and every iteration of an ICSR in a safety message must have a different timestamp. The most recent version of an ICSR will have the most recent date timestamp. Previous versions of an ICSR will have older date timestamps.
Conformance	Required
Data Type	Date
OID	None
Value Allowed	See Appendix II for further information.
Business Rule(s)	
	The date must be specified to the second(i.e. "CCYYMMDDhhmmss"). The date specified cannot refer to a future date.

1129 **A.1.4 Type of Report**

User Guidance	This field is intended to capture the type of report, and not the source. For cases from literature, a separate element for the designation of the source is covered in item A.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 A.5.4 (see the User Guidance for the field A.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	ich-type-of-report-oid
Value Allowed	1=Spontaneous report 2=Report from study 3=Other 4=Not available to sender (unknown)
Business Rule(s)	

1130

1131 **Note**: **There is a known gap between the numbers of the previous and next data elements.**

1132 **A.1.6 Date Report Was First Received from Source**

User Guidance	For organisations transmitting an initial case, this should be the date the information was received from the primary source 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, A.1.6 should be the date the retransmitter first received the information.
Conformance	Required
Data Type	Date
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.

A.1.7 Date of Most Recent Information for this report

User Guidance	This date should be changed each time follow-up information is received by the sender. However if the case is amended for any other reason (e.g. internal review by the sender or expert opinion) this date should not be changed but the field A.1.13 should be populated with the value "amendment" indicating that the case was amended by the sender. (See the User Guidance for field A.1.13) Because reports can be sent at different times to multiple receivers, the initial/follow-up status is dependent upon the receiver. For this reason an item to capture follow-up status is not included. However, the date of receipt of the most recent information taken together with the "sender identifier" (A.3.2) and "sender's (case) report unique identifier" (A.1.0.1) provide a mechanism for each receiver to identify whether the report being transmitted is an initial or follow-up report. For this reason these items are required for each transmission.
Conformance	Required
Data Type	Date
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 A.1.7 should not be changed in an amended or nullified report if no new information on the case has been *received*.

A.1.8 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. It is recognised that these documents might not be obtainable in many instances. Literature reference documents when available, are described in section A.4, and are not duplicated in A.1.8.

1141 **A.1.8.1 Are Additional Documents Available?**

User Guidance	When retransmitting information, the sender (retransmitter) indicates 'true' 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

1142 **A.1.8.1.r.1 Documents Held by Sender (repeat as necessary)**

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. It is recognised that these documents might not be obtainable in many instances.
Conformance	Optional, but required if A.1.8.1 is 'true'
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rule(s)	

1143 **A.1.8.1.r.2 Included documents**

User Guidance	This element contains the actual content of A.1.8.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 Value allowed will be defined by region.

1144 **A.1.9 Does this Case Fulfill the Local Criteria for an Expedited Report?**

User Guidance	The definition of expedited is dependent upon the sender's local regulatory requirements. This item should be used by the sender to indicate whether the case fulfils the local expedited requirements. When the countries of origin and destination of the transmission differ, the receiver should be aware that the 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)	
	"Null Flavor" is only allowed when sender convert a case report from R2 to R3 where A.1.9 was not populated, in other cases, false or true should be used.

A.1.10 Worldwide Unique Case Identification

Both A.1.10.1 and A.1.10.2 should always be populated and should never be changed in any subsequent re-transmission.

When a sender has not previously received a valid electronic ICSR, the identifiers (content and format) in A.1.0.1 and A.1.10.1 are identical.

Retransmitters should use their own sender's (case) safety report unique identifier in field A.1.0.1, but not change the values in fields A.1.10.1 and A.1.10.2.

When a regulator is the initial sender, A.1.10.2 should be flagged as 1=Regulator.

When an entity other than a regulator is the initial sender, A.1.10.2 should be flagged as 2=Other.

A.1.10.1 Worldwide Unique Case Identification number

User Guidance	Original transmitters (initial senders) should use the same identifier used in A.1.0.1. Retransmitters MUST NOT change A.1.10.1 and A.1.10.2.
Conformance	Required
Data Type	100AN
OID	ich-worldwide-case-identifier-oid
Value Allowed	Free text (see A.1.0.1 *User Guidance* for format)
Business Rule(s)	
	Both the Sender's (case) Safety Report Unique Identifier (A.1.0.1) and the Worldwide Unique Case Identification (A.1.10) data elements are mapped to the repeatable XML attribute <id> in the "investigationEvent" entity in the HL7 ICSR model. (See the Reference Instance) The HL7 model uses two values - " ich-senders-safety-report-identifier-oid " and "ich-worldwide-case-identifier-oid " in the root portion of the investigationEvent.id to distinguish A.1.0.1 and A.1.10. The following notation will be used to represent A.1.0.1: <id extension="country code-company name-sequence no" root=" ich-senders-safety-report-identifier-oid "/> And the following for A.1.10: <id extension="country code-company name-sequence no" root=" ich-worldwide-case-identifier-oid "/> The attribute <id> can repeat in the message, but there must be a single instance of the <id> attribute with the root value of "worldWideCaseIdOid" for a particular case safety report.

	Retransmitters should use their own sender's (case) safety report unique identifier (A.1.0.1), but must not change A.1.10.1 and A.1.10.2.

1161 **A.1.10.2 First Sender of this Case**

User Guidance	A.1.10.2 should be used to document the identity of the original sender of the case. When a regulator is the initial sender, A.1.10.2 should be flagged as "Regulator." When an entity other than a regulator is the initial sender, A.1.10.2 should be flagged as "Other."
Conformance	Required
Data Type	1N
OID	ich-first-sender-of-this-case-oid
Value Allowed	1=Regulator 2=Other
Business Rule(s)	

1162

1163 **A.1.11 Other Case Identifiers in Previous Transmissions**

User Guidance	This item should be completed only if the answer is "true". 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 field A.1.11.r.2 and the organisations name should be captured in field A.1.11.r.1.
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	
	False is not an option as value allowed. This field should either be true or "null flavor" .

1164 **A.1.11.r.1 Source(s) of the Case Identifier (repeat as necessary)**

User Guidance	This repeatable item should be used in conjunction with A.1.11.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 A.1.11.r.1 (and A.1.11.r.2) should be present. In addition the identifier of the previous sender (A.1.0.1) should be included here by the retransmitter.
Conformance	Required if A.1.11='true'
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	

1165 **A.1.11.r.2 Case Identifier(s)**

User Guidance	This repeatable item should be used in conjunction with A.1.11.r.1 to provide all other case identifiers electronically transmitted, perhaps by multiple other senders (transmitters and retransmitters). If the case has been received from another sender all other case identifiers included in A.1.11.r.1 (and A.1.11.r.2) should be present. In addition, the case identifier provided by the previous sender (A.1.0.1) should be included here by the retransmitter.
Conformance	Required if A.1.11= 'true'
Data Type	100AN
OID	None
Value Allowed	Free text (see A.1.0.1 *User Guidance* for format)
Business Rule(s)	

A.1.12.r Identification Number of the Report Which Is Linked to this Report (repeat as necessary)

User Guidance	This section should be used to identify reports or cases that warrant being evaluated together. 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, and several similar reports from same reporter (cluster). The reason for the linkage between ICSRs should be provided in B.5.4. For example, if a sender wishes to reference an ICSR A in ICSR B then the sender populates field A.1.12.r, in both reports to cross-reference each other. In this example for ICSR A the field A.1.12.r should capture the value of the field A.1.10.1of ICSR B, and in ICSR B the field A.1.12.r should capture the value of field A.1.10.1 of ICSR A. This field should be populated in both ICSRs when possible, although there might be cases in which one case does not have a conformant E2B Worldwide Unique Case Identification Number (e.g. legacy paper report).
Conformance	Optional
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	

A.1.13 Report Nullification / Amendment

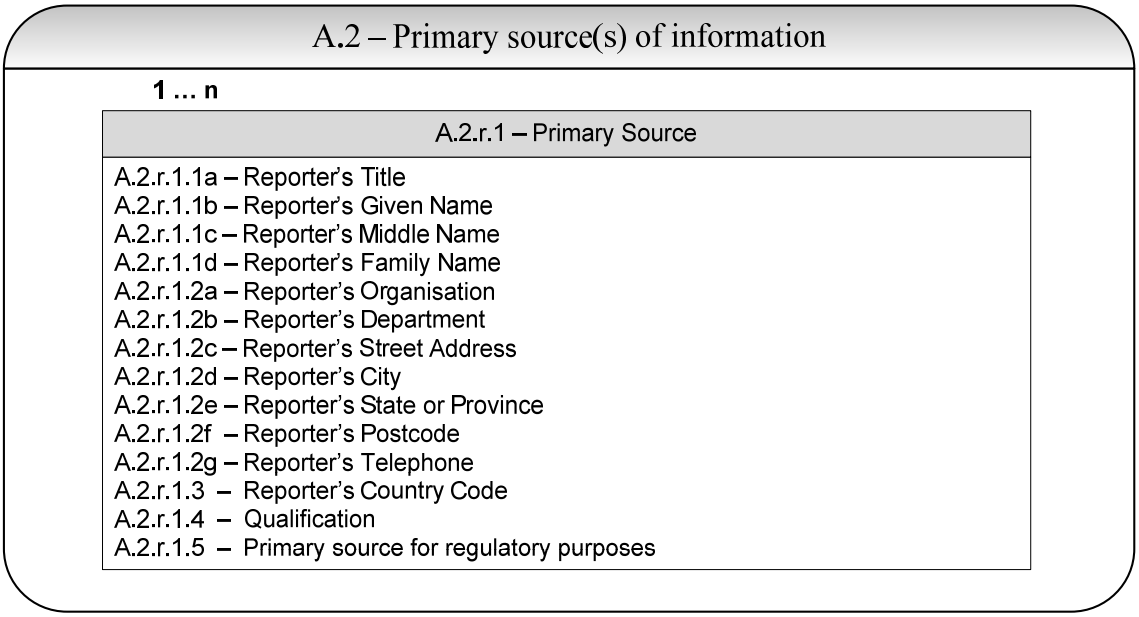
User Guidance	This item should be used to indicate that a previously transmitted ICSR is either considered completely void (nullified), (for example when the whole case was found to be erroneous), or amended, (for example when after an internal review or according to an expert opinion some items have been modified such as adverse event/reaction terms, seriousness, seriousness criteria or causality assessment). It is important to use the same Worldwide Unique Identifier previously submitted in A.1.10.1. The date originally reported in A.1.7 should not be changed in an amended or nullified report if no new information on the case has been received
Conformance	Optional
Data Type	1N
OID	ich-report-nullification-amendment-oid
Value Allowed	1=Nullification 2=Amendment
Business Rule(s)	

A.1.13.1 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 event terms, seriousness, seriousness criteria or causality assessment). It is important to use the same Worldwide Unique Identifier previously submitted in A.1.10.1. The date originally reported in A.1.7 should not be changed in an amended report.
Conformance	Optional, but required when A.1.13 is populated.
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rule(s)	

A.2 PRIMARY SOURCE(S) OF INFORMATION

The primary source of the information is the person who initially reports the facts. In case of multiple sources, the primary source for regulatory purposes is the person who first reports the facts to the sender and this should be indicated in A.2.r.1.5. The primary source should be distinguished from senders (secondary sources), who subsequently transmit the case report, e.g. industry to a regulatory authority.



1181 **A.2.r.1 Primary Source(s) (repeat as necessary)**

	Reporter identifiers	Reporter's address and telephone	Country	Qualification	Primary source for regulatory purposes
Data Element	A.2.r.1.1a A.2.r.1.1b A.2.r.1.1c A.2.r.1.1d	A.2.r.1.2a A.2.r.1.2b A.2.r.1.2c A.2.r.1.2d A.2.r.1.2e A.2.r.1.2f A.2.r.1.2g	A.2.r.1.3	A.2.r.1.4	A.2.r.1.5
User Guidance	The identification of the reporter (primary source) could be prohibited by certain national or international confidentiality requirements. The information should be provided when it is in conformance with confidentiality requirements. However, at least one subsection should be completed to ensure that there is an identifiable reporter. If only the name of the reporter is known and confidentiality requirements prohibit transmission of the reporter's full name, initials or values indicating the data has been masked (nullFlavor) can be used to populate A.2.r.1.1b, A.2.r.1.1c, and/or A.2.r.1.1d, 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 fields should be left blank with nullFlavor = MSK. Please see Section 3.4.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.				

1182 **A.2.r.1.1a Reporter's Title**

User Guidance	The reporter's title should be used.
Conformance	Optional
Data Type	50AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK, UNK

Business Rule(s)	
	See the detailed user guidance and business rule(s) above under A.2.r.1.

1183 **A.2.r.1.1b Reporter's Given Name**

User Guidance	The reporter's given name should be used.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Each ICSR shall identify the primary reporter's given name for regulatory purposes in conformance with regional confidentiality requirements. See the detailed user guidance and business rule(s) above under A.2.r.1.

1184 **A.2.r.1.1c Reporter's Middle Name**

User Guidance	The reporter's middle name should be used.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Each ICSR shall identify the primary reporter's middle name for regulatory purposes in conformance with regional confidentiality requirements. See the detailed user guidance and business rule(s) above under A.2.r.1.

1185 **A.2.r.1.1d Reporter's Family Name**

User Guidance	The reporter's family name should be used.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Each ICSR shall identify the primary reporter's family name for regulatory purposes in conformance with regional confidentiality requirements. See the detailed user guidance and business rule(s) above under A.2.r.1.

1186 **A.2.r.1.2a Reporter's Organisation**

User Guidance	The reporter's contact information should be used.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Each ICSR shall identify the primary reporter's organisation for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.2.r.1.

1187 **A.2.r.1.2b Reporter's Department**

User Guidance	The reporter's contact information should be used.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Each ICSR shall identify the primary reporter's department for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.2.r.1.

1188 **A.2.r.1.2c Reporter's Street**

User Guidance	The reporter's contact information should be used.
Conformance	Optional
Data Type	100AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Each ICSR shall identify the primary reporter's street for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.2.r.1.

1189 **A.2.r.1.2d Reporter's City**

User Guidance	The reporter's contact information should be used.
Conformance	Optional
Data Type	35AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Each ICSR shall identify the primary reporter's city for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.2.r.1.

1190 **A.2.r.1.2e Reporter's State or Province**

User Guidance	The reporter's contact information should be used.
Conformance	Optional
Data Type	40AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Each ICSR shall identify the primary reporter's state or province for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.2.r.1.

1191 **A.2.r.1.2f Reporter's Postcode**

User Guidance	The reporter's contact information should be used.
Conformance	Optional
Data Type	15AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Each ICSR shall identify the primary reporter's postcode for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.2.r.1.

1192 **A.2.r.1.2g Reporter's Telephone**

User Guidance	Reporter's telephone including the country code and any extension. The reporter's contact information should be used. Numbers should be entered in a fashion that allows for international dialling and not include any domestic trunk prefix, e.g. for those countries which only use the leading zero domestically this should be stripped. For example, local 0xx-yyy-zzzz becomes international +cc-xx-yyy-zzzz. When entering a phone number, do not include domestic international dialling prefixes (00 in Europe, 011 in US, 010 in Japan). Begin with the International Telecommunications Union plus sign (+) notation for country code. Additional visual separators for human readability are not required. If used these characters should be limited to parenthesis '( )', dashes '-' or decimal points.
Conformance	Optional
Data Type	33AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	Each ICSR shall identify the primary reporter's telephone for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.2.r.1.

1193 **A.2.r.1.3 Reporter's Country Code**

User Guidance	Use the two letter ISO 3166 Part 1 code (ISO 3166-1 alpha-2) to represent the names of the country.
Conformance	Optional, but required if A.2.r.1.5 is populated = 1
Data Type	2A
OID	1.0.3166.1.2.2
Value Allowed	ISO 3166-1 alpha-numeric nullFlavor: MSK, ASKU, NASK, UNK
Business Rule(s)	
	A two character country code will be used in all instances. An ISO country code does not exist for the "EU". In this case, "EU" will be accepted as the country code.

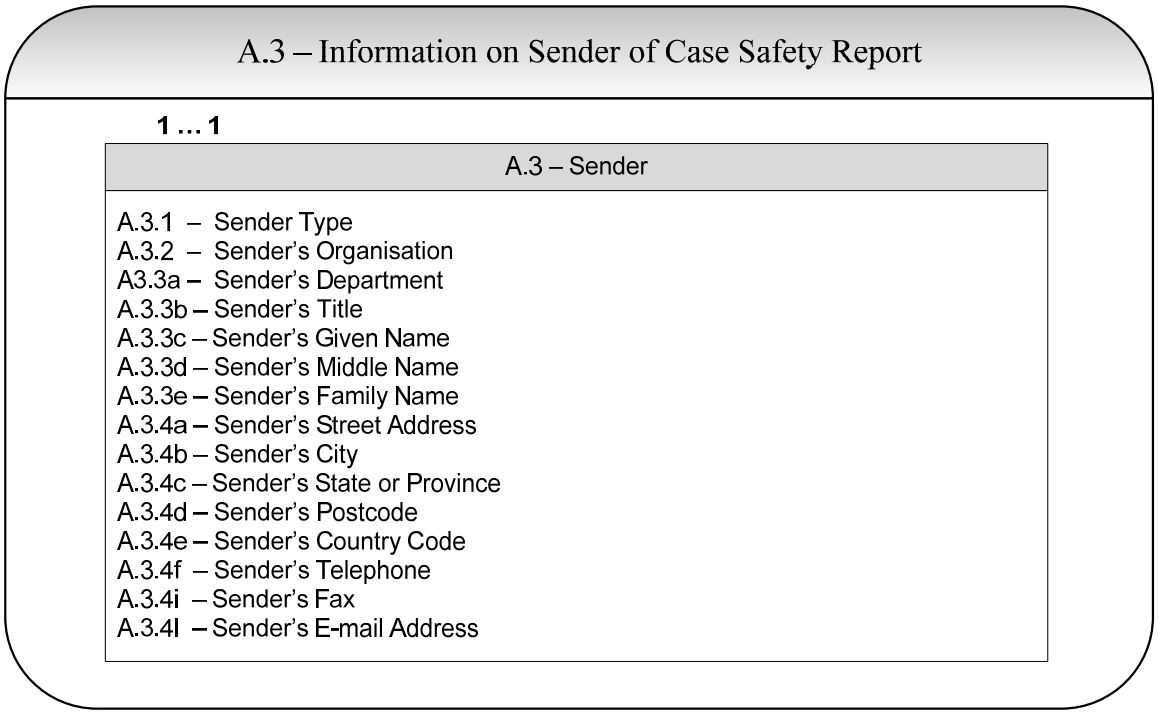
1194 **A.2.r.1.4 Qualification**

User Guidance	The reporter qualification does not preclude the reportability of the case; reportability depends on local regulations.
Conformance	Required if A.2.r.1.5=1 (Yes)
Data Type	1N
OID	ich-qualification-oid
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 field 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.

1195 **A.2.r.1.5 Primary source for regulatory purposes**

User Guidance	For regulatory purposes, in case of multiple sources, the primary source will identify world wide case unique identifier. This source should identify where the case occurred. This determines where the case will be reported as a domestic case and where the case will be reported as a foreign case using the country of the reporter.
Conformance	Optional, but required for one instance of this element
Data Type	1N
OID	None
Value Allowed	1 = primary
Business Rule(s)	
	It is required that one source be flagged as Primary. Therefore this field must be set to "1" once, and only once, for one A.2 block within the message. A.2 is a repeatable block of elements, and there can be multiple sources, but only one is the Primary source. If there is only one source, and only one A.2 block in the message, then this field should be flagged as "1". If there are multiple sources, and multiple A.2 blocks in the message, then this element will be set to "1" for a single A.2 block and will be empty in all the other A.2 blocks. Do not enter any other information in this element for any A.2 block. Do not use this element to rank sources hierarchically.

A.3 INFORMATION ON SENDER OF CASE SAFETY REPORT



A.3.1 Sender Type

User Guidance	In this context, "Pharmaceutical company" includes biotechnology companies and other manufacturers required to submit ICSRs.
Conformance	Required
Data Type	1N
OID	ich-sender-type-oid
Value Allowed	1 = Pharmaceutical Company 2 = Regulatory Authority 3 = Health Professional 4 = Regional Pharmacovigilance Center 5 = WHO collaborating center for international drug monitoring 6 = Other (e.g. distributor, study sponsor, contract research organisation, or non-commercial organisation) 7 = Patient / Consumer
Business Rule(s)	
	Each transmission shall identify the type of the sender organisation or individual.

1199 **A.3.2 Sender's Organisation**

User Guidance	Identifies the sender (e.g. company name or regulatory authority name).
Conformance	Required if A.3.1 Sender Type is not coded as 7 (Patient / Consumer)
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	Each transmission shall identify the name of the sender organisation or individual.

1200 **A.3.3 Person Responsible for Sending the Report**

	Sender Department	Title	Given name	Middle name	Family name
Data Element	A.3.3a	A.3.3b	A.3.3c	A.3.3d	A.3.3e
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 mask some of the elements used to identify the person responsible for sending the report in the transmitted message. If the elements that are being used to identify the Sender cannot be transmitted due to data privacy requirements, then those fields 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.				

1201 **A.3.3a Sender's Department**

User Guidance	Name of the department
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, NI
Business Rule(s)	
	The identification of the sender's department could be subject to confidentiality requirements. See the detailed user guidance and business rule(s) above under A.3.3.

A.3.3b Sender's Title

User Guidance	Sender's title
Conformance	Optional
Data Type	50AN
OID	None
Value Allowed	Free text nullFlavor: MSK, NI
Business Rule(s)	
	The identification of the sender's title could be subject to confidentiality requirements. See the detailed user guidance and business rule(s) above under A.3.3.

A.3.3c Sender's Given Name

User Guidance	Sender's given name
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, NI
Business Rule(s)	
	The identification of the sender's given name could be subject to confidentiality requirements. See the detailed user guidance and business rule(s) above under A.3.3.

A.3.3d Sender's Middle Name

User Guidance	Sender's middle name.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, NI
Business Rule(s)	
	The identification of the sender's middle name could be subject to confidentiality requirements. See the detailed user guidance and business rule(s) above under A.3.3.

A.3.3e Sender's Family Name

User Guidance	Sender's family name.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, NI

Business Rule(s)	
	The identification of the sender's family name could be subject to confidentiality requirements. See the detailed user guidance and business rule(s) above under A.3.3.

1206 **A.3.4 Sender's Address, Fax, Telephone and E-mail Address**

	Street Address	City	State or Province	Postcode	Country Code	Telephone	Fax	E-mail Address
Data Element	A.3.4a	A.3.4b	A.3.4c	A.3.4d	A.3.4e	A.3.4f	A.3.4.i	A.3.4l
User Guidance	The sender's contact information should be provided in conformance with local or international confidentiality requirements.							
Business Rule(s)								
	Depending on the local legal requirements regarding confidentiality, it might be necessary to mask some of the elements used to specify the Sender's contact details 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 fields 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.							

1207 **A.3.4a Sender's Street Address**

User Guidance	Sender's street address.
Conformance	Optional
Data Type	100AN
OID	None
Value Allowed	Free text nullFlavor: MSK, NI
Business Rule(s)	
	Each ICSR shall identify the Sender's street address for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.3.4.

1208 **A.3.4b Sender's City**

User Guidance	Sender's city.
Conformance	Optional
Data Type	35AN
OID	None
Value Allowed	Free text nullFlavor: MSK, NI
Business Rule(s)	

	Each ICSR shall identify the Sender's city for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.3.4.

1209

1210 **A.3.4c Sender's State or Province**

User Guidance	Sender's state or province.
Conformance	Optional
Data Type	40AN
OID	None
Value Allowed	Free text nullFlavor: MSK, NI
Business Rule(s)	
	Each ICSR shall identify the Sender's state or province for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.3.4.

1211 **A.3.4d Sender's Postcode**

User Guidance	Sender's postcode.
Conformance	Optional
Data Type	15AN
OID	None
Value Allowed	Free text nullFlavor: MSK, NI
Business Rule(s)	
	Each ICSR shall identify the Sender's postcode for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.3.4.

1212

1213 **A.3.4e Sender's Country Code**

User Guidance	Use the two letter ISO 3166 Part 1 code (ISO 3166-1 alpha-2) to represent the names of the sender's country. The identification of the sender's country code could be subject to confidentiality requirements. See user guidance in A.3.4.
Conformance	Optional
Data Type	2A
OID	1.0.3166.1.2.2
Value Allowed	ISO 3166-1 alpha-numeric nullFlavor: MSK
Business Rule(s)	
	A two character country code will be used in all instances. An ISO country code does not exist for the "EU". In this case, "EU" will be accepted as the country code.

	See the detailed user guidance and business rule(s) above under A.3.4.

1214 **A.3.4f Sender's Telephone**

User Guidance	Include the country code and any extension number. Numbers should be entered in a fashion that allows for international and not include any domestic trunk prefix, e.g. for those countries which only use the leading zero domestically this should be stripped. For example, local 0xx-yyy-zzzz becomes international +cc-xx-yyy-zzzz. When entering a phone number, do not include domestic international dialling prefixes (00 in Europe, 011 in US, 010 in Japan). Begin with the International Telecommunications Union plus sign (+) notation for country code. Additional visual separators for human readability are not required. If used these characters should be limited to parenthesis '( )', dashes '-' or decimal points.
Conformance	Optional
Data Type	33AN
OID	None
Value Allowed	Free text nullFlavor: MSK, NI
Business Rule(s)	
	Each ICSR shall identify the Sender's telephone number for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.3.4.

1215

1216 **Note: There is a known gap between the numbers of the previous and next data elements.**

1217 **A.3.4i Sender's Fax**

User Guidance	Include the country code and any extension number. Numbers should be entered in a fashion that allows for international dialling and not include any domestic trunk prefix, e.g. for those countries which only use the leading zero domestically this should be stripped. For example, local 0xx-yyy-zzzz becomes international +cc-xx-yyy-zzzz. When entering a phone number, do not include domestic international dialling prefixes (00 in Europe, 011 in US, 010 in Japan). Begin with the International Telecommunications Union plus sign (+) notation for country code. Additional visual separators for human readability are not required. If used these characters should be limited to parenthesis '( )', dashes '-' or decimal points.
Conformance	Optional

Data Type	33AN
OID	None
Value Allowed	Free text nullFlavor: MSK, NI
Business Rule(s)	
	Each ICSR shall identify the Sender's fax number for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.3.4.

1218

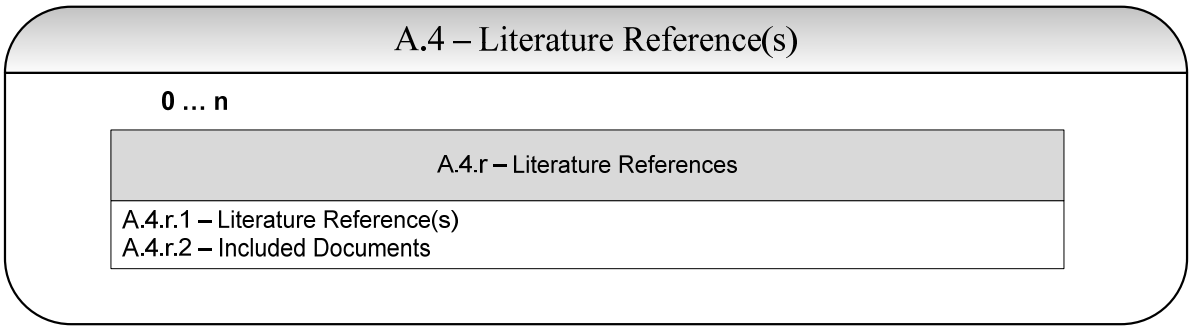
1219 **Note: There is a known gap between the numbers of the previous and next data elements.**

1220 **A.3.4l Sender's E-mail Address**

User Guidance	Sender's email address.
Conformance	Optional
Data Type	100AN
OID	None
Value Allowed	Free text nullFlavor: MSK, NI
Business Rule(s)	
	Each ICSR shall identify the Sender's email address for regulatory purposes in conformance with confidentiality requirements. See the detailed user guidance and business rule(s) above under A.3.4.

1221

1222 ## A.4 LITERATURE REFERENCE(S)



1223

1224 **A.4.r.1 Literature Reference(s) (repeat as necessary)**

User Guidance	This field should be used for literature article(s) that describe individual case(s), but not for articles used for data analysis. References should be provided in the style specified by the Vancouver Convention, known as "Vancouver style" and which have 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. Updated instructions are provided in the National Library of Medicine citing medicine home page: http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=citmed.TOC&depth=2.
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.

1225

1226 **A.4.r.2 Included documents**

User Guidance	This element contains the actual content referenced inA.4.r.1 if the sender chooses to send 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 Value allowed will be defined by region.

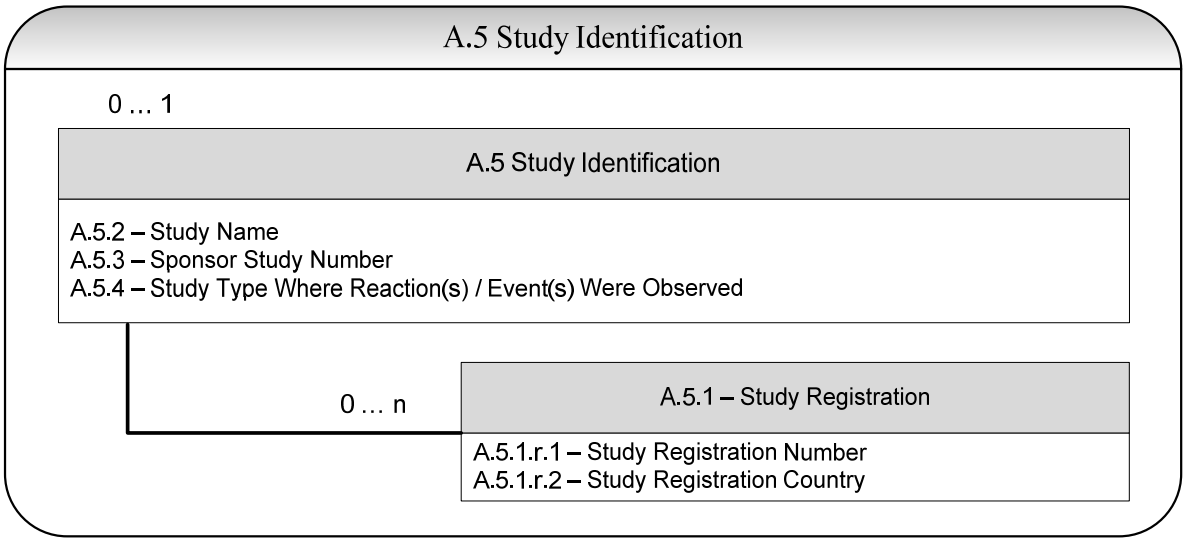
1227

1228

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

1229

A.5 STUDY IDENTIFICATION



A.5.1 Study Registration (repeat as necessary)

A.5.1.r.1 Study Registration Number

User Guidance	This field should be populated with the study registration number as assigned in the reporting region, e.g. EudraCT number for reporting in the European Economic Area (EEA).
Conformance	Optional
Data Type	50AN
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.

A.5.1.r.2 Study Registration Country

User Guidance	This field should be populated with the country that assigned the Study Registration Number presented in A.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-numeric nullFlavor: ASKU, NASK
Business Rule(s)	
	A two character country code will be used in all instances. An ISO country code does not exist for the "EU". 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.

A.5.2 Study Name

User Guidance	This field 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.

A.5.3 Sponsor Study Number

User Guidance	This section 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	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.

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

User Guidance	This information should be provided if the field A.1.4 Type of report has been populated with "Report from study".
Conformance	Required if A.1.4=2 (Report from study)
Data Type	1N
OID	ich-study-type-oid
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)	
	N/A

B.1 PATIENT CHARACTERISTICS (HEADER / ENTITY)

This section describes the subject who experienced one or several adverse events/reactions.

In cases where a foetus or nursing 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 B.1 fields below apply only to the parent (mother or father) who experienced the adverse reaction/event.

  Example: Mother suffers from pre-eclampsia and the child has not 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 B.1. fields below apply to the mother. However, if suspect drug(s) were taken by the father this information should be indicated in the field B.4.k.10.

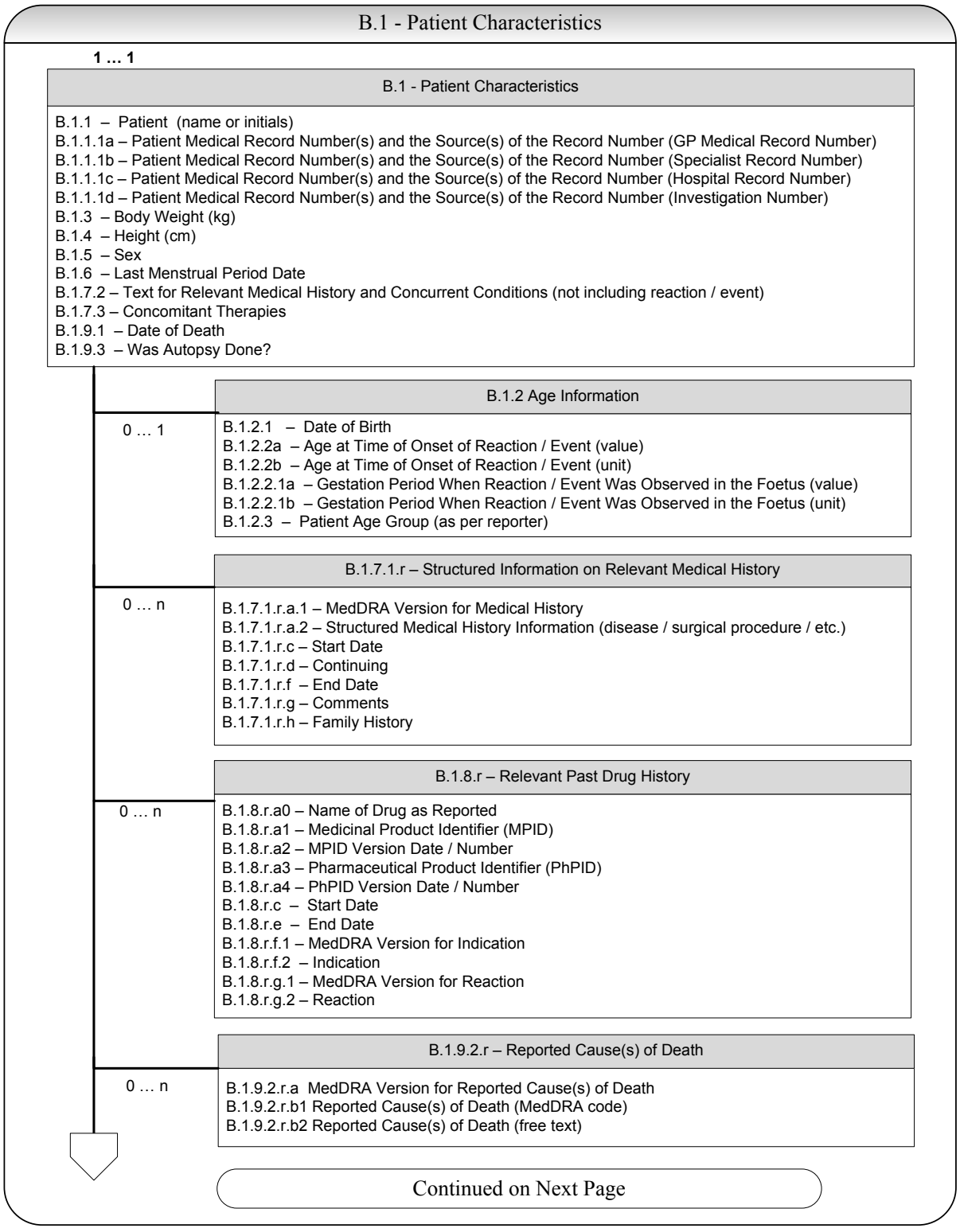
- If both the parent and the child/foetus sustain adverse event(s)/reaction(s), two separate reports, e.g. one for the parent (mother or father) and one for the child/foetus, should be provided and should be linked by using sections A.1.12.r in each report.

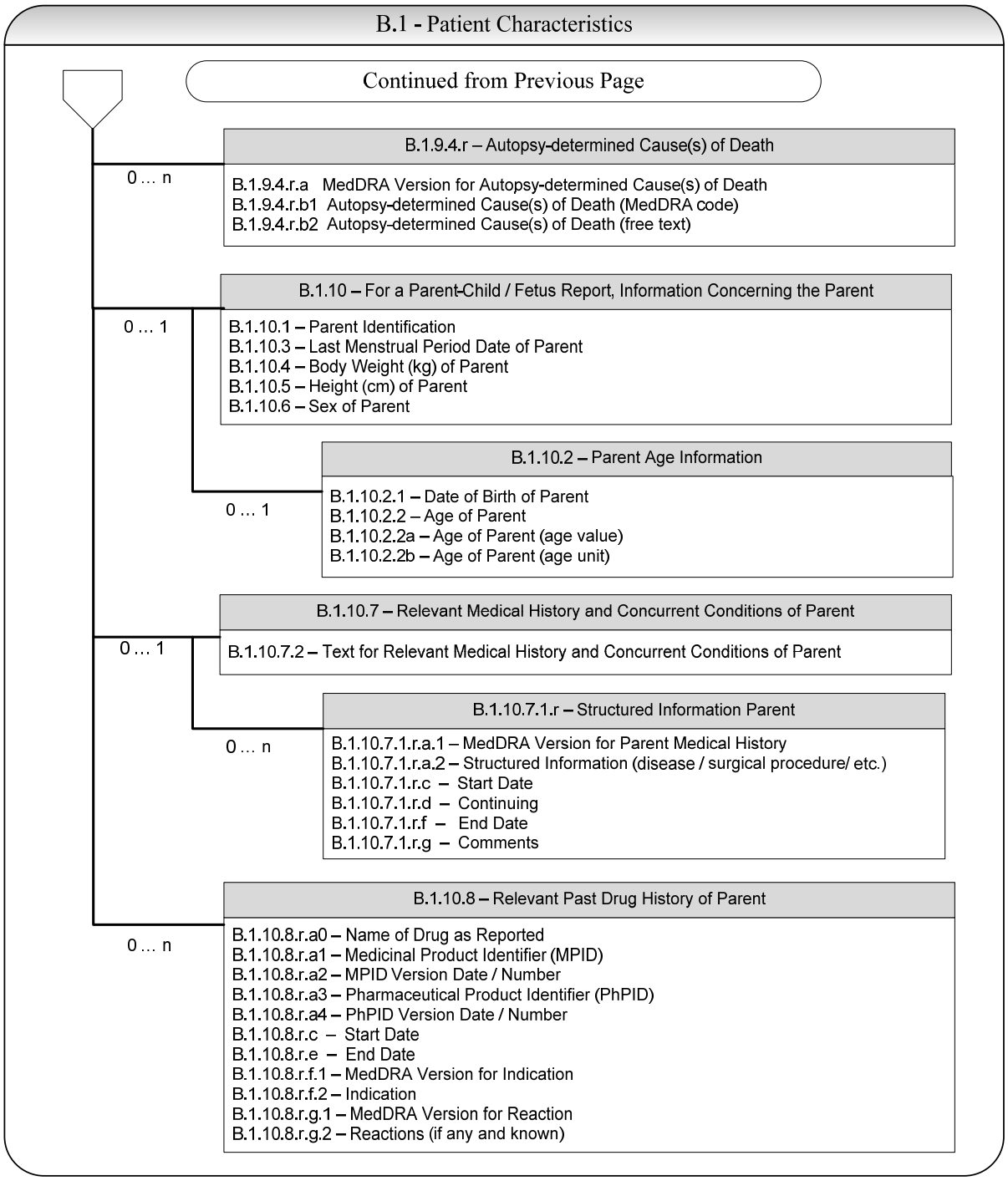
  Example: Mother suffers from pre-eclampsia and, at parturition, the baby had a low birth weight and club foot. Two linked ICSRs should be submitted: The mother's report should have the adverse event/reaction of pre-eclampsia; the report for the baby should have event/reaction terms for low birth weight and club foot. The term pre-eclampsia would only apply to the mother's case. Section A.1.12 (ID number of the linked report) should be completed for both the mother and baby's case.

- 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 B.1.10.

  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 B.1.10.1 with the Caesarean section as relevant medical history (B.1.10.7).

- 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 B.1.10 and the case narrative (section B.5.1) should describe the entire case, including the father's information.


B.1 - Patient Characteristics
1 ... 1
B.1 - Patient Characteristics
B.1.1 – Patient (name or initials)
B.1.1.1a – Patient Medical Record Number(s) and the Source(s) of the Record Number (GP Medical Record Number)
B.1.1.1b – Patient Medical Record Number(s) and the Source(s) of the Record Number (Specialist Record Number)
B.1.1.1c – Patient Medical Record Number(s) and the Source(s) of the Record Number (Hospital Record Number)
B.1.1.1d – Patient Medical Record Number(s) and the Source(s) of the Record Number (Investigation Number)
B.1.3 – Body Weight (kg)
B.1.4 – Height (cm)
B.1.5 – Sex
B.1.6 – Last Menstrual Period Date
B.1.7.2 – Text for Relevant Medical History and Concurrent Conditions (not including reaction / event)
B.1.7.3 – Concomitant Therapies
B.1.9.1 – Date of Death
B.1.9.3 – Was Autopsy Done?
B.1.2 Age Information
0 … 1
B.1.2.1 – Date of Birth
B.1.2.2a – Age at Time of Onset of Reaction / Event (value)
B.1.2.2b – Age at Time of Onset of Reaction / Event (unit)
B.1.2.2.1a – Gestation Period When Reaction / Event Was Observed in the Foetus (value)
B.1.2.2.1b – Gestation Period When Reaction / Event Was Observed in the Foetus (unit)
B.1.2.3 – Patient Age Group (as per reporter)
B.1.7.1.r – Structured Information on Relevant Medical History
0 … n
B.1.7.1.r.a.1 – MedDRA Version for Medical History
B.1.7.1.r.a.2 – Structured Medical History Information (disease / surgical procedure / etc.)
B.1.7.1.r.c – Start Date
B.1.7.1.r.d – Continuing
B.1.7.1.r.f – End Date
B.1.7.1.r.g – Comments
B.1.7.1.r.h – Family History
B.1.8.r – Relevant Past Drug History
0 … n
B.1.8.r.a0 – Name of Drug as Reported
B.1.8.r.a1 – Medicinal Product Identifier (MPID)
B.1.8.r.a2 – MPID Version Date / Number
B.1.8.r.a3 – Pharmaceutical Product Identifier (PhPID)
B.1.8.r.a4 – PhPID Version Date / Number
B.1.8.r.c – Start Date
B.1.8.r.e – End Date
B.1.8.r.f.1 – MedDRA Version for Indication
B.1.8.r.f.2 – Indication
B.1.8.r.g.1 – MedDRA Version for Reaction
B.1.8.r.g.2 – Reaction
B.1.9.2.r – Reported Cause(s) of Death
0 … n
B.1.9.2.r.a MedDRA Version for Reported Cause(s) of Death
B.1.9.2.r.b1 Reported Cause(s) of Death (MedDRA code)
B.1.9.2.r.b2 Reported Cause(s) of Death (free text)
Continued on Next Page


B.1 - Patient Characteristics
Continued from Previous Page
B.1.9.4.r – Autopsy-determined Cause(s) of Death
0 … n
B.1.9.4.r.a MedDRA Version for Autopsy-determined Cause(s) of Death
B.1.9.4.r.b1 Autopsy-determined Cause(s) of Death (MedDRA code)
B.1.9.4.r.b2 Autopsy-determined Cause(s) of Death (free text)
B.1.10 – For a Parent-Child / Fetus Report, Information Concerning the Parent
0 … 1
B.1.10.1 – Parent Identification
B.1.10.3 – Last Menstrual Period Date of Parent
B.1.10.4 – Body Weight (kg) of Parent
B.1.10.5 – Height (cm) of Parent
B.1.10.6 – Sex of Parent
B.1.10.2 – Parent Age Information
0 … 1
B.1.10.2.1 – Date of Birth of Parent
B.1.10.2.2 – Age of Parent
B.1.10.2.2a – Age of Parent (age value)
B.1.10.2.2b – Age of Parent (age unit)
B.1.10.7 – Relevant Medical History and Concurrent Conditions of Parent
0 … 1
B.1.10.7.2 – Text for Relevant Medical History and Concurrent Conditions of Parent
B.1.10.7.1.r – Structured Information Parent
0 … n
B.1.10.7.1.r.a.1 – MedDRA Version for Parent Medical History
B.1.10.7.1.r.a.2 – Structured Information (disease / surgical procedure/ etc.)
B.1.10.7.1.r.c – Start Date
B.1.10.7.1.r.d – Continuing
B.1.10.7.1.r.f – End Date
B.1.10.7.1.r.g – Comments
B.1.10.8 – Relevant Past Drug History of Parent
0 … n
B.1.10.8.r.a0 – Name of Drug as Reported
B.1.10.8.r.a1 – Medicinal Product Identifier (MPID)
B.1.10.8.r.a2 – MPID Version Date / Number
B.1.10.8.r.a3 – Pharmaceutical Product Identifier (PhPID)
B.1.10.8.r.a4 – PhPID Version Date / Number
B.1.10.8.r.c – Start Date
B.1.10.8.r.e – End Date
B.1.10.8.r.f.1 – MedDRA Version for Indication
B.1.10.8.r.f.2 – Indication
B.1.10.8.r.g.1 – MedDRA Version for Reaction
B.1.10.8.r.g.2 – Reactions (if any and known)

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B.1.1 Patient (name or initials)

User Guidance	It is important that this field 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. This also applies to medical record number(s) (B.1.1.1).
Conformance	Required
Data Type	60AN
OID	None
Value Allowed	Free text nullFlavor: MSK, ASKU, NASK, UNK
Business Rule(s)	
	• If the initials of the patient are unknown to the sender, this field should be left blank with nullFlavor = UNK. • If the initials are known to the sender but cannot be transmitted due to data privacy requirements, this field 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.

B.1.1.1 Patient Medical Record Number(s) and the 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 source of the number should be specified to ensure the possibility of retrieval when possible and desirable.

The patient identification in a clinical trial can be transmitted in field B.1.1.1d 'Patient investigation number'. Note that multiple elements from the source database, like Center- Patient and random number, should be concatenated in this element to assure a unique patient identification.

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

User Guidance	*See Section B.1.1.1 above.*
Conformance	Optional
Data Type	20AN
OID	ich-gp-medical-record-number-oid
Value Allowed	Free text nullFlavor: MSK, 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 B.1.1.1a: <id extension="**B.1.1.1a**" root="ich-gp-medical-record-number-oid" />

B.1.1.1b Patient Medical Record Number(s) and the Source(s) of the Record Number (Specialist Record Number)

User Guidance	*See Section B.1.1.1 above.*
Conformance	Optional
Data Type	20AN
OID	ich-specialist-medical-record-number-oid
Value Allowed	Free text nullFlavor: MSK, 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 B.1.1.1b: <id extension="**B.1.1.1b**" root="ich-specialist-record-number-oid" />

B.1.1.1c Patient Medical Record Number(s) and Source(s) of the Record Number (Hospital Record Number)

User Guidance	*See Section B.1.1.1 above.*
Conformance	Optional
Data Type	20AN
OID	ich-hospital-medical-record-number-oid
Value Allowed	Free text nullFlavor: MSK, 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 B.1.1.1c: <id extension="**B.1.1.1c**" root="ich-hospital-record-number-oid" />

B.1.1.1d Patient Medical Record Number(s) and Source(s) of the Record Number (Investigation Number)

User Guidance	*See Section B.1.1.1 above.*
Conformance	Optional
Data Type	20AN
OID	ich-investigation-medical-record-number-oid
Value Allowed	Free text nullFlavor: MSK, 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 B.1.1.1d: <id extension="**B.1.1.1d**" root="ich-investigation-number-oid" />

B.1.2 Age Information (header)

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.

B.1.2.1 Date of Birth

User Guidance	A full precision date should be used (e.g. day, month, year). If the full date of birth is not known, an approximate age can be captured in section B.1.2.2. Alternatively, field B.1.2.3 'Patient age group (as per reporter)' can be used to indicate the age of the patient.
Conformance	Optional
Data Type	Date
OID	None
Value Allowed	See Appendix II for further information. nullFlavor: MSK, ASKU, NASK
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 field 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.

B.1.2.2 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 next item B.1.2.2.1 "Gestation period when reaction/event was observed in the foetus" should be used.

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

B.1.2.2a Age at Time of Onset of Reaction / Event (value)

User Guidance	*See Section B.1.2.2 above.*
Conformance	Optional, but required if B1.2.2b is populated.
Data Type	5N
OID	None
Value Allowed	Numeric
Business Rule(s)	
	N/A

B.1.2.2b Age at Time of Onset of Reaction / Event (unit)

User Guidance	*See Section B.1.2.2 above.*
Conformance	Optional, but required if B1.2.2a is populated.
Data Type	50AN
OID	2.16.840.1.113883.6.8
Value Allowed	UCUM codes for Decade, Year, Month, Week, Day, and Hour
Business Rule(s)	

B.1.2.2.1 Gestation Period When Reaction / Event Was Observed in the Foetus

Gestation period when reaction/event was observed in the foetus should be expressed by providing both a number and designation of units of days, weeks, months or trimester. The gestation period at the time of exposure is captured in section B.4.k.6.

B.1.2.2.1a Gestation Period When Reaction / Event Was Observed in the Foetus (value)

User Guidance	*See Section B.1.2.2.1 above.*
Conformance	Optional, but required if B.1.2.2.1b is populated.
Data Type	3N
OID	None
Value Allowed	Numeric
Business Rule(s)	
	N/A

B.1.2.2.1b Gestation Period When Reaction/Event Was Observed in the Foetus (unit)

User Guidance	*See Section B.1.2.2.1 above.*
Conformance	Optional, but required if B.1.2.2.1a is populated.
Data Type	50AN
OID	UCUM: 2.16.840.1.113883.6.8
Value Allowed	UCUM codes for Month, Week, Day, 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}.

B.1.2.3 Patient Age Group (as per reporter)

User Guidance	These terms are not defined in this document and are intended to be used as they were reported by the primary source. This section should be completed only when the age is not provided more specifically in sections B.1.2.1 or B.1.2.2.
Conformance	Optional
Data Type	1N
OID	ich-patient-age-group-oid
Value Allowed	0= Foetus 1=Neonate (Preterm and Term newborns) 2=Infant 3=Child 4=Adolescent 5=Adult 6=Elderly
Business Rule(s)	
	N/A

B.1.3 Body Weight (kg)

User Guidance	Body weight in kilograms at the time of the event/reaction.
Conformance	Optional
Data Type	6N
OID	None
Value Allowed	Numeric
Business Rule(s)	
	• ICH defines that the unit of weight is "kg". • Fractions or decimals are allowed using a period. No commas are allowed in this numeric field

B.1.4 Height (cm)

User Guidance	Height in centimetres at the time of the event/reaction.
Conformance	Optional
Data Type	3N
OID	None
Value Allowed	Numeric
Business Rule(s)	
	• ICH defines that the unit of height is "cm". • Fractions or decimals are allowed using a period. No commas are allowed in this numeric field

B.1.5 Sex

User Guidance	In case of ambiguity, e.g. if the gender cannot be identified with certainty, use "0=Unknown".
Conformance	Required
Data Type	1N
OID	1.0.5218
Value Allowed	1=Male 2=Female 0=Unknown nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	If the gender is known to the sender but cannot be transmitted due to data privacy requirements, then leave the field 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.

B.1.6 Last Menstrual Period Date

User Guidance	Imprecise dates can be included, (e.g. month, and year or year only). Relevant information on menopause or conditions related to menopause should be captured in the field B.1.7.1.r using the MedDRA LLT. If this report is for a mother and baby, then B.1.10.3 must be populated.
Conformance	Optional

Data Type	Date
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.

B.1.7 Relevant Medical History and Concurrent Conditions (not including reaction / event) (header)

B.1.7.1.r Structured Information on Relevant Medical History (repeat as necessary)

Medical judgment should be exercised in completing this section. 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 should be recorded in the comments. If precise dates are not known and a text description is pertinent in understanding the medical history, or if concise additional information is helpful in showing the relevance of the past medical history, this information can be included in the Comments (B.1.7.r.g). In order to identify relevant medical information of the family (e.g. hereditary diseases), the data element "Family History" (B.1.7.1.r.h) should be set to "true" (Yes) for the appropriate disease(s).

If there is no relevant medical history and no concurrent conditions for inclusion in B.1.7.1 then B.1.7.2 is required. If the reason is that the relevant medical history is not documented at the time of the report then the value for B.1.7.2 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.

MedDRA LLT code should be used in B.1.7.r.a.2. 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 medical history term. For example, if two conditions are reported, the first condition would be described in items B.1.7.1.1.a.1 through B.1.7.1.1.h, and the other condition would be described in items B.1.7.1.2.a.1 through B.1.7.1.2.h.

1352 **B.1.7.1.r.a.1 MedDRA Version for Medical History**

User Guidance	Provide the MedDRA version for B.1.7.1.r.a.2.
Conformance	Optional, but required if B.1.7.1.r.a.2 is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. The value allowed is limited to a MedDRA version code that is defined by the organisation that maintains the terminology.

1353 **B.1.7.1.r.a.2 Structured Medical History Information (disease / surgical procedure / etc.)**

User Guidance	The information pertinent to understanding the case is desired (such as diseases, conditions such as pregnancy, surgical procedures, psychological trauma, risk factors, etc.). See Section B.1.7.1.r above. MedDRA LLT code should be used.
Conformance	Optional, but required if B.1.7.1.r.a.1 is populated.
Data Type	8N
OID	MedDRA=2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	
	The code is dictated by the organisation that maintains the terminology.

1354 **B.1.7.1.r.c Start Date**

User Guidance	Imprecise dates can be used for both start and end dates. Highest precision is desirable.
Conformance	Optional
Data Type	Date
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.

1355 **B.1.7.1.r.d Continuing**

User Guidance	Indicate if the 'medical condition' in B.1.7.1.r.a.2 is still present at the time of this report.
Conformance	Optional
Data Type	Boolean
OID	None
Value Allowed	false true nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	In the case of "Yes", the value should be "Boolean: true". In the case of "No", the value should be "Boolean: false". Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

1356 **B.1.7.1.r.f End Date**

User Guidance	Imprecise dates can be used for both start and end dates. Highest precision is desirable.
Conformance	Optional
Data Type	Date
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.

1357 **B.1.7.1.r.g Comments**

User Guidance	Provide additional comments about the 'medical condition' in B.1.7.1.r.a.2 that could not be captured in structured field. 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)	

B.1.7.1.r.h Family History

User Guidance	Identify relevant medical information of the family (e.g., hereditary diseases), with “true” (Yes). When Parent Medical history is provided (B.1.10.7), do not include those terms under this section with this data element set to “true” (Yes).
Conformance	Optional
Data Type	Boolean
OID	None
Value Allowed	true
Business Rule(s)	

B.1.7.2 Text for Relevant Medical History and Concurrent Conditions (not including reaction / event)

User Guidance	The term "None" should be used here when there is no relevant medical history and no concurrent conditions. If a relevant medical history is not documented at the time of the report then this field is unknown and should not be confused with “None”. If structured information is not available in the sender’s database, this field should be used. Otherwise, it is preferable to send structured data in segment B.1.7.1.r.
Conformance	Optional, but required if B.1.7.1 section 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, this field 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.

B.1.7.3 Concomitant Therapies

User Guidance	This field is to be populated according to information provided by the reporter to indicate the presence of concomitant therapies such as radiotherapy or drug class not otherwise specified. In case of concomitant medication(s) the structured information on the medicinal product(s) should be provided in the fields B.4.k.2.1 to B.4.k.2.4. In case of other administered therapies that cannot be structured the information should be provided in the narrative section B.5.1.
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 the fields B.4.k.2.1 to B.4.k.2.4. In case of other administered therapies that cannot be structured the information should be provided in the narrative section B.5.1.

B.1.8 Relevant Past Drug History (repeat as necessary) (header / entity)

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 that particular patient (for example, a patient with known renal or liver impairment) .Information concerning concomitant and other suspect drugs should be included in section B.4. The information provided here can also include previous experience with similar drugs. When completing the item concerning the name of the drug, it is important to use the words provided by the primary source. Trade name, generic name or class of drug can be used.

To standardise this information, the ICH M5 guideline should be used. Based on the medicinal product name as reported by the primary source, the most specific identifier, being either 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 fields should be left blank.

MedDRA LLT numeric code should be used for the Indication (B.1.8.r.f.2) and Reaction (B.1.8.r.g.2). 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 B.1.8.1.a0 through B.1.8.1.g.2, and the other drug would be described in items B.1.8.2.a0 through B.1.8.2.g.2.

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 the narrative.

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 (B.1.8). 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.

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	A history of allergy to a particular drug is preferably reported in section B.1.8 "Relevant Past Drug History ", using the suspect drug name and MedDRA terms in the indication and reactions fields. The information could also be reported in section B.1.7.1 "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". This latter field is not searchable in most databases and thus this is not the preferred option. If it is the first allergic reaction for the patient and allergy testing results are available, they can be recorded along with other ADR-related terms. For example, the reaction itself is coded to the LLT "Drug hypersensitivity" (or a more descriptive LLT) in B.2.i.1 "Reaction/event in MedDRA Terminology ". In addition, the testing results are recorded by use of the LLT "Skin test positive", or "Allergy test positive" (or their more descriptive LLTs) in B.2.i.1.

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1400 **B.1.8.r.a0 Name of Drug as Reported**

User Guidance	The name should be that 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	Optional
Data Type	250AN
OID	None
Value Allowed	Free text nullFlavor: NA
Business Rule(s)	
	Null flavor=NA should be used when there is no previous exposure to a drug or vaccine. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

1401 **B.1.8.r.a1 Medicinal Product Identifier (MPID)**

User Guidance	Based on B.1.8.r.a0 and ICH M5 guideline, the most specific identifier, being *either* the MPID *or* the PhPID should be provided. If an MPID or a PhPID for the reported medicinal product is not available, these fields should be left blank.
Conformance	Optional, not allowed if B.1.8.r.a3 is populated
Data Type	Refer to M5 guideline
OID	Refer to M5 guideline

Value Allowed	Refer to M5 guideline
Business Rule(s)	
	Any given drug entry will have either MPID or PhPID, but NOT both.

1402 **B.1.8.r.a2 MPID Version Date/Number**

User Guidance	Provide the version date for B.1.8.r.a1.
Conformance	Optional, but required if B.1.8.r.a1 is populated
Data Type	Refer to M5 guideline
OID	None
Value Allowed	Refer to M5 guideline
Business Rule(s)	
	N/A

1403 **B.1.8.r.a3 Pharmaceutical Product Identifier (PhPID)**

User Guidance	Based on B.1.8.r.a0 and ICH M5 guideline, the most specific identifier, being *either* the MPID *or* the PhPID should be provided. If a MPID or a PhPID for the reported medicinal product is not available, these fields should be left blank.
Conformance	Optional, not allowed if B.1.8.r.a.1 is populated
Data Type	Refer to M5 guideline
OID	Refer to M5 guideline
Value Allowed	Refer to M5 guideline
Business Rule(s)	
	Any given drug entry will have either MPID or PhPID, but NOT both.

1404 **B.1.8.r.a4 PhPID Version Date/Number**

User Guidance	Provide the version date for B.1.8.r.a3.
Conformance	Optional, but required if B.1.8.r.a3 is populated
Data Type	Refer to M5 guideline
OID	None
Value Allowed	Refer to M5 guideline
Business Rule(s)	

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1406 **Note: There is a known gap between the numbers of the previous and next data elements.**

1407 **B.1.8.r.c Start Date**

User Guidance	Imprecise dates can be used for both start and end dates.
Conformance	Optional
Data Type	Date
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.

1408 **B.1.8.r.e End Date**

User Guidance	Imprecise dates can be used for both start and end dates.
Conformance	Optional
Data Type	Date
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.

1409 **B.1.8.r.f.1 MedDRA Version for Indication**

User Guidance	Provide the MedDRA version for B.1.8.r.f.2.
Conformance	Optional, but required if B.1.8.r.f.2 is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. The value allowed is limited to a MedDRA version code that is defined by the organisation that maintains the terminology.

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B.1.8.r.f.2 Indication

User Guidance	MedDRA LLT code should be used.
Conformance	Optional, but required if B.1.8.r.f.1 is populated.
Data Type	8N
OID	MedDRA=2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	
	The code is dictated by the organisation that maintains the terminology.

B.1.8.r.g.1 MedDRA Version for Reaction

User Guidance	Provide the MedDRA version for B.1.8.r.g.1.
Conformance	Optional, but required if B.1.8.r.g.2 is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. The value allowed is limited to a MedDRA version code that is defined by the organisation that maintains the terminology.

B.1.8.r.g.2 Reaction

User Guidance	Medical judgment should be exercised in completing this section. The information provided here describes previous experience with the drug described in B.1.8.r.a. *See Section B.1.8 above.* MedDRA LLT code should be used.
Conformance	Optional, but required if B.1.8.r.g.1 is populated.
Data Type	8N
OID	MedDRA=2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	
	The code is dictated by the organisation that maintains the terminology.

B.1.9 In Case of Death (header / entity)

B.1.9.1 Date of Death

User Guidance	An imprecise date can be used.
Conformance	Optional
Data Type	Date
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.

B.1.9.2.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 B.1.9.2.1.a through B.1.9.2.1.b and the other cause would be described in items B.1.9.2.2.a through B.1.9.2.2.b.

B.1.9.2.r.a MedDRA Version for Reported Cause(s) of Death

User Guidance	Provide the MedDRA version for B.1.9.2.r.b.
Conformance	Optional, but required if B.1.9.2.r.b1 is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. The value allowed is limited to a MedDRA version code that is defined by the organisation that maintains the terminology.

B.1.9.2.r.b1 Reported Cause(s) of Death (MedDRA code)

User Guidance	MedDRA LLT code should be used.
Conformance	Optional, but required if B.1.9.2.r.a is populated.
Data Type	8N
OID	MedDRA=2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	
	The code is dictated by the organisation that maintains the terminology.

B.1.9.2.r.b2 Reported Cause(s) of Death (free text)

User Guidance	The original reporter's words and/or short phrases used to describe the cause of death should be provided in an English translation for international transmission.
Conformance	Optional
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

B.1.9.3 Was Autopsy Done?

User Guidance	Indicate if an autopsy was done.
Conformance	Optional, but required if B.1.9.1 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.

1425 **B.1.9.4.r Autopsy-determined Cause(s) of Death (repeat as necessary)**

1426 **B.1.9.4.r.a MedDRA Version for Autopsy-determined Cause(s) of Death**

User Guidance	Provide the MedDRA version for B.1.9.4.r.b.
Conformance	Optional, but required if B.1.9.4.r.b1 is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. The value allowed is limited to a MedDRA version code that is defined by the organisation that maintains the terminology.

1427 **B.1.9.4.r.b1 Autopsy-determined Cause(s) of Death (MedDRA code)**

User Guidance	MedDRA LLT code should be used.
Conformance	Optional, but required if B.1.9.4.r.a is populated.
Data Type	8N
OID	MedDRA=2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	
	The code is dictated by the organisation that maintains the terminology.

1428 **B.1.9.4.r.b2 Autopsy-determined Cause(s) of Death (free text)**

User Guidance	The original reporter's words and/or short phrases used to describe the autopsy-determined cause of death should be provided in an English translation for international transmission.
Conformance	Optional
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

B.1.10 For a Parent-child / Foetus Report, Information Concerning the Parent (Header/entity)

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 user guidance for section B.1. Guidance regarding confidentiality is provided in B.1.1, and should be considered before providing the parent identification. For the subsections B.1.10.4 through B.1.10.8.r, the guidance provided for B.1.3 through B.1.5 and B.1.7 through B.1.8.r should be reviewed.

B.1.10.1 Parent Identification

User Guidance	*See Section B.1.10 above.* The identification of the parent 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	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 field should beleft blank with nullFlavor=UNK. • If the name or initials are known to the sender but cannot be transmitted due to data privacy requirements, this field 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.

B.1.10.2 Parent Age Information (header)

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.

If the full date of birth is not known, an incomplete date can be used. If only an approximate age is available this information can be captured in section B.1.10.2.2.

B.1.10.2.1 Date of Birth of Parent

User Guidance	If the full date of birth is not known, an incomplete date can be used.
Conformance	Optional
Data Type	Date
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 field 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.

1443 **B.1.10.2.2 Age of Parent**

1444 **B.1.10.2.2a Age of Parent (age value)**

User Guidance	See Section B.1.10.2 above
Conformance	Optional, but required if B.1.10.2.2b is populated.
Data Type	3N
OID	None
Value Allowed	Numeric
Business Rule(s)	

1445 **B.1.10.2.2b Age of Parent (age unit)**

User Guidance	See Section B.1.10.2 above.
Conformance	Optional, but required if B.1.10.2.2a is populated.
Data Type	50AN
OID	2.16.840.1.113883.6.8
Value Allowed	UCUM code for Year
Business Rule(s)	

1446 **B.1.10.3 Last Menstrual Period Date of Parent**

User Guidance	Indicate the date for the Parent's last menstrual period.
Conformance	Optional
Data Type	Date
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.

1447 **B.1.10.4 Body Weight (kg) of Parent**

User Guidance	See Section B.1.10 above.
Conformance	Optional
Data Type	6N
OID	None
Value Allowed	Numeric
Business Rule(s)	
	ICH defines that the unit of weight is "kg".

1448 **B.1.10.5 Height (cm) of Parent**

User Guidance	See Section B.1.10 above.
Conformance	Optional
Data Type	3N
OID	None
Value Allowed	Numeric
Business Rule(s)	
	ICH defines that the unit of height is "cm".

B.1.10.6 Sex of Parent

User Guidance	See Section B.1.10 above.
Conformance	Required if any data element in B.1.10 section is populated
Data Type	1N
OID	1.0.5218
Value Allowed	1=Male 2=Female 0=Unknown nullFlavor: MSK, ASKU, NASK
Business Rule(s)	
	If the gender of the parent is known to the sender but cannot be transmitted due to data privacy requirements, this field 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.

B.1.10.7 Relevant Medical History and Concurrent Conditions of Parent (header/entity)

B.1.10.7.1.r Structured Information (parent) (repeat as necessary)

MedDRA LLT code should be used in B.1.10.7.1.r.a.2. See the User Guidance provided for B.1.7 above.

B.1.10.7.1.r.a1 MedDRA Version for Parent Medical History

User Guidance	See Section B.1.10.7.1.r above.
Conformance	Optional, but required if B.1.10.7.1.r.a2 is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. The value allowed is limited to a MedDRA version code that is defined by the organisation that maintains the terminology.

B.1.10.7.1.r.a2 Structured Information (disease / surgical procedure / etc.)

User Guidance	See Section B.1.10.7.1.r above.
Conformance	Optional, but required if B.1.10.7.1.r.a1 is populated
Data Type	8N
OID	MedDRA=2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	
	The code is dictated by the organisation that maintains the terminology.

Note: There is a known gap between the numbers of the previous and next data elements.

B.1.10.7.1.r.c Start Date

User Guidance	See Section B.1.10.7.1.r above.
Conformance	Optional
Data Type	Date
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.

B.1.10.7.1.r.d Continuing

User Guidance	See Section B.1.10.7.1.r above.
Conformance	Allowed only if B.1.10.7.1.r.f is null
Data Type	Boolean
OID	None
Value Allowed	false true nullFlavor: ASKU, NASK
Business Rule(s)	
	In the case of "Yes", the value should be "Boolean: true". In the case of "No", the value should be "Boolean: false". In the case of "Unknown", this optional element is **not** transmitted. Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information.

B.1.10.7.1.r.f End Date

User Guidance	See Section B.1.10.7.1.r above.
Conformance	Optional
Data Type	Date
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.

B.1.10.7.1.r.g Comments

User Guidance	See Section B.1.10.7.1.r above.
Conformance	Optional
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	N/A

B.1.10.7.2 Text for Relevant Medical History and Concurrent Conditions of Parent

User Guidance	See Section B.1.10 above.
Conformance	Optional
Data Type	10000AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	N/A

B.1.10.8 Relevant Past Drug History of Parent (header / entity)

To standardise this information, the ICH M5 guideline should be used for drug information (MPID and PhPID). Based on the medicinal product name as reported by the primary source, the most specific identifier, being either the MPID or the PhPID should be provided. If an MPID or a PhPID for the reported medicinal product is not available, these fields should be left blank. MedDRA LLT codes should be used for the Indication (B.1.10.8.r.f) and Reaction (B.1.10.8.r.g).

B.1.10.8.r.a0 Name of Drug as Reported

User Guidance	The name should be that used 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 B.1.10.8 above.
Conformance	Optional
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	N/A

B.1.10.8.r.a1 Medicinal Product Identifier (MPID)

User Guidance	See Section B.1.10.8 above.

Conformance	Optional, not allowed if B.1.10.8.r.a3 is populated.
Data Type	Refer to M5 guideline
OID	Refer to M5 guideline
Value Allowed	Refer to M5 guideline
Business Rule(s)	
	Any given drug entry will have either MPID or PhPID, but NOT both.

1471 **B.1.10.8.r.a2 MPID Version Date/Number**

User Guidance	See Section B.1.10.8 above.
Conformance	Optional, but required if B.1.10.8.r.a1 is populated.
Data Type	Refer to M5 guideline
OID	None
Value Allowed	Refer to M5 guideline
Business Rule(s)	
	N/A

1472 **B.1.10.8.r.a3 Pharmaceutical Product Identifier (PhPID)**

User Guidance	See Section B.1.10.8 above.
Conformance	Optional, not allowed if B.1.10.8.r.a.1 is populated.
Data Type	Refer to M5 guideline
OID	Refer to M5 guideline
Value Allowed	Refer to M5 guideline
Business Rule(s)	
	Any given drug entry will have either MPID or PhPID, but NOT both.

1473 **B.1.10.8.r.a4 PhPID Version Date/Number**

User Guidance	See Section B.1.10.8 above.
Conformance	Optional, but required if B.1.10.8.r.a3 is populated.
Data Type	Refer to M5 guideline
OID	None
Value Allowed	Refer to M5 guideline
Business Rule(s)	

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1475 **Note: There is a known gap between the numbers of the previous and next data elements.**

1476 **B.1.10.8.r.c Start Date**

User Guidance	Start date of relevant past drug history of Parent.
Conformance	Optional
Data Type	Date
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.

Note: There is a known gap between the numbers of the previous and next data elements.

B.1.10.8.r.e End Date

User Guidance	End date of relevant past drug history of parent.
Conformance	Optional
Data Type	Date
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.

B.1.10.8.r.f.1 MedDRA Version for Indication

User Guidance	Provide the MedDRA version for B.1.10.8.r.f.2.
Conformance	Optional, but required if B.1.10.8.r.f.2 is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. The value allowed is limited to a MedDRA version code that is defined by the organisation that maintains the terminology.

B.1.10.8.r.f.2 Indication

User Guidance	See Section B.1.10.8 above.
Conformance	Optional, but required if B.1.10.8.r.f.1 is populated.
Data Type	8N
OID	MedDRA=2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	
	The code is dictated by the organisation that maintains the terminology.

B.1.10.8.r.g.1 MedDRA Version for Reaction

User Guidance	Provide the MedDRA version for B.1.10.8.r.g.2

Conformance	Optional, but required if B.1.10.8.r.g.2 is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. The value allowed is limited to a MedDRA version code that is defined by the organisation that maintains the terminology.

B.1.10.8.r.g.2 Reactions (if any and known)

User Guidance	See Section B.1.10.8 above.
Conformance	Optional, but required if B.1.10.8.r.g.1 is populated.
Data Type	8N
OID	MedDRA=2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	
	The code is dictated by the organisation that maintains the terminology.

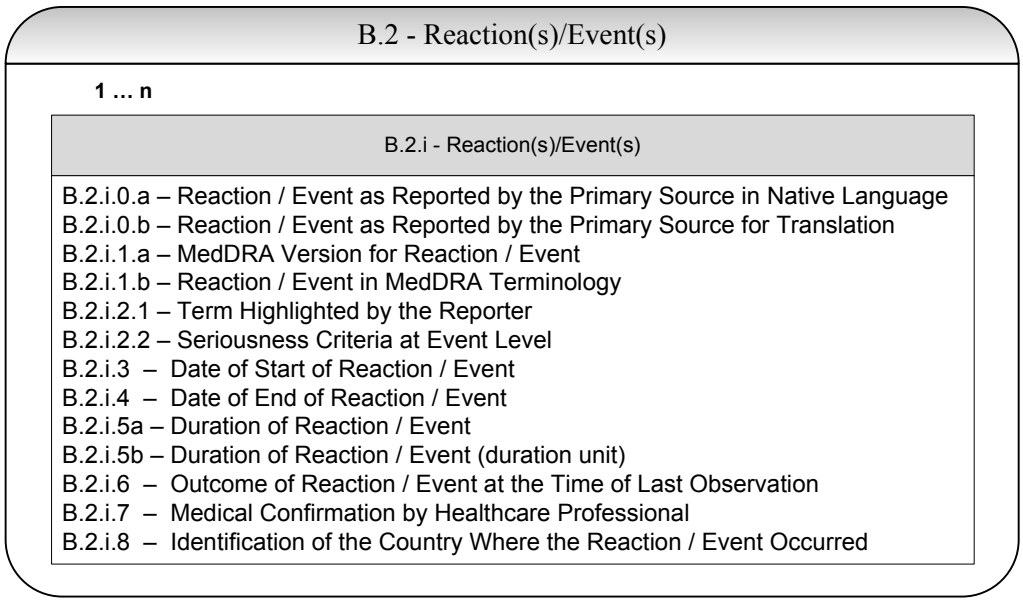
B.2 REACTION(S)/EVENT(S)

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

Note: For an observation required by regional guidance which does not contain a reaction/event B.2 must still be coded. Examples can include medication error without exposure, reporting drug misidentification, etc.

	For technical reason, each reaction / event should be assigned an internal ID so that B.4.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 B.2.1.0 through B.2.1.8, and the other reaction would be described in items B.2.2.0 through B.2.2.8.



1495

1496 **B.2.i.0.a1 Reaction / Event as Reported by the Primary Source in Native Language**

User Guidance	The original reporter's words and/or short phrases used to describe the reaction/event should be provided in a native language.
Conformance	Optional
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

1497 **B.2.i.0.a2 Reaction / Event as Reported by the Primary Source Language**

User Guidance	Provide the language used in B.2.i.0.a1 by using the International Standard, Codes for the representation of names of languages-- Part 2: alpha-3 codes (ISO 639-2/RA, alpha-3).
Conformance	Optional, but required if B.2.i.0.a1 is populated.
Data Type	3A
OID	2.16.840.1.113883.6.100
Value Allowed	ISO 639-2 Code
Business Rules	
	N/A

1498 **B.2.i.0.b Reaction / Event as Reported by the Primary Source for Translation**

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

1499 **B.2.i.1.a MedDRA Version for Reaction / Event**

User Guidance	Provide the MedDRA version for B.2.i.1.b.
Conformance	Required
Data Type	4AN
OID	None
Value Allowed	Numeric
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. The value allowed is limited to a MedDRA version code that is defined by the organisation that maintains the terminology.

1500 **B.2.i.1.b Reaction / Event in MedDRA Terminology**

User Guidance	Only the MedDRA Lowest Level Term (LLT) most closely corresponding to the reaction/event as reported by the primary source should be provided. 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). MedDRA LLT code should be used.
Conformance	Required
Data Type	8N
OID	MedDRA=2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	
	The code is dictated by the organisation that maintains the terminology.

B.2.i.2.1 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 field should be correlated with medical concept(s) listed in field B.2.i.0. and categorise the reactions/events as to whether the medical concept was the reason the reporter contacted the sender. This field is intended for the identification of a specific diagnosis as identified by the reporter e.g. if 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.
Conformance	Optional
Data Type	1N
OID	ich-term-highlighted-oid
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)	

B.2.i.2.2 Seriousness Criteria at Event Level (more than one can be chosen)

The seriousness criteria of the reaction/event should be based on the definitions provided in the ICH E2A and E2D guidelines. If the event is not serious, all of these fields should be left blank (which equates to a Boolean value of "null flavour = NI"). It is assumed that the event seriousness is assessed by the reporter; otherwise, it is assessed by the sender.

In case of miscarriage (where the ICSR should be prepared only for the parent, see section **B.1 Patient Characteristics**), the seriousness criterion is "other medically important condition". Depending on the parent's condition, the seriousness criterion could also be life-threatening and/or hospitalisation.

(Results in Death)

User Guidance	See Section B.2.i.2.2 Seriousness criteria at event level
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	

1513 **(Life Threatening)**

User Guidance	See Section B.2.i.2.2 Seriousness criteria at event level
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	

1514 **(Caused / Prolonged Hospitalisation)**

User Guidance	See Section B.2.i.2.2 Seriousness criteria at event level
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	

1515 **(Disabling / Incapacitating)**

User Guidance	See Section B.2.i.2.2 Seriousness criteria at event level
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	

1516 **(Congenital Anomaly / Birth Defect)**

User Guidance	See Section B.2.i.2.2 Seriousness criteria at event level
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	

(Other Medically Important Condition)

User Guidance	See Section B.2.i.2.2 Seriousness criteria at event level
Conformance	Required
Data Type	Boolean
OID	None
Value Allowed	true nullFlavor: NI
Business Rule(s)	

B.2.i.3 Date of Start of Reaction / Event

User Guidance	When a diagnosis is reported together with multiple symptoms, if the reporter does not provide a specific onset date for each reaction/event, this field should be populated with the start date and time of the first symptom. Refer also to item B.5.3.r.
Conformance	Optional
Data Type	Date
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.

1521 **B.2.i.4 Date of End of Reaction / Event**

User Guidance	This field corresponds to the date the reaction/event is assessed as resolved/recovered or resolved/recovered with sequelae (B.2.i.6). When a diagnosis is reported together with multiple symptoms, if the reporter does not provide a specific end date for each reaction/event, this field should be populated with the end date and time of the last symptom. Refer also to item B.5.3.r.
Conformance	Optional
Data Type	Date
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.

1522 **B.2.i.5a Duration of Reaction / Event**

User Guidance	Although 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 date field (start or end date) and this field.
Conformance	Optional, but required if B.2.i.5b is populated.
Data Type	5N
OID	None
Value Allowed	Numeric
Business Rule(s)	

1523 **B.2.i.5b Duration of Reaction / Event (duration unit)**

User Guidance	Provide the time unit for the value recorded in B.2.i.5a.
Conformance	Optional, but required if B.2.i.5a is populated.
Data Type	50AN
OID	2.16.840.1.113883.6.8
Value Allowed	UCUM
Business Rule(s)	
	Select the most appropriate UCUM code.

1524 **B.2.i.6 Outcome of Reaction / Event at the Time of Last Observation**

User Guidance	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, to the reaction/event, 'fatal' should not be selected here, but death should be reported only under section B.1.9.
Conformance	Required
Data Type	1N
OID	ich-outcome-of-reaction-event-oid
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)	

1525 **B.2.i.7 Medical Confirmation by Healthcare Professional**

User Guidance	If an event is reported by a non healthcare professional (e.g. lawyers, consumers), this field can be used to indicate whether the occurrence of the event is confirmed by a healthcare professional.
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.

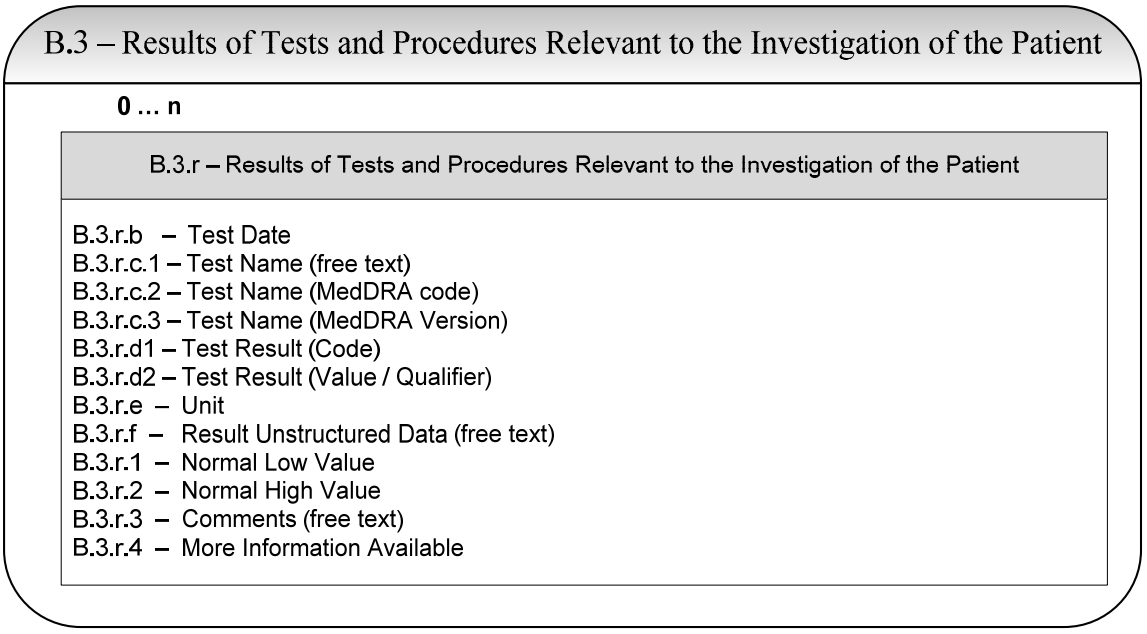
1526 **B.2.i.8 Identification of the Country Where the Reaction / Event Occurred**

User Guidance	This should be 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. Field A.2.r.1.3 should be populated with country C, and field B.2.i.8 should be populated with country B. Use the two letter ISO 3166 Part 1 code (ISO 3166-1 alpha-2) to represent the names of countries.
Conformance	Optional
Data Type	2A
OID	1.0.3166.1.2.2
Value Allowed	ISO 3166-1 alpha-numeric
Business Rule(s)	
	A two character country code will be used in all instances.

B.3 RESULTS OF TESTS AND PROCEDURES RELEVANT TO THE INVESTIGATION OF THE PATIENT

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 B.3.1.b through B.3.1.4, and the other test would be described in items B.3.2.b through B.3.2.4.



1544 **B.3.r.b Test Date**

User Guidance	Provide the date of the test or procedure. Imprecise dates can be used.
Conformance	Optional, but required if B.3.r.c is populated.
Data Type	Date
OID	None
Value Allowed	nullFlavor = UNK See Appendix II for further information.
Business Rules	
	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.

1545 **B.3.r.c Test Name**

1546 A Test Name is required for each B.3 block. While structured information for the Test Name is
1547 preferable using a MedDRA LLT code, provisions are made to transmit the information as free text.

1548 **B.3.r.c1 Test Name (free text)**

User Guidance	Provide a free text description of the test when an appropriate MedDRA code is unavailable.
Conformance	Optional, but required if B.3.r.b is populated and B.3.r.c2 is not populated.
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rules	
	N/A

1550 **B.3.r.c2 Test Name (MedDRA code)**

User Guidance	MedDRA LLT code is recommended for test name, but if there is not an appropriate MedDRA code, free text is allowed to use for test name.
Conformance	Optional, but required when B.3.r.b is populated and B.3.r.c1 is not populated.
Data Type	8N
OID	MedDRA=2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rules	
	The code is dictated by the organisation that maintains the terminology.

B.3.r.c3 MedDRA Version for Test Name

User Guidance	Provide the MedDRA version for B.3.r.c1.
Conformance	Optional, but required when B.3.r.c2 is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric
Business Rules	
	Only 1 MedDRA version is allowed per ICSR. The value allowed is limited to a MedDRA version code that is defined by the organisation that maintains the terminology.

B.3.r.d Test Result

A Test Result is required for each B.3 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, B.3.r.f should be used.

B.3.r.d1 Test Result (Code)

User Guidance	Provide the code from this controlled vocabulary for the test result.
Conformance	Optional, but required if B.3.r.c is populated, and B.3.r.d2 and B.3.r.f is not populated.
Data Type	1N
OID	ich-test-result-code-oid
Value Allowed	1 = Positive 2 = Negative 3 = Borderline 4 = Inconclusive
Business Rules	
	This data element can be used when a numeric value cannot describe the result.

B.3.r.d2 Test Result (Value / Qualifier)

User Guidance	Provide the value for the test result. possibly qualified with an operator such as ‘greater than’.
Conformance	Optional, but required if B.3.r.c is populated, and B.3.r.d1 and B.3.r.f is not populated.
Data Type	50N
OID	None
Value Allowed	Numeric
Business Rules	
	If results and units cannot be split, B.3.r.f should be used. The supported qualifiers are “greater than”, “less than”, “greater than or equal to” and “less than or equal to”.

B.3.r.e Unit

User Guidance	When a UCUM code is not suitable, or results (B.3.r.d2) and units (B.3.r.e) cannot be split, B.3.r.f should be used.
Conformance	Optional, but required if B.3.r.d2 is populated.
Data Type	50AN
OID	2.16.840.1.113883.6.8
Value Allowed	UCUM
Business Rules	
	Select the most appropriate UCUM code.

1560 **B.3.r.f Result Unstructured Data (free text)**

User Guidance	Use if results and units cannot be split or UCUM code is not available for test unit. For example, for the test 'protein excretion', the result could be recorded here as '125mg / 24 hours'.
Conformance	Optional, but required if B.3.r.c is populated, and B.3.r.d is not populated.
Data Type	2000AN
OID	None
Value Allowed	Free text.
BusinessRules	

1561 **B.3.r.1 Normal Low Value**

User Guidance	The same units as used in B.3.r.e are implied.
Conformance	Optional
Data Type	50AN
OID	None
Value Allowed	Free text
Business Rules	

1562 **B.3.r.2 Normal High Value**

User Guidance	The same units as used in B.3.r.e are implied.
Conformance	Optional
Data Type	50AN
OID	None
Value Allowed	Free text
Business Rules	

1563 **B.3.r.3 Comments (free text)**

User Guidance	Provide any relevant comments made by the reporter about this test result.
Conformance	Optional
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rules	

1564 **B.3.r.4 More Information Available**

User Guidance	"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 field is set to "true", then A.1.8.1 should set to "true".
Conformance	Optional
Data Type	Boolean
OID	None
Value Allowed	false true
Business Rules	

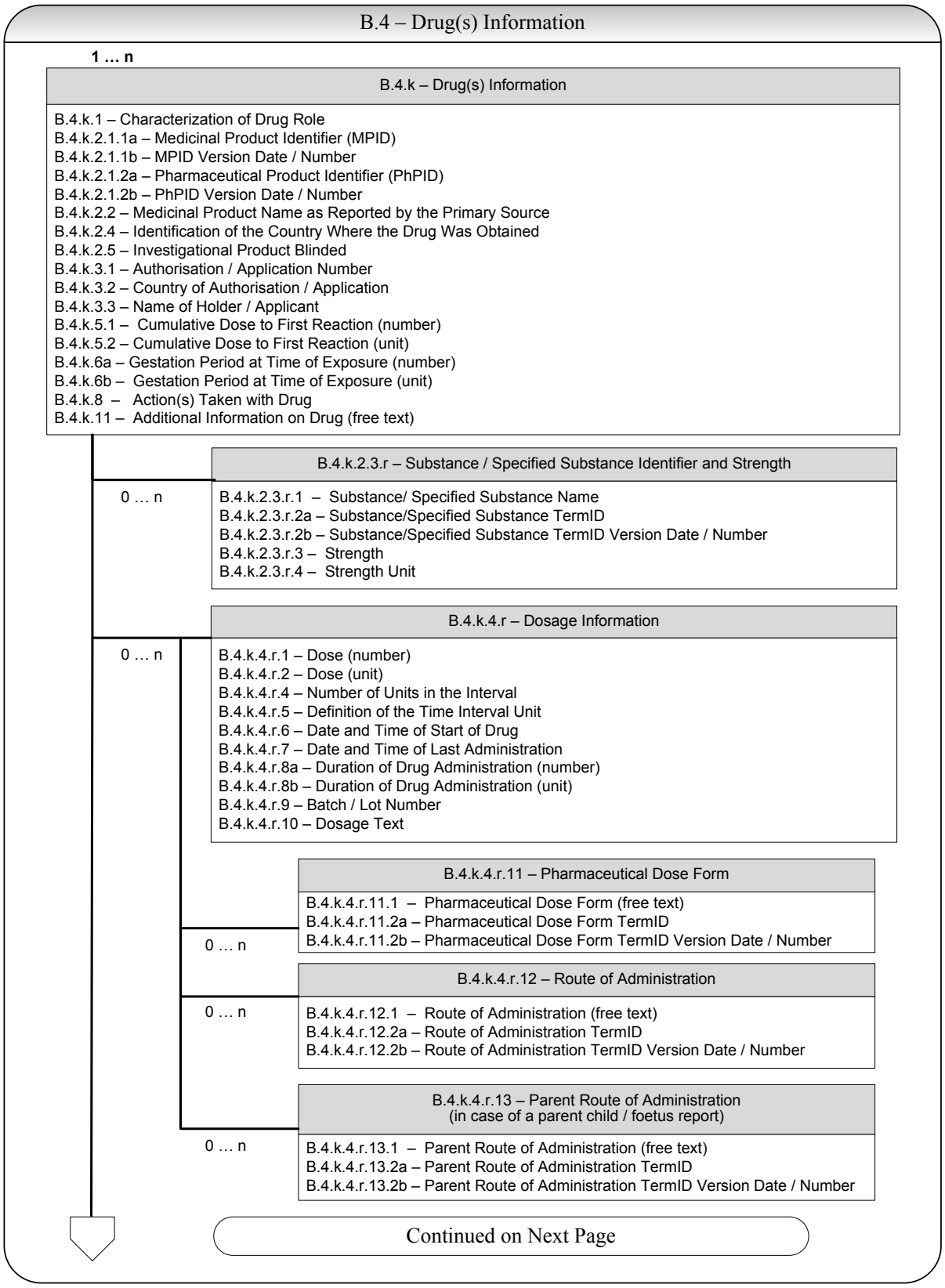
B.4 DRUG(S) INFORMATION (REPEAT AS NECESSARY)

This section covers both suspect and concomitant medications (including biologics). In addition, the section can be used to identify drugs suspected to have an interaction. A minimum of one suspect medication needs to be provided for each valid ICSR. Medications used to treat the reaction/event should not be included here.

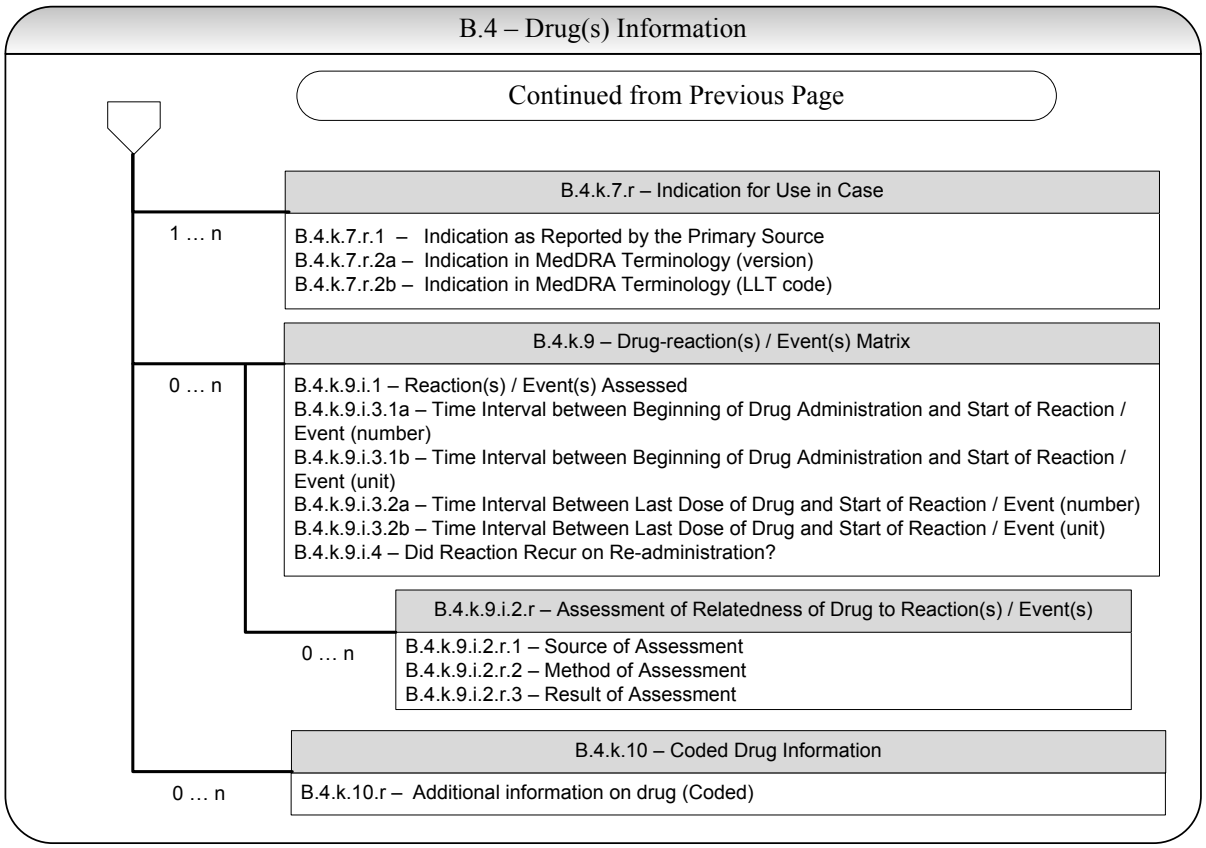
For each drug, the characterisation of the drug role (B.4.k.1) is that indicated or implied by the primary reporter, (e.g. the original source of the information). Suspect medications are those health products taken by the patient and suspected by the reporter to have contributed to the adverse reaction described in section B.2. 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 B.1.8.

As for the designation "i" in section B.2 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".

	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 drug. Drugs used to treat the reaction/event should not be included here.


B.4 – Drug(s) Information
1 … n
B.4.k – Drug(s) Information
B.4.k.1 – Characterization of Drug Role
B.4.k.2.1.1a – Medicinal Product Identifier (MPID)
B.4.k.2.1.1b – MPID Version Date / Number
B.4.k.2.1.2a – Pharmaceutical Product Identifier (PhPID)
B.4.k.2.1.2b – PhPID Version Date / Number
B.4.k.2.2 – Medicinal Product Name as Reported by the Primary Source
B.4.k.2.4 – Identification of the Country Where the Drug Was Obtained
B.4.k.2.5 – Investigational Product Blinded
B.4.k.3.1 – Authorisation / Application Number
B.4.k.3.2 – Country of Authorisation / Application
B.4.k.3.3 – Name of Holder / Applicant
B.4.k.5.1 – Cumulative Dose to First Reaction (number)
B.4.k.5.2 – Cumulative Dose to First Reaction (unit)
B.4.k.6a – Gestation Period at Time of Exposure (number)
B.4.k.6b – Gestation Period at Time of Exposure (unit)
B.4.k.8 – Action(s) Taken with Drug
B.4.k.11 – Additional Information on Drug (free text)
B.4.k.2.3.r – Substance / Specified Substance Identifier and Strength
0 … n
B.4.k.2.3.r.1 – Substance/ Specified Substance Name
B.4.k.2.3.r.2a – Substance/Specified Substance TermID
B.4.k.2.3.r.2b – Substance/Specified Substance TermID Version Date / Number
B.4.k.2.3.r.3 – Strength
B.4.k.2.3.r.4 – Strength Unit
B.4.k.4.r – Dosage Information
0 … n
B.4.k.4.r.1 – Dose (number)
B.4.k.4.r.2 – Dose (unit)
B.4.k.4.r.4 – Number of Units in the Interval
B.4.k.4.r.5 – Definition of the Time Interval Unit
B.4.k.4.r.6 – Date and Time of Start of Drug
B.4.k.4.r.7 – Date and Time of Last Administration
B.4.k.4.r.8a – Duration of Drug Administration (number)
B.4.k.4.r.8b – Duration of Drug Administration (unit)
B.4.k.4.r.9 – Batch / Lot Number
B.4.k.4.r.10 – Dosage Text
B.4.k.4.r.11 – Pharmaceutical Dose Form
0 … n
B.4.k.4.r.11.1 – Pharmaceutical Dose Form (free text)
B.4.k.4.r.11.2a – Pharmaceutical Dose Form TermID
B.4.k.4.r.11.2b – Pharmaceutical Dose Form TermID Version Date / Number
B.4.k.4.r.12 – Route of Administration
0 … n
B.4.k.4.r.12.1 – Route of Administration (free text)
B.4.k.4.r.12.2a – Route of Administration TermID
B.4.k.4.r.12.2b – Route of Administration TermID Version Date / Number
B.4.k.4.r.13 – Parent Route of Administration
(in case of a parent child / foetus report)
0 … n
B.4.k.4.r.13.1 – Parent Route of Administration (free text)
B.4.k.4.r.13.2a – Parent Route of Administration TermID
B.4.k.4.r.13.2b – Parent Route of Administration TermID Version Date / Number
Continued on Next Page

1586



B.4.k.1 Characterisation of Drug Role

User Guidance	This field 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 1.5). 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 event(s) resulting from the suspected interaction, as well as the type of interaction (e.g. drug interaction, food interaction, alcohol interaction, etc.) should be captured with the appropriate MedDRA LLT(s) in section *B.2 Reaction(s) / Event(s)*. "***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. In general the adverse event should be reported as per the trial procedure. In that case, only sections B.4.k.1 and B.4.k.2 are to be filled out for that B.4 block. The information on the suspect cause of the event should be provided in the narrative field B.5.1. In addition comments can be provided by the reporter in the field B.5.2 and the sender in the field B.5.4. **Medication error:** if the patient did not receive the actual prescribed drug but another one, repeatable B.4 sections 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 *B.2 Reaction(s) / Event(s)*.

Conformance	Required
Data Type	1N
OID	ich-characterisation-of-drug-role-oid
Value Allowed	1 = Suspect 2 = Concomitant 3 = Interacting 4 = Drug Not Administered
Business Rules	
	Each ICSR must contain at least one “Suspect” or “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 B.2. 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 B.1.8.

B.4.k.2 Drug Identification

Medicinal product names or active ingredient names should be provided in B.4.k.2.2 as they were reported by the primary source. To standardise the identification of medicinal products, the ICH M5 guideline should be used. When available, the most precise structured information should be provided when identifying medicinal products. Although the most complete information should be provided, redundant information does not have to be repeated. For example, if a MPID is provided in B.4.k.2.1.1, there is no need to provide a PhPID in B.4.k.2.1.2. Likewise, if a PhPID is provided, there is no need to provide information such as Strength or termIDs for Pharmaceutical dose form and Substance name, etc.

In case of investigational drugs, only an unstructured code might be known and provided in B.4.k.2.2 and B.4.k.2.3.r.1.

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 B.4.k.2.3 as necessary.

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

1608 **B.4.k.2.1.1 Medicinal Product Unique Identifier**

1609 **B.4.k.2.1.1a Medicinal Product Identifier (MPID)**

User Guidance	Based on B.4.k.2.2 and ICH M5 guideline, the most specific identifier, being *either* the Medicinal Product Identifier (MPID, B.4.k.2.1.1) *or* the Pharmaceutical Product Identifier(s) (PhPID, B.4.k.2.1.2) should be provided. If a MPID or PhPID(s) for the reported medicinal product is not available, these fields should be left blank. Until M5 is available, this field will be left blank.
Conformance	Optional
Data Type	Refer to M5 guideline
OID	Refer to M5 guideline
Value Allowed	Refer to M5 guideline
Business Rules	

1610 **B.4.k.2.1.1b MPID Version Date / Number**

User Guidance	Provide the version date for B.4.k.2.1.1a.
Conformance	Required if B.4.k.2.1.1a MPID is provided.
Data Type	Refer to M5 guideline
OID	None
Value Allowed	Refer to M5 guideline
Business Rules	

1611 **B.4.k.2.1.2 Pharmaceutical Product Unique Identifier(s)**

1612 **B.4.k.2.1.2a Pharmaceutical Product Identifier (PhPID)**

User Guidance	Based on B.4.k.2.2 and ICH M5 guideline, the most specific identifier, being *either* the Medicinal Product Identifier (MPID, B.4.k.2.1.1) *or* the Pharmaceutical Product Identifier(s) (PhPID, B.4.k.2.1.2) should be provided. If a MPID or PhPID(s) for the reported medicinal product is not available, these fields should be left blank. Until M5 is available, this field will be left blank.
Conformance	Optional
Data Type	Refer to M5 guideline
OID	Refer to M5 guideline
Value Allowed	Refer to M5 guideline
Business Rules	

1613 **B.4.k.2.1.2b PhPID Version Date/Number**

User Guidance	Provide the version date for B.4.k.2.1.2a.
Conformance	Required if B.4.k.2.1.2a PhPID is provided.
Data Type	Refer to M5 guideline
OID	None

Value Allowed	Refer to M5 guideline
Business Rules	

1614

	When a **PhPID (B.4.k.2.1.1)** is provided, the remainder of section B.4.k.2.1.2 and B.4.k.2.3.r.x (data elements B.4.k.2.3.r.1 through B.4.k.2.3.r.4c) should be blank.

1615 **B.4.k.2.2 Medicinal Product Name as Reported by the Primary Source**

User Guidance	Provide the medicinal product name as reported by the source.
Conformance	Required
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

1616 **B.4.k.2.3.r Substance/Specified Substance Identifier and Strength (repeat as necessary)**

1617 Each active ingredient should be specified individually by repeating this section. For each active
1618 ingredient, the ICH M5 substance/specified substance TermID should be provided if available. If the
1619 substance/specified substance TermID is not available, the INN or the active ingredient name or the
1620 drug identification code should be provided

1621 **B.4.k.2.3.r.1 Substance/ Specified Substance Name**

User Guidance	If a B.4.k.2.3.r.2a Substance Name TermID is not available, provide a text description of the substance. A medical device can be described here.
Conformance	Required if both B.4.k.2.1.1 PhPID and B.4.k.2.3.r.2a Substance Name TermID are unavailable.
Data Type	250 AN
OID	None
Value Allowed	Free text
Business Rule(s)	

1622 **B.4.k.2.3.r.2a Substance/Specified Substance TermID**

User Guidance	If B.4.k.2.1.2 PhPID is unavailable, use the Substance Name TermID. Until M5 is available, this field will be left blank.
Conformance	Optional
Data Type	Refer to M5 guideline
OID	Refer to M5 guideline
Value Allowed	Refer to M5 guideline
Business Rule(s)	

1623 **B.4.k.2.3.r.2b Substance/Specified Substance TermID Version Date/Number**

User Guidance	Provide the version date for the Substance Name TermID.
Conformance	Required if B.4.k.2.3.r.2a Substance Name TermID is provided.
Data Type	Refer to M5 guideline
OID	None
Value Allowed	Refer to M5 guideline
Business Rule(s)	

1624 **B.4.k.2.3.r.3 Strength**

User Guidance	If B.4.k.2.1.2 PhPID is unavailable, provide the lower numerator of the strength for the substance. If not a range, provide the numerator of the strength.
Conformance	Optional
Data Type	10N
OID	None
Value Allowed	Numeric
Business Rule(s)	

1625 **B.4.k.2.3.r.4 Strength Unit**

User Guidance	Provide the unit for B.4.k.2.3.r.3 Strength.
Conformance	Optional, but required if B.4.k.2.3.r.3 is populated.
Data Type	50AN
OID	2.16.840.1.113883.6.8
Value Allowed	UCUM
Business Rule(s)	
	Select the most appropriate UCUM code.

1626 **B.4.k.2.4 Identification of the Country Where the Drug Was Obtained**

User Guidance:	Use the two letter ISO 3166 Part 1 code (ISO 3166-1 alpha-2) to represent the country where the drug was obtained.
Conformance	Optional
Data Type	2A
OID	None
Value Allowed	ISO 3166-1 alpha-numeric
Business Rule(s)	
	A two character country code will be used in all instances. An ISO country code does not exist for the "EU". In this case, "EU" will be accepted as the country code.

1627

	Technically, data type of B.4.k.2.4 is defined as string instead of code by HL7. To ensure data quality, this Implementation Guide requires use of ISO country code instead of free text.

1628

1629 **B.4.k.2.5 Investigational Product Blinded**

User Guidance	This field should be used only for 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 even a blinded case safety report during a clinical trial, this field should be used as follows: until the investigational product is un-blinded, the status "blinded" should be indicated by using 'true' in this field. When this field is 'true', the fields of section B.4.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 B.4.k blocks. After un-blinding, if appropriate, "placebo" should be reported in B.4.k.2.3.r as a suspect drug.
Conformance	Optional
Data Type	Boolean
OID	None
Value Allowed	true
Business Rules	
	The value for this field 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 element should not be transmitted.

1630

1631 **B.4.k.3.1 Authorisation / Application Number**

User Guidance	If B.4.k.2.1.1 MPID is unavailable, provide the Authorisation or Application number of the medicinal product in the country where it was obtained when the case report is sent to that country. This applies to both applications and authorisations. Pharmaceutical companies should provide this information at least for their own suspect drug(s).
Conformance	Optional
Data Type	35 AN
OID	None
Value Allowed	Free text
Business Rules	
	N/A

1632 **B.4.k.3.2 Country of Authorisation / Application**

User Guidance	If B.4.k.2.1.1 MPID is unavailable, provide the country where the drug was authorised when the case report is sent to that country. Use the two letter ISO 3166 Part 1 code (ISO 3166-1 alpha-2) to represent the name of the country.
Conformance	Required if B.4.k.3.1 Authorisation / Application Number is provided.
Data Type	2A
OID	1.0.3166.1.2.2
Value Allowed	ISO 3166-1 alpha-numeric

Business Rules	
	A two character country code will be used in all instances. An ISO country code does not exist for the "EU". In this case, "EU" will be accepted as the country code.

B.4.k.3.3 Name of Holder / Applicant

User Guidance	Provide a name of licence holder as indicated on the package.
Conformance	Optional
Data Type	60AN
OID	N/A
Value Allowed	Free text
Business Rule(s)	
	N/A

B.4.k.4.r Dosage Information (repeat as necessary)

Data elements B.4.k.4.r.1 through B.4.k.4.r.5 should be used to provide dosage information. For example, 5mg (in one dose) every other day, subsections B.4.k.4.r.1 through B.4.k.4.r.5 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 B.4.k.4.r.1 through B.4.k.4.r.5 would be 5, mg, 0.25, day, respectively.

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 (B.4.k.4.r.1 to B.4.k.4.r.8b) relates to how the mother took the medication(s). If both parents are the source of the suspect drug(s) then the dosage information reflects how the parent ingested or was administered the drug(s).

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 B.4.k.4.r.10.

Note: Dose examples are provided in Appendix V (B)

B.4.k.4.r.1 Dose (number)

User Guidance	If any of the following pieces of information B.4.k.4.r.1 or B.4.k.4.r.2 is unknown both fields should be left blank.
Conformance	Optional
Data Type	8N
OID	None
Value Allowed	Numeric
Business Rule(s)	
	N/A

B.4.k.4.r.2 Dose (unit)

User Guidance	Provide the unit for B.4.k.4.r.1
Conformance	Optional, but required if B.4.k.4.r.1 is populated.

Data Type	50AN
OID	2.16.840.1.113883.6.8
Value Allowed	UCUM
Business Rules	
	Select the most appropriate UCUM code. If an arbitrary unit code [arb`U] is used, the unit should be described in B.4.k.4.r.10.

1655 **B.4.k.4.r.4 Number of Units in the Interval**

User Guidance	Provide a time interval between the drug administrations in B.4.k.4.r.4 and unit in B.4.k.4.r.5. If either B.4.k.4.r.4 or B.4.k.4.r.5 is unknown, both fields should be left blank unless the definition of the interval unit is "cyclical", "as necessary", or "total" and either B.4.k.4.r.1 or B.4.k.4.r.2 is known, for example "20 mg in total".
Conformance	Optional
Data Type	4N
OID	None
Value Allowed	Numeric
Business Rule(s)	
	N/A

1656 **B.4.k.4.r.5 Definition of the Time Interval Unit**

User Guidance	Provide the UCUM code that best describes the type of interval for B.4.4.r.4. Alternatively, "Cyclical", "As Necessary", and "Total" can be used.
Conformance	Optional, but required if B.4.k.4.r.4 is populated.
Data Type	50AN
OID	UCUM:2.16.840.1.113883.6.8
Value Allowed	UCUM codes and Cyclical, As Necessary, and Total
Business Rules	
	When UCUM code is encoded, select the most appropriate UCUM code UCUM allows to use non-unit expression for symbols not in UCUM. In this case, this Implementation Guide uses {Cyclical}, {As Necessary}, and {Total} where applicable.

1657 **B.4.k.4.r.6 Date and Time of Start of Drug**

User Guidance	Provide the date and time when drug administration started.
Conformance	Optional
Data Type	Date
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.

1658 **B.4.k.4.r.7 Date and Time of Last Administration**

User Guidance	Provide 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 Action(s) taken with drug (B.4.k.8) should be used. If drug administration is stopped but the date is unknown, apply the appropriate nullFlavor to B.4.k.4.r.7. See Appendix V (B) for examples.
Conformance	Optional
Data Type	Date
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.

1659 **B.4.k.4.r.8a Duration of Drug Administration (number)**

User Guidance	Although this section can usually be computed from start/end of administration, both dates and duration can be useful for a short duration, 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. The information requested is the overall duration of drug administration and covers intermittent administration.
Conformance	Optional, but required if B.4.k.4.r.8b is populated.
Data Type	5N
OID	None
Value Allowed	Numeric
Business Rule(s)	

1660 **B.4.k.4.r.8b Duration of Drug Administration (unit)**

User Guidance	Provide the unit for **B.4.k.r.8a Duration of Drug Administration**.
Conformance	Required if B.4.k.4.r.8a is populated
Data Type	50AN
OID	2.16.840.1.113883.6.8
Value Allowed	UCUM
Business Rule(s)	
	Select the most appropriate UCUM code.

1661 **B.4.k.4.r.9 Batch / Lot Number**

User Guidance	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 additional information on drug (B.4.k.11).
Conformance	Optional
Data Type	35AN
OID	None
Value Allowed	Free text
Business Rule(s)	

1662 **B.4.k.4.r.10 Dosage Text**

User Guidance	This item should be used in cases where provision of structured dosage information is not possible or to provide more detail on structured dosage fields. There is no need to duplicate information provided in the dosage fields.
Conformance	Optional
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rule(s)	

1663 **B.4.k.4.r.11 Pharmaceutical Dose Form**

1664 **B.4.k.4.r.11.1 Pharmaceutical Dose Form (free text)**

User Guidance	If a Pharmaceutical Dose Form TermID (B.4.k.4.r.11.2a) is not available, free text should be used in this field. 'Not specified' or 'Unknown' can be used if the source has not provided or does not know the information, respectively.
Conformance	Required if B.4.k.2.1.2 PhPID is unavailable.
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.

1665 **B.4.k.4.r.11.2a Pharmaceutical Dose Form TermID**

User Guidance	If B.4.k.2.1.2 PhPID is unavailable, the pharmaceutical dose form should be provided as a TermID using the ICH M5 Pharmaceutical Dose Form controlled vocabulary. If the Pharmaceutical Dose Form TermID is not available, free text in B.4.k. 4.r.11.1 should be used.
Conformance	Optional
Data Type	Refer to M5 guideline
OID	Refer to M5 guideline
Value Allowed	Refer to M5 guideline
Business Rule(s)	

1666 **B.4.k.4.r.11.2b Pharmaceutical Dose Form TermID Version Date/Number**

User Guidance	Provide the version date for the Pharmaceutical Dose Form TermID
Conformance	Required if B.4.k.4.r.11.2a Pharmaceutical Dose Form TermID is provided.
Data Type	Refer to M5 guideline
OID	None
Value Allowed	Refer to M5 guideline
Business Rule(s)	

1667 **B.4.k.4.r.12 Route of Administration**

1668 **B.4.k.4.r.12.1 Route of Administration (free text)**

User Guidance	If a B.4.k.4.r.12.2a Route of Administration TermID is not available, free text should be used in this field. 'Not specified' or 'Unknown' can be used if the source has not provided or does not know the information, respectively.
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.

B.4.k.4.r.12.2a Route of Administration TermID

User Guidance	Route of administration should be provided as TermID using the ICH M5 Route of administration controlled vocabulary. Until M5 is available, use the existing code list attached in Appendix VI. If the route of administration TermID is not available, free text in B.4.k.4.r.12.1 should be used. 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 B.4.k.4.r.13.
Conformance	Optional
Data Type	Refer to M5 guideline Until M5 is available, this is 3N
OID	Refer to M5 guideline Until M5 is available, use ich-route-of-administration-oid
Value Allowed	Refer to M5 guideline Until M5 is available, use code list in Appendix VI
Business Rule(s)	

B.4.k.4.r.12.2b Route of Administration TermID Version Date

User Guidance	Provide the version date for the Route of Administration TermID.
Conformance	Optional
Data Type	Refer to M5 guideline
OID	None
Value Allowed	Refer to M5 guideline Until M5 guideline is available, this field should not be provided
Business Rule(s)	

B.4.k.4.r.13 Parent Route of Administration (in case of a parent child / foetus report)

Note: Text regarding how parent information is linked through association with the associated person will be inserted here in a future version of this document (as per HL7).

B.4.k.4.r.13.1 Parent Route of Administration (free text)

User Guidance	If a B.4.k.4.r.13.2a Route of Administration TermID is not available, free text should be used in this field. 'Not specified' or 'Unknown' can be used if the source has not provided or does not know the information, respectively.
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.

1675 **B.4.k.4.r.13.2a Parent Route of Administration TermID**

User Guidance	This section should be used in a parent-child/foetus report to indicate the known route of administration of the drug as taken by the parent for the dosage described in B.4.k.4.r.1 to B.4.k.4.r.5. The parent route of administration should be provided as TermID using the ICH M5 Route of administration controlled vocabulary. Until M5 is available, use the existing code list attached in Appendix VI. If the Route of administration TermID is not available, free text in B.4.k.4.r.13.1 should be used.
Conformance	Optional
Data Type	Refer to M5 guideline Until M5 is available, this is 3N
OID	Refer to M5 guideline Until M5 is available, use ich-route-of-administration-oid
Value Allowed	Refer to M5 guideline Until M5 is available, use code list in Appendix VI
Business Rule(s)	

1676 **B.4.k.4.r.13.2b Parent Route of Administration TermID Version Date**

User Guidance	Provide the version date for the Route of Administration TermID.
Conformance	Optional
Data Type	Refer to M5 guideline
OID	None
Value Allowed	Refer to M5 guideline Until M5 guideline is available, this field should not be provided
Business Rule(s)	

1677 **B.4.k.5.1 Cumulative Dose to First Reaction (number)**

User Guidance	The cumulative dose provided should be the total dose administered until the onset of the first sign, symptom or reaction/event where this can be calculated.
Conformance	Optional, but required if B.4.k.5.2 is populated.
Data Type	10N
OID	None
Value Allowed	Numeric
Business Rule(s)	

1678 **B.4.k.5.2 Cumulative Dose to First Reaction (unit)**

User Guidance	Provide the unit for B.4.k. 5.1
Conformance	Optional, but required if B.4.k. 5.1 is populated.
Data Type	50AN
OID	2.16.840.1.113883.6.8
Value Allowed	UCUM
Business Rule(s)	
	Select the most appropriate UCUM code.

1679 **B.4.k.6a Gestation Period at Time of Exposure (number)**

User Guidance	The gestational age at the time of the earliest exposure should be used. This should be expressed by providing both a number and designation of units of days, weeks, months or trimester.
Conformance	Optional, but required if B.4.k.6b is populated.
Data Type	3N
OID	None
Value Allowed	Numeric
Business Rules	

1680 **B.4.k.6b Gestation Period at Time of Exposure (unit)**

User Guidance	Provide the unit for B.4.k.6a
Conformance	Optional, but required if B.4.k.6a is populated.
Data Type	50AN
OID	UCUM: 2.16.840.1.113883.6.8
Value Allowed	UCUM codes for Month, Week, Day, and Trimester
Business Rule(s)	
	Select the most appropriate UCUM code. Units commonly used in clinical practice but not defined in UCUM can be transmitted using curly braces like e.g. {trimester}.

1681 **B.4.k.7 Indication for use in case (repeat as necessary)**

1682 **B.4.k.7.r.1 Indication as Reported by the Primary Source**

User Guidance	The original reporter's words and/or short phrases used to describe the indication for drug use should be provided in an English translation for international transmission. These can also be included in the narrative B.5.1. 'Not specified' or 'Unknown' can 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.

1683 **B.4.k.7.r.2a Indication in MedDRA Terminology (version)**

User Guidance	Provide the MedDRA version for B.4.k.7.r.2a
Conformance	Optional, but required if B.4.k.7.r.2a is populated
Data Type	4AN

OID	None
Value Allowed	Numeric
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. The value allowed is limited to a MedDRA version code that is defined by the organisation that maintains the terminology.

1684 **B.4.k.7.r.2b Indication in MedDRA Terminology (LLT code)**

User Guidance	Provide the MedDRA Lowest Level Term (LLT) most closely corresponding to the indication described B.4.k.7.r.1.
Conformance	Optional, but required if B.r.k.7.r.1 is provided.
Data Type	8N
OID	MedDRA=2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rule(s)	
	When the indication is unknown the MedDRA term "Drug use for unknown indication (10057097)" should be used.

1685 **B.4.k.8 Action Taken with Drug**

User Guidance	This information describes the action taken with the drug as a result of the suspected reaction. The value '1'(Drug withdrawn'), taken together with the outcome of the reaction (B.2.i.6), 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/event.
Conformance	Optional
Data Type	1N
OID	ich-action-taken-with-drug-oid
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)	

1686 **B.4.k.9 Drug-reaction(s) / Event(s) Matrix (repeat as necessary)**

1687 This section provides the means to transmit the degree of suspected relatedness of the drug (k) with a
1688 suspect role to each reaction(s)/event(s) (i) in section B.2. The repeating items (r) are used to provide
1689 the assessment of relatedness by different sources or methods of assessment. For the purpose of
1690 reporting, there is an implied suspicion of causality for spontaneous reports. It is recognised that
1691 information concerning the relatedness, especially for spontaneous reports, is often subjective and
1692 might not be available.
1693
1694 The following example illustrates the functionality contained in this section.
1695 • Assume the patient has had three adverse events: Event1, Event2, and Event3

- The reporter provided assessment of causality for events Event1 & 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 B.4.k.9.i.2.r.x (where x equals the 3 subfields 1-3). Please note the subfields 1-3 are repeatable. For subsection B.4.k.9.i.1, a technical reference to the reaction / event in B.2.i should be used. Subsections B.4.k.9.i.2.r.1, B.4.k.9.i.2.r.2 and B.4.k.9.i.2.r.3 do not call for a standardised methodology or vocabulary.

B.4.k.9.i.1	B.4.k.9.i.2.r.1	B.4.k.9.i.2.r.2	B.4.k.9.i.2.r.3
technical reference to event 1 in B.2.i	reporter	global introspection	related
	Company	algorithm	possibly related
	Company	Bardi	0.76
technical reference to event 2 in B.2.i	reporter	global introspection	not related
	Company	algorithm	possibly related
	Company	Bardi	0.48
technical reference to event 3 in B.2.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, fields B.4.k.9.i.1 through B.4.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 fields B.4.k.9.i.1 through B.4.k.9.i.2.r.3. Additionally, field B.5.4 Sender's Comments 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.

B.4.k.9.i.1 Reaction(s) / Event(s) Assessed

User Guidance	This is not a user entered element. This is a technical reference within the message that is used to identify reaction / event in B.2.i that is being assessed.
Conformance	Optional
Data Type	N/A
OID	None
Value Allowed	N/A
Business Rule(s)	
	The observation id for reaction / event populated in B.2.i is applied to this value.

B.4.k.9.i.2.r Assessment of Relatedness of Drug to Reaction(s) / Event(s) (repeat as necessary)

1711 **B.4.k.9.i.2.r.1 Source of Assessment**

User Guidance	Indicate the source of the assessment provided in B.4.k.9.i.2.r.3.
Conformance	Optional
Data Type	60AN
OID	None
Value Allowed	Free text
Business Rule(s)	

1712 **B.4.k.9.i.2.r.2 Method of Assessment**

User Guidance	Indicate the method of the assessment provided in B.4.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)	

1713 **B.4.k.9.i.2.r.3 Result of Assessment**

User Guidance	Provide the 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)	

1714 **B.4.k.9.i.3.1a Time Interval between Beginning of Drug Administration and Start of Reaction /**
1715 **Event (number)**

User Guidance	Dates, if available, should be transmitted in the appropriate items, rather than intervals. However there are circumstances when dates are known but the interval is very short (e.g. 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 B.4.k.9.i.3.1b is populated.
Data Type	5N
OID	None
Value Allowed	Numeric
Business Rule(s)	

1716 **B.4.k.9.i.3.1b Time Interval between Beginning of Drug Administration and Start of Reaction /**
1717 **Event (unit)**

User Guidance	Provide the unit for B.4.k.9.i.3.1a.

Conformance	Optional, but required if B.4.k.9.i.3.1a is populated.
Data Type	50AN
OID	2.16.841.1.113883.6.8
Value Allowed	UCUM
Business Rules	
	Select the most appropriate UCUM code.

1718 **B.4.k.9.i.3.2a Time Interval between Last Dose of Drug and Start of Reaction / Event (number)**

User Guidance	*Please refer to B.4.k.9.i.3.1 above.*
Conformance	Optional, but required if B.4.k.9.i.3.2a is populated.
Data Type	5N
OID	None
Value Allowed	Numeric
Business Rules	

1719 **B.4.k.9.i.3.2b Time Interval between Last Dose of Drug and Start of Reaction / Event (unit)**

User Guidance	Provide the unit for B.4.k.9.i.3.2a
Conformance	Optional, but required if B.4.k.9.i.3.2a is populated.
Data Type	50AN
OID	2.16.841.1.113883.6.8
Value Allowed	UCUM
Business Rules	
	Select the most appropriate UCUM code.

1720 **B.4.k.9.i.4 Did Reaction Recur on Re-administration?**

User Guidance	Indicate if the patient was rechallenged with the drug and the outcome if known. This field should not be coded if it was not reported whether or not a rechallenge was done.
Conformance	Optional
Data Type	1N
OID	ich-recur-on-readministration-oid
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 Rules	
	If the sender does not know whether a rechallenge was performed, this data element should not be transmitted.

1721 **B.4.k.10.r Additional information on drug (Coded) (repeat as necessary)**

User Guidance	This field should be used to specify any additional information pertinent to the case that is not covered by the sections above. For cases where the suspect drug was taken by the father, this should be indicated in this field as '3' (Drug taken by the father). If the additional information cannot be described by B.4.k.10.r then use the field B.4.k.11.
Conformance	Optional
Data Type	2N
OID	ich-addional-info-on-drug-code-oid
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 Rules	

1722 **B.4.k.11 Additional Information on Drug (free text)**

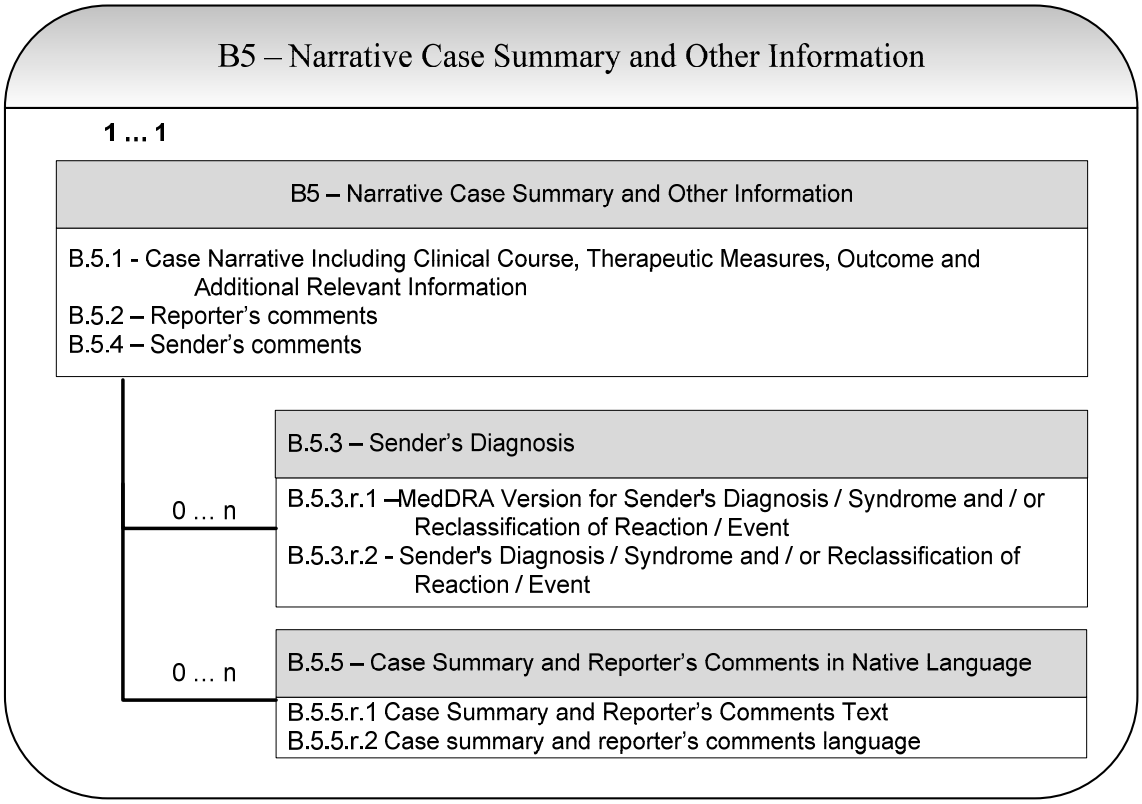
User Guidance	This is a free text field used to provide other additional drug information not described in B.4.k.10.r. For example, expiry date for the lot number described in B.4.k.4.r.9.
Conformance	Optional
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rules	
	If provided, this element needs to be separated and independent from any value selected in the code list for B.4.k.10.r.

1723

1724

B.5 NARRATIVE CASE SUMMARY AND FURTHER INFORMATION

Sections B.5.3 and B.5.5 are repeatable to allow for sufficient space to describe and comment on the reaction/event and to accommodate for the use of different languages.



B.5.1 Case Narrative Including Clinical Course, Therapeutic Measures, Outcome and Additional Relevant Information

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

B.5.2 Reporter's Comments

User Guidance	This item should be used to include 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	

Rules	

B.5.3 Sender's Diagnosis

B.5.3.r.1 MedDRA Version for Sender's Diagnosis / Syndrome and / or Reclassification of Reaction / Event (repeat as necessary)

User Guidance	Provide the MedDRA version for B.5.3.r.2.
Conformance	Optional, but required if B.5.3.r.2 is populated.
Data Type	4AN
OID	None
Value Allowed	Numeric
Business Rule(s)	
	Only 1 MedDRA version is allowed per ICSR. The value allowed is limited to a MedDRA version code that is defined by the organisation that maintains the terminology.

B.5.3.r.2 Sender's Diagnosis / Syndrome and / or Reclassification of Reaction / Event (repeat as necessary)

User Guidance	This section provides the sender with an opportunity to combine signs and symptoms that were reported into a succinct diagnosis. The reasoning would be included in section B.5.4. MedDRA LLT code should be used.
Conformance	Optional, but required if B.5.3.r.1 is populated.
Data Type	8N
OID	MedDRA=2.16.840.1.113883.6.163
Value Allowed	Numeric
Business Rules	
	The code is dictated by the organisation that maintains the terminology.

B.5.4 Sender's Comments

User Guidance	This section provides information concerning 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). In case of linkage of multiple ICSRs using A.1.12, the reason should be provided in these comments.
Conformance	Optional
Data Type	2000AN
OID	None
Value Allowed	Free text
Business Rules	

B.5.5 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 reporter's comments on the case in a language different from that used in B.5.1, B.5.2, and B.5.4.

B.5.5.r.1 and B.5.5.r.2 are used in combination to transmit the sender's and receiver's comments in another language other than English as required in some countries and regions.

B.5.5.r.1 Case Summary and Reporter's Comments Text

User Guidance	*Please refer to B.5.5 above.*
Conformance	Optional
Data Type	100000AN
OID	None
Value Allowed	Free text
Business Rules	

B.5.5.r.2 Case Summary and Reporter's Comments Language

User Guidance	Provide the language used in B.5.5.r.1 by using the International Standard, Codes for the representation of names of languages-- Part 2: alpha-3 codes (ISO 639-2/RA, alpha-3).
Conformance	Required if B.5.5.r.1 is populated.
Data Type	3A
OID	2.16.840.1.113883.6.100
Value Allowed	ISO 639-2 Code
Business Rules	

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 a clinical document provided from a primary source is available as an attachment then A.1.8.1 should be "true," the title of the document in the attachment is required in A.1.8.1.r.1 and the document file type should be identified in A.1.8.1.r.2.

When a literature article is sent as an attachment, the literature citation in Vancouver style is only required in A.4.r.1 and the document file type is required in A.4.r.2, rather than in A.1.8.1.r.2. (Please refer to section 3.4 for detailed specification of each data element.)

Within one ICSR, multiple document titles (A.1.8.1.r) and literature titles (A.4.r) can be provided, as well as the associated materials.

Although several types of document files (e.g. PDF, jpeg, tiff, and DICOM) are *technically* permissible as attachments, each region will determine the file types that can process.

Because documents might not be available at the time of ICSR reporting, attachments can be transmitted separately from the ICSR transmission. When the sender transmits an attachment

separately, the original ICRS along with all the *same* medical information captured in E2B(R3) data elements is retransmitted as an 'amendment' (see guidance for element A.1.13) If the data elements in E2B(R3) have changed, then the attachment is transmitted as a follow-up.

3.5.2 Technical specification

It is always required that documents for attachments should be provided in-line, therefore, providing a hyperlink to the document source stored separately is not acceptable.
Attachments should be enclosed in a message with its document file type, which is captured in A.1.8.1.r.2 and A.4.r.2. Three properties for document file type are available, and the appropriate properties should be provided in a message.

i) MediaType: Identifies the type of the encapsulated data and identifies a method to interpret or render the data. This property indicates the data format standardised by RFC 2046 (http://www.ietf.org/rfc/rfc2046.txt), (e.g. application/PDF, image/jpeg, application/DICOM. The default value for mediaType 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 Sample XML

When an ICSR includes two documents for attachment, its XML instance is given like the following way.
Attachment 1 : PDF file document
Attachment 2 : compressed JPEG file document

```
<reference typeCode="REFR">
    <document classCode="DOC" moodCode="EVN">
        <code code="ADDITIONAL_DOCUMENT" codesystem="0. 2. 999. 5. 9"/>
        <title>A.1.8.1.r.1_1</title>
        <text mediaType='application/pdf'  representation='B64'>
        omSJUEdmde9j44zmMiromSJUEdmde9j44zmMirdMDSsWdIJdksIJR3373jeu836edjzMMIjdMDSsW
        dIJdksIJR3373jeu83MNYD83jmMdomSJUEdmde9j44zmMir...MNYD83jmMdomSJUEdmde9j44zm
        Mir6edjzMMIjdMDSsWdIJdksIJR3373jeu834zmMir6edjzMMIjdMDSsWdIJdksIJR3373jeu83==
        </text>
    </document>
</reference>
<reference typeCode="REFR">
    <document classCode="DOC" moodCode="EVN">
        <code code="ADDITIONAL_DOCUMENT" codesystem="0. 2. 999. 5. 9"/>
        <title>A.1.8.1.r.1_2</title>
        <text mediaType='image/jpeg' representation='B64' compression="DF">
        omSJUEdmde9j44zmMiromSJUEdmde9j44zmMirdMDSsWdIJdksIJR3373jeu836edjzMMIjdMDSsW
        dIJdksIJR3373jeu83MNYD83jmMdomSJUEdmde9j44zmMir...MNYD83jmMdomSJUEdmde9j44zm
        Mir6edjzMMIjdMDSsWdIJdksIJR3373jeu834zmMir6edjzMMIjdMDSsWdIJdksIJR3373jeu83==
        </text>
    </document>
</reference>
```

4.0 RULES FOR IMPLEMENTATION

4.1 Mandatory Data Elements within the ICSR Schema

There are numerous mandatory data elements and attributes that must be expressed to create a valid ICH ICSR XML message. If these data elements and attributes are not provided in an appropriate format, the XML instance of the message will not parse properly. If the message does not parse properly, the message will be rejected with an error. Proper application of tools to create the message should prevent this problem from occurring. The inventory of mandatory data elements is provided in two formats. The first form will identify all the data elements that are mutually exclusive, mutually inclusive, conditionally required or required. The second format will provide a table of HL-7 ICSR schema elements that are required for business or technical reasons. The schema elements mandatory for business reasons are based on the table provided in section 4.1.2.

4.1.1 Inventory of Mandatory Data Elements

The inventory of mandatory data elements is derived from the conformance identified for each data element in section 3.4.0a: ICH ICSR Data Element Attribute List. In general, the inventory will identify those fields that are required. In some cases, there mutually inclusive fields that must be provided together (or not at all), and there are also cases where sets of fields are mutually exclusive and only one of the sets can be provided. In other cases, one field could be conditionally required based on the value of another field. These special cases are identified in the conformance column of the tables below.

4.1.1.1 Mutually Exclusive Data Elements

These data elements are mutually exclusive, and can not be provided together in the ICSR message. A valid ICSR message can contain either element, but not both. For example, if the value of Element ID 1 is known, then a value for the field listed under Element ID 2 can not be provided. Providing both values in an ICSR instance will yield the resulting ICSR invalid.

Element id 1	Description	Element id 2	Description
B.1.8.r.a1	Medicinal Product Identifier (MPID)	B.1.8.r.a3	Pharmaceutical product Identifier (PhPID)
B.1.10.8.r.a1	Medicinal Product Identifier MPID	B.1.10.8.r.a3	Pharmaceutical product Identifier (PhPID)
B.4.k.2.1.1a	Medicinal Product Identifier MPID	B.4.k.2.1.2a	Pharmaceutical product Identifier (PhPID)

4.1.1.2 Mutually Inclusive Data Elements

The data elements below are mutually inclusive. If data is provided for the field listed under 'Element ID 1', then the element listed under 'Element ID 2' must also be provided. Failure to provide both data elements together in an ICSR instance will yield the instance invalid. With the exception of data element B.1.9.4.r (Autopsy-determined Cause(s) of Death) and B.1.9.3 (Was Autopsy Done?), the field under 'Element ID 2' must not be provided without providing the data element listed under 'Element ID 1.' Except as noted above, providing the field 'Element ID 2' without 'Element ID 1' will result in an invalid ICSR message.

Element id 1	Description	Element id 2	Description
B.1.2.2a	Age at Time of Onset of Reaction / Event (value)	B.1.2.2b	Age at Time of Onset of Reaction / Event (unit)
B.1.2.2.1a	Gestation Period When	B.1.2.2.1b	Gestation Period When

Element id 1	Description	Element id 2	Description
	Reaction / Event was Observed in the Foetus (value)		Reaction / Event was Observed in the Foetus (unit)
B.1.7.1.r.a.1	MedDRA Version for Medical History	B.1.7.1.r.a.2	Structured Medical Information (disease / surgical procedure / etc.)
B.1.8.r.a1	Medicinal Product Identifier (MPID)	B.1.8.r.a2	MPID Version Date/Number
B.1.8.r.a3	Pharmaceutical Product Identifier (PhPID)	B.1.8.r.a4	PhPID Version Date/Number
B.1.8.r.f.1	MedDRA version for Indication	B.1.8.r.f.2	Indication
B.1.8.r.g.1	MedDRA version for Reaction	B.1.8.r.g.2	Reaction
B.1.9.2.r.a	MedDRA version for Reported Cause(s) of Death	B.1.9.2.r.b1	Reported Cause(s) of Death (MedDRA code)
B.1.9.4.r	Autopsy-determined cause(s) of death (repeat as necessary)	B.1.9.3	Was autopsy done?
B.1.9.4.r.a	MedDRA Version for Autopsy-determined Cause(s) of Death	B.1.9.4.r.b1	Autopsy-determined Cause(s) of Death (MedDRA code)
B.1.10.2.2a	Age of Parent (age value)	B.1.10.2.2b	Age of Parent (age unit)
B.1.10.7.1.r.a.1	MedDRA Version for Parent Medical History	B.1.10.7.1.r.a.2	Structured Information (disease / surgical procedure/ etc.)
B.1.10.8.r.a1	Medicinal Product Identifier (MPID)	B.1.10.8.r.a2	MPID Version Date/Number
B.1.10.8.r.a3	Pharmaceutical Product Identifier (PhPID)	B.1.10.8.r.a4	PhPID Version Date/Number
B.1.10.8.r.f.1	MedDRA Version for Indication	B.1.10.8.r.f.2	Indication
B.1.10.8.r.g.1	MedDRA Version for Reaction	B.1.10.8.r.g.2	Reactions (if any and known)
B.2.i.5a	Duration of Reaction / Event	B.2.i.5b	Duration of Reaction / Event (duration unit)
B.3.r.c2	Test Name (MedDRA code)	B.3.r.c3	MedDRA Version for Test Name
B.4.k.2.1.1a	Medicinal Product Identifier (MPID)	B.4.k.2.1.1b	MPID Version Date/Number
B.4.k.2.1.2a	Pharmaceutical Product Identifier (PhPID)	B.4.k.2.1.2b	PhPID Version Date/Number
B.4.k.2.3.r.2a	Substance/Specified Substance TermID	B.4.k.2.3.r.2b	Substance/Specified Substance TermID Version Date/Number
B.4.k.2.3.r.3	Strength	B.4.k.2.3.r.4	Strength Unit
B.4.k.4.r.8a	Duration of Drug Administration (number)	B.4.k.4.r.8b	Duration of Drug Administration (unit)
B.4.k.4.r.11.2a	Pharmaceutical Dose Form TermID	B.4.k.4.r.11.2b	Pharmaceutical Dose Form TermID Version Date/Number
B.4.k.4.r.12.2a	Route of Administration	B.4.k.4.r.12.2b	Route of Administration

Element id 1	Description	Element id 2	Description
	TermID		TermID Version Date/Number
B.4.k.4.r.13.2a	Parent Route of Administration TermID	B.4.k.4.r.13.2b	Parent Route of Administration TermID Version Date/Number
B.4.k.5.1	Cumulative Dose to First Reaction (number)	B.4.k.5.2	Cumulative Dose to First Reaction (unit)
B.4.k.7.r.2a	Indication in MedDRA Terminology (LLT code)	B.4.k.7.r.2b	Indication in MedDRA Terminology (version)
B.4.k.9.i.3.1a	Time Interval between Beginning of Drug Administration and Start of Reaction / Event (number)	B.4.k.9.i.3.1b	Time Interval between Beginning of Drug Administration and Start of Reaction / Event (unit)
B.4.k.9.i.3.2a	Time Interval between Last Dose of Drug and Start of Reaction / Event (number)	B.4.k.9.i.3.2b	Time Interval between Last Dose of Drug and Start of Reaction / Event (unit)

4.1.1.3 Conditionally Required

These data elements might be required depending upon the value of the fields identified in the conformance column. The conditions in the conformance column will indicate the conditions which render the element mandatory.

Element id	Description	Conformance
A.1.8.1.r.1	Documents Held by Sender	Required if A.1.8.1 is 'true'
A.1.11.r.1	Source(s) of the Case Identifier	Required if A.1.11 is 'true'
A.1.11.r.2	Case Identifier(s)	Required if A.1.11 is 'true'
A.1.13.1	Reason for Nullification / Amendment	Required when A.1.13 is *not null*
A.2.r.1.4	Qualification	Required when A.2.r.1.5='1' (yes)
A.5.4	Study Type where Reaction(s) / Event(s) Were Observed	Required when A.1.4=2 (*Report from study)*
B.1.7.2	Text for Relevant Medical History and Concurrent Conditions (not including reaction / event)	Required if B.1.7.1 section is null
B.1.10.7.1.r.d	Continuing	Allowed only if B.1.10.7.1.r.f is null
B.3.r.b	Test date	Required when B.3.r.c is populated
B.3.r.c1	Test name (Free text)	Required if B.3.r.b is populated and B.3.r.c2 is not populated
B.3.r.c2	Test name (MedDRA code)	Required if B.3.r.b is populated and B.3.r.c1 is not populated
B.3.r.d1	Test Result (code)	Required when B.3.r.c is populated, and B.3.r.d2 and B.3.r.f is not populated.

Element id	Description	Conformance
B.3.r.d2	Test Result (value and qualifier)	Required when B.3.r.c is populated, and B.3.r.d1 and B.3.r.f is not populated.
B.3.r.e	Unit	Required when B.3.r.d2 populated.
B.3.r.f	Result Unstructured Data (free text)	Required when B.3.r.c is populated and B.3.r.d is not populated.
B.3.r.4	More Information Available	Required if B.3.r.c is populated
B.4.k.3.2	Country of authorisation / application	Required when B.4.k.3.1 is populated.
B.5.5.r.2	Case summary and reporter's comments language	Required if B.5.5.r.1 is populated

1857 **4.1.1.4 Required Data Elements**

1858 The data elements listed below are mandatory as per the E2B(R3) business rules and must be provided
1859 as part of the message in order for the message to properly parse. Failure to provide any of the
1860 mandatory data elements will result in an invalid ICSR message instance.

1861 **4.1.1.4.1 ICH ICSR Transmission Identification & Message Header (Batch Wrapper)**

Element id	Description	Conformance
M.1.1	Type of Messages in Batch	Required
M.1.4	Batch number	Required
M.1.5	Batch sender identifier	Required
M.1.6	Batch receiver identifier	Required
M.1.7	Date of Batch Transmission	Required
M.2.r.4	Message Identifier	Required
M.2.r.5	Message Sender Identifier	Required
M.2.r.6	Message Receiver Identifier	Required
M.2.r.7	Date of Message Creation	Required

1862 **4.1.1.4.2 Administrative and Identification Information**

1863 **4.1.1.4.2.1 Identification of the Case Safety Report (A.1)**

Element id	Description	Conformance
A.1.0.1	Sender's (case) safety report unique identifier	Required
A.1.3	Date of transmission	Required
A.1.4	Type of report	Required
A.1.6	Date report was first received from source	Required
A.1.7	Date of most recent information for this case	Required
A.1.8.1	Are additional documents available?	Required
A.1.9	Does this case fulfill the local criteria for an expedited report?	Required
A.1.10.1	Worldwide unique case identification number	Required
A.1.10.2	First sender of this case	Required
A.1.11	Other case identifiers in previous transmissions	Required

4.1.1.4.2.2 Primary Sources of Information (A.2)

Element id	Description	Conformance
A.2.r.1.5	Primary source for regulatory purposes	Required

4.1.1.4.2.3 Sender (A.3)

Element id	Description	Conformance
A.3.1	Sender type	Required
A.3.2	Sender's organisation	Required

4.1.1.4.2.4 Literature References (A.4)

No mandatory data elements.

4.1.1.4.2.5 Study Identification (A.5)

No mandatory data elements.

4.1.1.4.3 Information on the Case

4.1.1.4.3.1 Patient Characteristics (B.1)

Element id	Description	Conformance
B.1.1	Patient (name or initials)	Required
B.1.5	Sex	Required
B.1.8.r.a0	Name of drug as reported	Required

4.1.1.4.3.2 Reaction(s) / Event(s) (B.2)

Element id	Description	Conformance
B.2.i.1.a	MedDRA version for reaction / event	Required
B.2.i.1.b	Reaction/event in MedDRA terminology	Required
B.2.i.6	Outcome of Reaction / Event at the Time of Last Observation	Required

4.1.1.4.3.3 Results of Tests and Procedures Relevant to the Investigation of the Patient (B.3)

No mandatory data elements.

4.1.1.4.3.4 Drug(s) Information (repeat as necessary) (B.4)

Element id	Description	Conformance
B.4.k.1	Characterisation of Drug Role	Required
B.4.k.9	Action taken with drug	Required

4.1.1.4.3.5 Narrative Case Summary and Further Information (B.5)

Element id	Description	Conformance
B.5.1	Case narrative including clinical course, therapeutic measures, outcome and additional relevant information	Required

4.1.2 HL-7 Mandatory / Required Elements

The tables below provide a schema centric view of the mandated / required data elements. The mandatory attributes require some values and not allow null flavours while, required attributes require some values including null flavours. The set of attributes and elements in the table below are required to be present in an ICSR instance in order for that instance to properly parse and validate. If any of the set of attributes and elements is not provided, the ICSR instance is not valid. There are two primary reasons an element or attribute is listed in the table below. If the element or attribute will contain data for one of the data elements identified in section 4.1.1.4, it will be identified in the table below. In addition to the XML elements and attributes required for the mandatory elements, the presence of these elements could require the presence of additional elements. These additional elements are also identified. These tables will then consist of the minimum set of XML elements and attributes required for a valid ICSR instance.

4.1.2.1 HL-7 Mandatory Elements

Element ID	Element/Attribute	XPath
M1.4	id	/MCCI_IN200100UV01/id
M1.7	creationTime	/MCCI_IN200100UV01/creationTime
A.1.10.2	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/souceOf/relatedInvestigation/code[@code="initialReport"]
B.3.r.1	interpretationCode	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="testsAndProceduresRelevantToTheInvestigation"]/component/observation/referenceRange/observationRange/interpretationCode
B.3.r.2	interpretationCode	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="testsAndProceduresRelevantToTheInvestigation"]/component/observation/referenceRange/observationRange/interpretationCode
B.4.k.9.i.3.1a B.4.k.9.i.3.1b	id	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/outboundRelationship1[@typeCode="SAS"]/actReference/id
B.4.k.9.i.3.2a B.4.k.9.i.3.2b	id	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/outboundRelationship1[@typeCode="SAE"]/actReference/id

Element ID	Element/Attribute	XPath
B.4.k.9.i.4	id	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/outboundRelationship2/observation/outboundRelationship1/actReference/id
B.4.k.7.r.1 B.4.k.7.r.2a B.4.k.7.r.2b	id	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/inboundRelationship/observation/outboundRelationship1/actReference/id
B.4.k.2.3.r.1 B.4.k.2.3.r.2a B.4.k.2.3.r.2b B.4.k.2.3.r.3 B.4.k.2.3.r.4	ingredientSubstance	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/consumable/instanceOfKind/kindOfProduct/ingredient/ingredientSubstance
B.4.k.3.3	playingOrganization	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/consumable/instanceOfKind/kindOfProduct/asManufacturedProduct/subjectOf/approval/holder/role/playingOrganization

4.1.2.1 HL-7 Required Elements

The elements below are required and nullFlavor can be used in the case of value is null.

Element ID	Element/Attribute	XPath
A.1.0.1	id	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/id
A.1.10.1	id	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/id
B.1.2.2a B.1.2.2b	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation/code[@code="age"]
B.1.2.2.1a B.1.2.2.1b	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation/code[@code="gestationPeriod"]
B.1.2.3	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation/code[@code="ageGroup"]
B.1.3	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActPr

Element ID	Element/Attribute	XPath
		ocess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation/code[@code="bodyWeight"]
B.1.4	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation/code[@code="height"]
B.1.6	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation/code[@code="lastMenstrualPeriodDate"]
B.1.7.1.r.a.1 B.1.7.1.r.a.2	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="relevantMedicalHistoryAndconcurrentConditions"]/component/observation/code
B.1.7.1.r.d	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="relevantMedicalHistoryAndconcurrentConditions"]/component/observation/inboundRelationship2/observation/code[@code="continuing"]
B.1.7.1.r.g	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="relevantMedicalHistoryAndconcurrentConditions"]/component/observation/outboundRelationship2/observation/code[@code="comment"]
B.1.7.1.r.h	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="relevantMedicalHistoryAndconcurrentConditions"]/component/observation/outboundRelationship2/observation/code[@code="10157-6"]
B.1.7.2	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="relevantMedicalHistoryAndconcurrentConditions"]/component/observation/code[@code="historyAndConcurrentConditionText]
B.1.7.3	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="relevantMedicalHistoryAndconcurrentConditions"]/component/observation/code[@code="concommitantTherapy"]
B.1.8.r.f.1 B.1.8.r.f.2	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugHistory"]/component/substanceAdministration/outboundRelationship2/observation/code[@code="indication

Element ID	Element/Attribute	XPath
		"]
B.1.8.r.g.1 B.1.8.r.g.2	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugHistory"]/component/substanceAdministration/outboundRelationship2/observation/code[@code="reaction"]
B.1.9.2.r.a B.1.9.2.r.b1 B.1.9.2.r.b2	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation/code[@code="reportedcauseOfDeath"]
B.1.9.3	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation/code[@code="autopsy"]
B.1.9.4.r.a B.1.9.4.r.b1 B.1.9.4.r.b2	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation[code/@code="autopsy"]/outboundRelationship2/observation/code[@code="causeOfDeath"]
B.1.10.2.2a B.1.10.2.2b	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/player1/role/subjectOf2/observation/code[@code="age"]
B.1.10.3	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/player1/role/subjectOf2/observation/code[@code="lastMenstrualPeriodDate"]
B.1.10.4	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/player1/role/subjectOf2/observation/code[@code="bodyWeight"]
B.1.10.5	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/player1/role/subjectOf2/observation/code[@code="height"]
B.1.10.7.1.r.a.1 B.1.10.7.1.r.a.2	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/player1/role/subjectOf2/organizer[code/@code="relevantMedicalHistoryAndconcurrentConditions"]/component/observation/code
B.1.10.7.1.r.d	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/player1/role/subjectOf2/organizer[code/@code="relevantMedicalHistoryAndconcurrentConditions"]/component/observation/inboundRelationship2/observation/code[@code="Continuing"]
B.1.10.7.1.r.g	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/player1/role/subjectOf2/organizer[code/@code="relevantMedicalHistoryAndconcurrentConditions"]/component/observation/outboundRelationship2/o

Element ID	Element/Attribute	XPath
		bservation/code[@code="comment"]
B.1.10.7.2	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/player1/role/subjectOf2/organizer[code/@code="relevantMedicalHistoryAndconcurrentConditions"]/component/observation/code[@code="historyAndConcurrentConditionText"]
B.1.10.8.r.f1 B.1.10.8.r.f2	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/player1/role/subjectOf2/organizer[code/@code="drugHistory"]/component/substanceAdministration/outboundRelationship2/observation/code[@code="indication"]
B.1.10.8.r.g1 B.1.10.8.r.g2	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/player1/role/subjectOf2/organizer[code/@code="drugHistory"]/component/substanceAdministration/outboundRelationship2/observation/code[@code="reaction"]
B.2.i.*	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation/code[@code="reaction"]
B.2.i.0.b	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation[code/@code="reaction"]/outboundRelationship2/observation/code[@code="reactionForTranslation"]
B.2.i.2.1	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation[code/@code="reaction"]/outboundRelationship2/observation/code[@code="termHighlightedByReporter"]
B.2.i.2.2.a	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation/code[@code="reaction"]/outboundRelationship2/observation/code[@code="resultsInDeath"]
B.2.i.2.2.b	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation[code/@code="reaction"]/outboundRelationship2/observation/code[@code="isLifeThreatening"]
B.2.i.2.2.c	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation[code/@code="reaction"]/outboundRelationship2/observation/code[@code="requiresInpatientHospitalization"]
B.2.i.2.2.d	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation[code

Element ID	Element/Attribute	XPath
		/@code="reaction"]/outboundRelationship2/observation/code[@code="resultsInPersistentOrSignificantDisability"]
B.2.i.2.2.e	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation[code/@code="reaction"]/outboundRelationship2/observation/code[@code="congenitalAnomalyBirthDefect"]
B.2.i.2.2.f	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation[code/@code="reaction"]/outboundRelationship2/observation/code[@code="otherMedicallyImportantCondition"]
B.2.i.6	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation[code/@code="reaction"]/outboundRelationship2/observation/code[@code="outcome"]
B.2.i.7	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation[code/@code="reaction"]/outboundRelationship2/observation/code[@code="medicalConfirmationByHealthProfessional"]
B.3.r.c1 B.3.r.c2 B.3.r.c3	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="testsAndProceduresRelevantToTheInvestigation"]/component/observation/code
B.3.r.3	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="testsAndProceduresRelevantToTheInvestigation"]/component/observation/outboundRelationship2/observation/code[@code="comment"]
B.3.r.4	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="testsAndProceduresRelevantToTheInvestigation"]/component/observation/outboundRelationship2/observation/code[@code="moreInformationAvailable"]
B.4.k.2.5	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/outboundRelationship2/observation/code[@code="blinded"]
B.4.k.4.r.13.2a B.4.k.4.r.13.2b B.4.k.4.r.13.1	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/outboundRelationship2/substanceAdministration/inboundRelationship/observation/code[/@code="parentRouteOfAd

Element ID	Element/Attribute	XPath
		ministration"]
B.4.k.5.1 B.4.k.5.2	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/outboundRelationship2/observation/code[@code="cumulativeDoseToReaction"]
B.4.k.6a B.4.k.6b	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/outboundRelationship2/observation/code[@code="gestationPeriod"]
B.4.k.7.r.1 B.4.k.7.r.2a B.4.k.7.r.2b	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/inboundRelationship/observation/code[@code="indication"]
B.4.k.9.i.4	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/outboundRelationship2/observation/code[@code="recurranceOfReaction"]
B.4.k.10.r	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/outboundRelationship2/observation/code[@code="codedDrugInformation"]
B.4.k.11	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/outboundRelationship2/observation/code[@code="additionalInformation"]
B.3.r.1	value	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="testsAndProceduresRelevantToTheInvestigation"]/component/observation/referenceRange/obsrevationRange[interpretationCode/@code="L"]/value
B.3.r.2	value	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="testsAndProceduresRelevantToTheInvestigation"]/component/observation/referenceRange/obsrevationRange[interpretationCode/@code="H"]/value
B.4.k.8	code	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAs

Element ID	Element/Attribute	XPath
		sessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/inboundRelationship/act/code
B.4.k.2.3.r.1	name	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/consumable/instanceOfKind/kindOfProduct/ingredient/ingredientSubstance/name
B.4.k.2.4	representedOrganization	/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/organizer[code/@code="drugInformation"]/component/substanceAdministration/consumable/instanceOfKind/subjectOf/productEvent/performer/assignedEntity/representedOrganization

5.0 THE ICSR ACKNOWLEDGEMENT TRANSACTION

The acknowledgment transaction will be sent after receipt of an ICH ICSR. The message includes a standard ICH ICSR header, an acknowledgment for the message, and a repeating detail section that provides information about specific problems found in the original 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 the batch.

Acknowledgement Message in HL7

Within HL7 messaging, this functionality is managed using the Response Batch Wrapper. Note: the response batch, like the batch wrapper and the transmission wrapper, contains a "stub" class that makes it possible to associate the batch with a variety of different message types. For our purposes, that message type will be the Application Response Message.
For the purposes of this guide, 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, MCCI_MT200101UV, and, as the stub, MCCI_MT002300UV. (Review the HL7 ballot package to determine necessary edits to the schemas provided) If you are working with the HL7 published schemas, COCT_MT040203UV (R_NotificationParty) and any contained schemas will be needed as well.

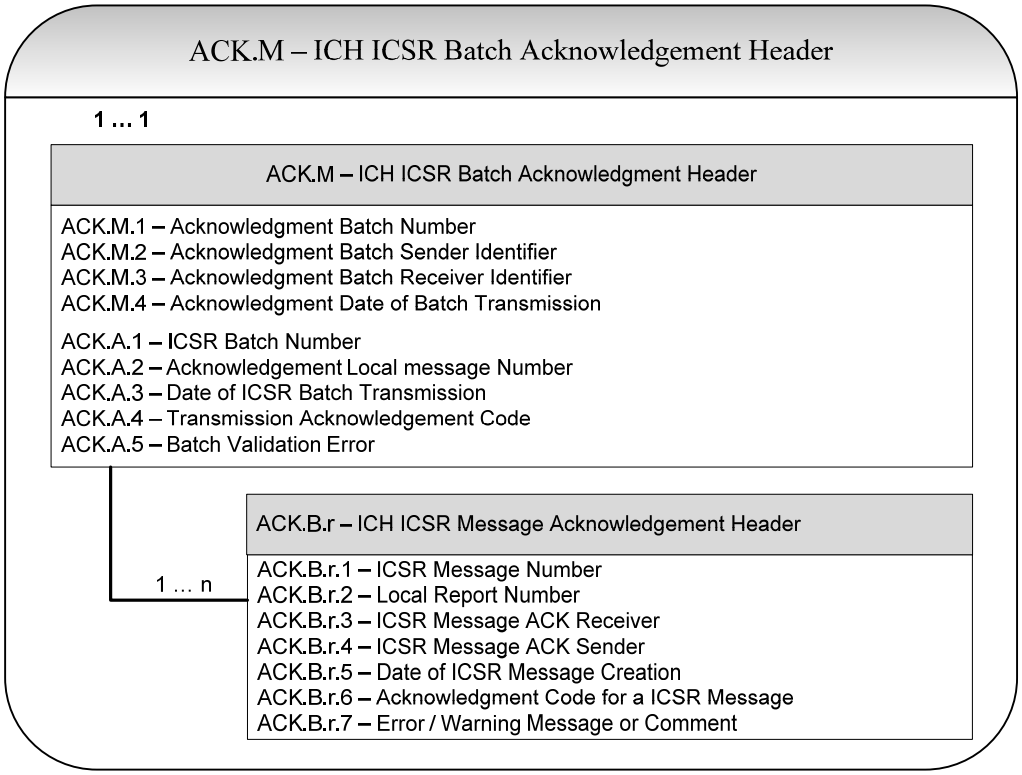
For the purposes of this guide, it will be assumed that all transactions are batched, and that all responses will refer to the original batch wrapper, as well as to the message.

ICH ICSR Acknowledgement Message

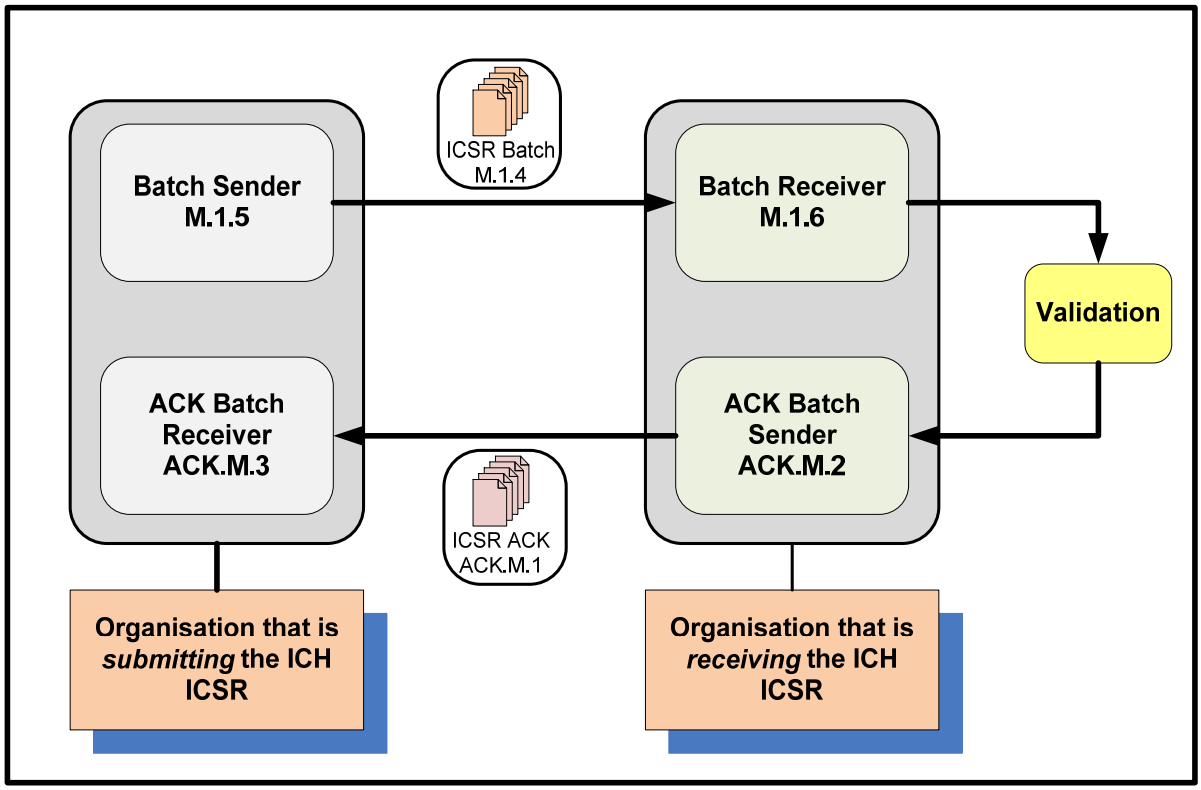
The Acknowledgement header contains core transactional information related to the receipt of batch transmission. The data elements used for the ICH ICSR Acknowledgement are described below.

Elements beginning with ACK.M contain technical information required for Acknowledgement message. 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, this structure provides information for the batch as opposed to each ICSR message. 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 messages within a batch, and with 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 submission. The diagram below illustrates the submission and acknowledgement transaction at the batch message level.



1932

1933 **ACK.M ICH ICSR Batch Acknowledgement Header**

1934 **ACK.M.1 Acknowledgement Batch Number**

User Guidance	The batch number is a unique tracking number assigned to a specific 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)	

1935 **ACK.M.2 Acknowledgement Batch Sender Identifier**

User Guidance	This field identifies the sender of the ICH ICSR Acknowlegement batch file (creator of ICH ICSR Acknowledgement batch file), e.g. company name or regulatory authority
Conformance	Required
Data Type	60AN
OID	ich-ack-batch-sender-identifier-oid
Value Allowed	Free text
Business Rule(s)	
	This should be the same identifier as M.1.6. The following notation will be used to represent ACK.M.2: <id extension="acknowledement sender identifier" root="ich-ack-batch-sender-identifier-oid"/>

	The sender identifier should be agreed between trading partners.

1936 **ACK.M.3 Acknowledgement Batch Receiver Identifier**

User Guidance	This field identifies the intended recipient of the transmission of ICSR batch file.
Conformance	Required
Data Type	60AN
OID	ich-ack-batch-receiver-identifier-oid
Value Allowed	Free text
Business Rule(s)	
	This should be the same identifier as M.1.5. The following notation will be used to represent ACK.M.3: <id extension="acknowledgement receiver identifier" root=" ich-ack-batch-receiver-identifier-oi "/> The sender identifier should be agreed between trading partners.

1937 **ACK.M.4 Acknowledgement Date of Batch Transmission**

User Guidance	The batch date is the date on which the ICH ICSR Acknowledgement batch file was transmitted.
Conformance	Required
Data Type	Date
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). The date specified cannot refer to a future date. The date should be local time at point of transmission of ICSR message.

1938

1939 **ACK.A.1 ICSR Batch Numberr**

User Guidance	A unique tracking number assigned to a specific ICH ICSR batch file by the sender. This ICSR batch number is unique to the sender of the ICH ICSR batch. It identifies the transaction (that is the batch) that is being acknowledged.
Conformance	Required
Data Type	100AN
OID	None
Value Allowed	N/A
Business Rule(s)	
	This should be the same number as M.1.4 of the batch being acknowleged.

1940 **ACK.A.2 Acknowledgement Local Message Number**

User Guidance	A value assigned to the ICH ICSR batch acknowledgement by the organisation sending the acknowledgement which is the receiver of the

	original ICH ICSR batch.
Conformance	Optional
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	

1941 **ACK.A.3 Date of ICSR Batch Transmission**

User Guidance	The date on which the transaction being acknowledged was originally sent.
Conformance	Required
Data Type	Date
OID	None
Value Allowed	See Appendix II for further information
Business Rule(s)	
	This should be the same date as M.1.7.

1942 **ACK.A.4 Transmission Acknowledgement Code**

User Guidance	A code to inform the sender of the submitted ICH ICSR batch whether to re-send the entire transaction, or to review the remainder of the acknowledgement to determine which ICSR messages are specifically cited.
Conformance	Required
Data Type	2A
OID	None
Value Allowed	AA – Application Acknowledgement Accept (message successfully processed) AE – Application Acknowledgment Error (error detected, error response has additional detail) AR – Application Acknowledgment Reject (parsing error, no data extracted)
Business Rule(s)	

1943 **ACK.A.5 Batch Validation Error**

User Guidance	A text field that can be used to describe ICH ICSR batch XML errors detected. This should contain the reason for AR in ACK.A.4.
Conformance	Optional
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

1944

1945 **ACK.B.r – ICH ICSR Message Acknowledgement Header**

1946 **ACK.B.r.1 ICSR Message Number**

User Guidance	The number assigned by the sender of the batch submitted to identify each ICH ICSR message (each message within a batch.)
Conformance	Required
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	
	This is the same as M.2.r.4

1947

1948 **ACK.B.r.2 Local Report Number**

User Guidance	A value assigned to the ICH ICSR message by the batch receiving organisation.
Conformance	Optional
Data Type	100AN
OID	None
Value Allowed	Free text
Business Rule(s)	

1949

1950 **ACK.B.r.3 ICSR Message ACK Receiver**

User Guidance	This field identifies the sender of the submitted ICH ICSR message (creator of ICH ICSR message), e.g. company name or regulatory authority
Conformance	Required
Data Type	60AN
OID	ich-ack-receiver-identifier-oid
Value Allowed	Free text
Business Rule(s)	
	This should be the same identifier as M.2.r.5. The following notation will be used to represent ACK.B.r.3: <id extension="ack receiver identifier" root="ich-ack-receiver-identifier-oid "/> The ACK receiver identifier should be agreed between trading partners.

1951 **ACK.B.r.4 ICSR Message ACK Sender**

User Guidance	This field identifies the recipient of the submitted ICSR message.
Conformance	Required
Data Type	60AN
OID	ich-ack-sender-identifier-oid
Value Allowed	Free text
Business Rule(s)	
	This should be the same identifier as M.2.r.6. The following notation will be used to represent ACK.B.r.4: <id extension="ack sender identifier" root="ich-ack-sender-identifier-oid"/> The ACK sender identifier should be agreed between trading partners.

1952 **ACK.B.r.5 Date of ICSR Message Creation**

User Guidance	The date of the ICSR message was created.
Conformance	Required
Data Type	Date
OID	None
Value Allowed	See Appendix II for fhuether information
Business Rule(s)	
	This should be the same as M.2.r.7.

1953

1954

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

User Guidance	An indication of whether or not the ICH ICSR message was successfully processed by the receiving application. A value of CR indicateds that the ICSR contains at least 1 fatal error that prevents the ICSR from being loaded.
Conformance	Required
Data Type	2AN
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	A brief description of the error or errors that were detected in a ICH ICSR message. This should contain the reason for CR in ACK.B.r.6. It can also contain non fatal warning messages even though ACK.B.r.6 is CA.
Conformance	Optional
Data Type	250AN
OID	None
Value Allowed	Free text
Business Rule(s)	

5.1 Example ICSR Acknowledgement Transaction

```
<?xml version="1.0" encoding="utf-8"?>
<!-- Reference Instance for ICSR ACK, v0.1 - 30/07/2010 -->
<MCCI_IN200101UV01 ITSVersion="XML_1.0" xsi:schemaLocation="urn:hl7-org:v3
MCCI_IN200101UV01.xsd" xmlns="urn:hl7-org:v3"
xmlns:fo="http://www.w3.org/1999/XSL/Format" xmlns:mif="urn:hl7-org:v3/mif"
xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
  <id extension="ACK.M.1" root="ich-ack-batch-number-oid"/>
  <!-- ACK.M.1: Acknowledgement Batch Number -->
  <creationTime value="20100729102030"/>
  <!-- ACK.M.4: Acknowledgement Date of Batch Transmission -->
  <responseModeCode code="D"/>
  <interactionId extension="MCCI_IN200100UV01" root="2.16.840.1.113883.1.6"/>
  <!-- Ack Message #1 -->
  <MCCI_IN000002UV01>
    <id extension="ACK.B.r.2" root="ich-local-report-number-oid"/>
    <!-- ACK.B.r.2 Local Report Number -->
    <creationTime value="20100729102030"/>
    <!-- ACK.M.4: Acknowledgement Date of Batch Transmission -->
    <interactionId extension="MCCI_IN000002UV01" root="2.16.840.1.113883.1.6"/>
    <processingCode code="P"/>
    <processingModeCode code="T"/>
```

```
    <acceptAckCode code="NE"/>
    <receiver typeCode="RCV">
      <device classCode="DEV" determinerCode="INSTANCE">
        <id extension="ACK.B.r3" root="ich-ack-receiver-identifier-oid"/>
        <!-- ACK.B.r.3: ICSR Message Ack Receiver -->
      </device>
    </receiver>
    <sender typeCode="SND">
      <device classCode="DEV" determinerCode="INSTANCE">
        <id extension="ACK.B.r.4" root="ich-ack-sender-identifier-oid"/>
        <!-- ACK.B.r.4: ICSR Message Ack Sender -->
      </device>
    </sender>
    <attentionLine>
      <keyWordText code="receiptDate" codeSystem="ich-date-of-creation-oid"/>
      <value xsi:type="TS" value="20100722"/>
      <!-- ACK.B.r.5: Date of ICSR Message Creation -->
    </attentionLine>
    <acknowledgement typeCode="AE">
      <!-- ACK.B.r.6::Acknowledgement Code for a ICSR Message -->
      <targetMessage>
        <id extension="ACK.B.r.1" root="ich-senders-safety-report-identifier-oid"/>
        <!-- ACK.B.r.1: ICSR Message Number -->
      </targetMessage>
      <acknowledgementDetail>
        <text>ACK.B.r.7</text>
        <!-- ACK.B.r.7: Error Message or Comment -->
      </acknowledgementDetail>
    </acknowledgement>
  </MCCI_IN000002UV01>
  <!-- Ack Message #1 -->
  <!-- Ack Message #2 -->
  <MCCI_IN000002UV01>
    <id extension="ACK.B.r.2" root="ich-local-report-number-oid"/>
    <!-- ACK.B.r.2 Local Report Number -->
    <creationTime value="20100729102030"/>
    <!-- ACK.M.4: Acknowledgement Date of Batch Transmission -->
    <interactionId extension="MCCI_IN000002UV01" root="2.16.840.1.113883.1.6"/>
    <processingCode code="P"/>
    <processingModeCode code="T"/>
    <acceptAckCode code="NE"/>
    <receiver typeCode="RCV">
      <device classCode="DEV" determinerCode="INSTANCE">
        <id extension="ACK.B.r3" root="ich-ack-receiver-identifier-oid"/>
        <!-- ACK.B.r.3: ICSR Message Ack Receiver -->
      </device>
    </receiver>
    <sender typeCode="SND">
      <device classCode="DEV" determinerCode="INSTANCE">
```

```
2028          <id extension="ACK.B.r.4" root="ich-ack-sender-identifier-oid"/>
2029          <!-- ACK.B.r.4: ICSR Message Ack Sender -->
2030        </device>
2031      </sender>
2032      <attentionLine>
2033        <keyWordText code="dateOfIcsrMessageCreation" codeSystem="ich-date-of-creation-
2034    oid"/>
2035        <value xsi:type="TS" value="20100722"/>
2036        <!-- ACK.B.r.5: Date of ICSR Message Creation -->
2037      </attentionLine>
2038      <acknowledgement typeCode="CR">
2039        <!-- ACK.B.r.6::Acknowledgement Code for a ICSR Message -->
2040        <targetMessage>
2041          <id extension="ACK.B.r.1" root="ich-senders-safety-report-identifier-oid"/>
2042          <!-- ACK.B.r.1: ICSR Message Number -->
2043        </targetMessage>
2044        <acknowledgementDetail>
2045          <text>ACK.B.r.7</text>
2046          <!-- ACK.B.r.7: Error Warning Message or Comment -->
2047        </acknowledgementDetail>
2048      </acknowledgement>
2049    </MCCI_IN000002UV01>
2050    <!-- Ack Message #2 -->
2051    <receiver typeCode="RCV">
2052      <device classCode="DEV" determinerCode="INSTANCE">
2053        <id extension="ACK.M.3" root="ich-ack-batch-receiver-identifier-oid"/>
2054        <!-- ACK.M.3: Acknowledgement Batch Receiver Identifier -->
2055      </device>
2056    </receiver>
2057    <sender typeCode="SND">
2058      <device classCode="DEV" determinerCode="INSTANCE">
2059        <id extension="ACK.M.2" root="ich-ack-batch-sender-identifier-oid"/>
2060        <!-- ACK.M.2: Acknowledgement Batch Sender Identifier -->
2061      </device>
2062    </sender>
2063    <attentionLine>
2064      <keyWordText code="acknowledgementLocalMessageNumber" codeSystem="ich-
2065    attentionLine-code-oid"/>
2066      <value xsi:type="II" extension="ACK.A.2" root="ich-ack-local-message-number-oid"/>
2067      <!-- ACK.A.2: Acknowledgement Local Message Number -->
2068    </attentionLine>
2069    <attentionLine>
2070      <keyWordText code="dateOfIcsrBatchTransmission" codeSystem="ich-attentionLine-
2071    code-oid"/>
2072      <value xsi:type="TS" value="20100722"/>
2073      <!-- ACK.A.3: Date of ICSR Batch Transmission -->
2074    </attentionLine>
2075    <acknowledgement typeCode="AE">
2076      <!-- ACK.A.4: Transmission Acknowledgement Code -->
```

```
    <targetBatch>
      <id extension="ACK.A.1" root="sender-identifier-value"/>
      <!-- ACK.A.1: ICSR Batch Number -->
      <!-- the sender-identifier-value is the batch sender value in M.1.4 -->
    </targetBatch>
    <acknowledgementDetail>
      <text>ACK.A.5</text>
      <!-- ACK.A.5: Batch Validation Error -->
    </acknowledgementDetail>
  </acknowledgement>
</MCCI_IN200101UV01>
```

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) – Backwards & Forwards Compatibility

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

Appendix I (B) – SGML & XML conversion

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

Appendix I (C) – ICH and HL7 Data Types

The following table lists the ICH data type and its corresponding HL7 data type by data element number.

ICH elements that require data type AN and require HL7 data type ED must use attribute mediaType set to text/plain. There are two exceptions A.1.8.1.r.1 and A.4.r.2, in these elements use appropriate mediaType for the included content.

Data Element Identifier	ICH Data Type	HL7 Data Type
B.4.k.1 Characterisation of Drug Role	ICH Data Type: 1N	HL7 Data Type: Coded With Equivalents (CE)
B.4.k.2.1.1a MPID	ICH Data Type: Refer to M5 guideline	HL7 Data Type: Coded With Equivalents (CE)
B.4.k.2.1.1b MPID Version Date	ICH Data Type: Refer to M5 guideline	HL7 Data Type: Coded With Equivalents (CE)
B.4.k.2.1.2a PhPID	ICH Data Type: Refer to M5 guideline	HL7 Data Type: Coded With Equivalents (CE)

Data Element Identifier	ICH Data Type	HL7 Data Type
B.4.k.2.1.2b PhPID Version Date	I ICH Data Type: Refer to M5 guideline	HL7 Data Type: Coded With Equivalents (CE)
B.4.k.2.2 Medicinal Product Name as Reported by the Primary Source	ICH Data Type: 250AN	HL7 Data Type: Product.name =Entity Name (EN)
B.4.k.2.3.r.1 Substance / Specified Substance Name	ICH Data Type: 250AN	HL7 Data Type: IngredientSubstance.name=Trivial Name (TN)
B.4.k.2.3.r.2a Substance / Specified Substance TermID	ICH Data Type: Refer to M5 guideline	HL7 Data Type: Substance.code=Coded With Equivalents (CE)
B.4.k.2.3.r.2b Substance/Specified Substance TermID Version Date	ICH Data Type: Refer to M5 guideline	HL7 Data Type: Substance.code=Coded With Equivalents (CE)
B.4.k.2.3.r.3 Strength	ICH Data Type: 10N	HL7 Data Type: Ingredient. quantity = Physical Quantity (PQ) value = REAL
B.4.k.2.3.r.4 Strength Unit	ICH Data Type: 50AN	HL7 Data Type: Ingredient. quantity = Physical Quantity (PQ) unit = Coded Simple Value (CS)
B.4.k.2.4 Identification of the Country Where the Drug Was Obtained	ICH Data Type: 2A	HL7 Data Type: Organization.add = Postal Address (AD)
B.4.k.2.5 Investigational Product Blinded	ICH Data Type: Boolean	HL7 Data Types: Observation value=Boolean (BL)
B.4.k.3.1 Authorisation / Application Number	ICH Data Type: 35AN	HL7 Data Type: ManufacturedProduct.id=Instance Identifier (II)
B.4.k.3.2 Country of Authorisation / Application	ICH Data Type: 2A	HL7 Data Type: Territory.code = Coded With Equivalents (CE)
B.4.k.3.3 Name of Holder / Applicant	ICH Data Type: 60AN	HL7 Data Type: Organization Name (ON)
B.4.k.4.r.1 Dose (number)	ICH Data Type: 8N	HL7 Data Type: DoseQuantity Value=REAL
B.4.k.4.r.2 Dose (unit)	ICH Data Type: 50AN	HL7 Data Type: doseQuantity Unit=Coded Simple Value (CS)
B.4.k.4.r.4 Number of Units in the Interval	ICH Data Type: 4N	HL7 Data Types: effectiveTime=General Timing Specification (GTS)
B.4.k.4.r.5 Definition of the Time Interval Unit	ICH Data Type: 50AN	HL7 Data Types: Time Interval Unit=Coded Simple Value (CS)
B.4.k.4.r.6 Date and Time of Start of Drug	ICH Data Type: Date	HL7 Data Types: effectiveTime=General Timing Specification (GTS) *Note GTS is further constrained to Interval of Point in Time (TS)

Data Element Identifier	ICH Data Type	HL7 Data Type
B.4.k.4.r.7 Date and Time of Last Administration	ICH Data Type: Date	HL7 Data Types: effectiveTime=General Timing Specification (GTS) *Note GTS is further constrained to Interval of Point in Time (TS)
B.4.k.4.r.8a Duration of Drug Administration (number)	ICH Data Type: 5N	HL7 Data Types: effectiveTime=General Timing Specification (GTS) *Note GTS is further constrained to Interval of Point in Time (TS)
B.4.k.4.r.8b Duration of Drug Administration (unit)	ICH: 50AN	HL7 Data Types: effectiveTime=General Timing Specification (GTS) *Note GTS is further constrained to Interval of Point in Time (TS)
B.4.k.4.r.9 Batch / Lot Number	ICH Data Type: 35AN	HL7 Data Type: lotNumberText=Character String (ST)
B.4.k.4.r.10 Dosage Text	ICH Data Type: 2000AN	HL7 Data Type: Encapsulated Data (ED)
B.4.k.4.r.11.1 Pharmaceutical Dose Form	ICH Data Type: 60AN	HL7 Data Type: originalText = Encapsulated Data (ED)
B.4.k.4.r.11.2a Pharmaceutical Dose Form TermID	ICH Data Type: Refer to M5 guideline	HL7 Data Type: formCode = Coded With Equivalents (CE)
B.4.k.4.r.11.2b Pharmaceutical Dose Form Term ID Version Date	ICH Data Type: Refer to M5 guideline	HL7 Data Type: Coded With Equivalents (CE)
B.4.k.4.r.12.1 Route of Administration	ICH Data Type: 60AN	HL7 Data Type: Coded With Equivalents (CE)
B.4.k.4.r.12.2a Route of Administration TermID	ICH Data Type: Refer to M5 guideline Until M5 is available, this is 3N	HL7 Data Type: Coded With Equivalents (CE)
B.4.k.4.r.12.2b Route of Administration TermID Version Date	ICH Data Type: Refer to M5 guideline	HL7 Data Type: Coded With Equivalents (CE)
B.4.k.4.r.13.1 Parent Route of Administration	ICH Data Type: 60AN	HL7 Data Type: Coded With Equivalents (CE)
B.4.k.4.r.13.2a Parent Route of Administration TermID	ICH Data Type: Refer to M5 guideline Until M5 is available, this is 3N	HL7 Data Type: Coded With Equivalents (CE)
B.4.k.4.r.13.2b Parent Route of Administration TermID Version Date	ICH Data Type: Refer to M5 guideline	HL7 Data Type: Coded With Equivalents (CE)
B.4.k.5.1 Cumulative Dose to First Reaction (number)	ICH Data Type: 10N	HL7 Data Type: Physical Quantity (PQ) Value = REAL

Data Element Identifier	ICH Data Type	HL7 Data Type
B.4.k.5.2 Cumulative Dose to First Reaction (unit)	ICH Data Type: 50AN	HL7 Data Type: Physical Quantity (PQ) Unit=Coded Simple Value (CS)
B.4.k.6a Gestation Period at Time of Exposure (number)	ICH Data Type: 3N	HL7 Data Type: Physical Quantity (PQ) Translation = Physical Quantity Representation (PQR)
B.4.k.6b Gestation Period at Time of Exposure (unit)	ICH Data Type: 50AN	HL7 Data Type: codeSystem = Unique Identifier String (UID)
B.4.k.7.r.1 Indication as Reported by the Primary Source	ICH Data Type: 250AN	HL7 Data Type: ANY
B.4.k.7.r.2a Indication in MedDRA Terminology (version)	ICH Data Type: 4AN	HL7 Data Type: Coded with Equivalents (CE)
B.4.k.7.r.2b Indication in MedDRA Terminology (LLT code)	ICH Data Type: 8AN	HL7 Data Type: ANY
B.4.k.8 Action Taken with Drug	ICH Data Type: 1N	HL7 Data Type: Coded with Equivalents (CE)
B.4.k.9.i.1 Reaction(s) / Event(s) Assessed	ICH Data Type: N/A	HL7 Data Type: N/A
B.4.k.9.i.2.r.1 Source of Assessment	ICH Data Type 60AN	HL7 Data Type: originalText = Encapsulated Data (ED)
B.4.k.9.i.2.r.2 Method of Assessment	ICH Data Type: 60AN	HL7 Data Type: originalText = Encapsulated Data (ED)
B.4.k.9.i.2.r.3 Result of Assessment	ICH Data Type: 60AN	HL7 Data Type: ANY
B.4.k.9.r.3.1a Time Interval between Beginning of Drug Administration and Start of Reaction / Event	ICH Data Type: 5N	HL7 Data Type: pauseQuantity.Value =REAL
B.4.k.9.i.3.1b Time Interval between Beginning of Drug Administration and Start of Reaction / Event (unit)	ICH Data Type: 50AN	HL7 Data Type: pauseQuantity.Unit = Coded Simple Value (CS)
B.4.k.9.i.3.2a Time Interval Between Last Dose of Drug and Start of Reaction / Event	ICH Data Type: 5N	HL7 Data Type: pauseQuantity.Value =REAL
B.4.k.9.i.3.2b Time Interval Between Last Dose of Drug and Start of Reaction / Event (unit)	ICH Data Type: 50AN	HL7 Data Type: pauseQuantity.Unit = Coded Simple Value (CS)
B.4.k.9.i.4 Did Reaction Recur on Re-administration	ICH Data Type: 1N	HL7 Data Type: Coded with Equivalents (CE)
B.4.k.10.r Additional information on drug (Coded)	ICH Data Type: 1N	HL7 Data Type: Coded with Equivalents (CE)
B.4.k.11 Additional Information on drug (Free text)	ICH Data Type: 2000AN	HL7 Data Type: Coded with Equivalents (CE)

Data Element Identifier	ICH Data Type	HL7 Data Type
B.5.1 Case Narrative Including Clinical Course, Therapeutic Measures, Outcome and Additional Relevant Information	ICH Data Type: 100000AN	HL7 Data Type: Encapsulated Data (ED)
B.5.2 Reporter's Comments	ICH Data Type: 20000AN	HL7 Data Type: Encapsulated Data (ED)
B.5.3.r.1 MedDRA Version for Sender's Diagnosis / Syndrome and / or Reclassification of Reaction / Event (repeat as necessary)	ICH Data Type: 4AN	HL7 Data Type: Coded with Equivalents (CE)
B.5.3.r2 Sender's Diagnosis / Syndrome and / or Reclassification of Reaction / Event (repeat as necessary)	ICH Data Type: 8N	HL7 Data Type: Coded with Equivalents (CE)

2111 **Appendix I (D) – HL7 Business Rule(s) For ICH Data Elements**

Data Element ID	Data Element Name	Related HL7 Business Rule
A.1.3	Date of Creation	There must one instance of element "effectiveTime" below "controlActProcess" per case safety report in the ICSR message.
A.1.4	Type of Report	There must one instance of element "code" below the element "investigationEvent" for each case safety report in the ICSR message.
A.1.8.1	Are Additional Documents Available?	The information is stored within the "obseverationEvent" field identified with a code value set to "DA" (Document Available).
A.1.8.1.r.1	Documents Held by Sender	• In the case of multiple documents, the element "pertainsTo" should repeat as needed to store the document information within separate fields. • Supplemental information can be provided by an attachment. If attaching an explanatory document, please refer to Section 3.5.
A.1.9	Does this Case Fulfill the Local Criteria for an Expedited Report?	The element "reference" can repeat but there must be a single occurrence of element "reference" containing an "observationEvent" with "code" set to "localCriteriaForExpedited".
A.1.10.2	First Sender of this Case	The element "support" can repeat but there must be a single occurrence of element "support" containing a "relatedReport" with "code" set to "INITIAL".
A.1.11	Other Case Identifiers in Previous Transmissions	The element "pertinentInformation" can repeat but there must be a single occurrence of element "pertinentInformation" containing a "reportingCriteria" with "code" set to "othercaseIDs".
A.1.11.r.1	Source(s) of the Case Identifier	The same "id" must be used for the source and identifier of the same case.

Data Element ID	Data Element Name	Related HL7 Business Rule
A.1.11.r.2	Case Identifier(s)	The same "id" must be used for the source and identifier of the same case.
A.1.12.r	Identification Number of the Report Which Is Linked to this Report	• The element "id" must repeat with the same observation code, e.g. "OTHER", for each linked report number applicable. • There must be a single "relatedReport" field with observation code set to "OTHER" for a given case safety report.
A.1.13	Report Nullification / Amendment	The element "pertinentInformation" can repeat but there must be a single occurrence of the element “pertinentInformation” containing a “reportingCriteria” with “code” set to “NullificationAmendmentCode”
A.1.13.1	Reason for Nullification / Amendment	The element "pertinentInformation" can repeat but there must be a single occurrence of the element “pertinentInformation” containing a “reportingCriteria” with “code” set to “nullificationAmmendmentReason”.
B.1.10.1	Parent Identification	If the information is “UNKNOWN”, then use nullFlavor element with “UNK” as unknown. In the case of “PRIVACY”, use nullFlavor element with “MSK” as masked.

APPENDIX II – DATE / TIME

ICH has elected to utilise the International Standard ISO 8601 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. ISO 8601 notation is the commonly recommended format for representing date and time as human-readable strings in communication protocols and file formats. Several standards and profiles have been derived from ISO 8601, including RFC 3339 and a W3C note on date and time formats.

ISO 8601 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. For ICH purposes, punctuation should be omitted utilising the more compact version of the ISO 8601 date and time format standards (Note: examples with punctuation have been omitted). This will help avoid confusion for international communication[14].

Appendix II (A) Date

The international standard date notation is **CCYYMMDD** where CCYY is the century and year in the usual Gregorian calendar, MM is the month of the year between 01 (January) and 12 (December), and DD is the day of the month between 01 and 31.

Example: the fourth day of February, 1995 is written as **19950204**

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

[14] “A summary of the international standard date and time notation,” Markus Kuhn, University of Cambridge Computer Laboratory, Cambridge, England, http://www.cl.cam.ac.uk/~mgk25/iso-time.html

Example: **199502**

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

Appendix II (B) Time

The international standard notation for the time-of-day is **hhmmss** where hh is the number of complete hours that have passed since midnight (00-24), mm is the number of complete minutes that have passed since the start of the hour (00-59), and ss is the number of complete seconds since the start of the minute (00-59). Note: If the hour value is 24, then the minute and second values must be zero.

Example: 235959 - represents the time one second before midnight.

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 or comma

Example: 235959.9942 is 5.8 ms before midnight

As every day both starts and ends 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.

In short, the syntax is "CCYYMMDDhhmmss. Common forms are "CCYYMMDD" and "CCYYMMDDHHMM."

Appendix II (C) 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. Universal Time (also known as "Zulu Time") was called Greenwich Mean Time (GMT) 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.

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

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

Appendix II (D) ISO 8601 Compliant Examples (traditionally used with HL7)

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:
1994-11-05T08:15:30-05:00 =19941105081530-0500
- or –
1994-11-05T13:15:30Z =19941105131530Z
To further illustrate date and time: June 1, 2005, at 3:31:15:05 pm Pacific Time Zone
To the millisecond: 20090601231150.5 or 200906011531150.5-0800
To the second: 20090601T33115Z
To the minute: 20090601T2331Z
To the hour: 20090601T23Z
To the day: 20090601
To the month: 200906
To the year: 2009

APPENDIX III - 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 / Adverse experience	Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment.
Acknowledgement of Receipt	The acknowledgement of receipt is the procedure by which on receipt of the safety message the syntax and semantics are checked. [EMEA]
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. [EMEA]

Term	Definition
Adverse Drug Reaction (ADR) or Adverse Reaction	In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) can not 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).
Case	An observation requiring investigation, and includes problems that might or might not involve individual or groups of investigative subjects. [HL7 Patient Safety]
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][15]
Drug	(See Medicinal Product)
Electronic Data Interchange (EDI)	US draft: The computer-to-computer interchange of strictly formatted messages that represent documents other than monetary instruments. EDI implies a sequence of messages between two parties, either of whom can serve as originator or recipient. The formatted data representing the documents can be transmitted from originator to recipient via telecommunications or physically transported on electronic storage media. EU draft: EDI is the electronic transfer, from computer to computer, of commercial and administrative data using an agreed standard to structure an EDI message. EDI is based on the use of structured and coded messages, the main characteristic of which is their ability to be processed by computers and transmitted automatically and without ambiguity. This makes EDI specific in comparison with other data exchange such as electronic mail.
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. [EMEA]

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

Term	Definition
The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)	The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is a project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration. The Observers are WHO, EFTA, and Canada (represented by Health Canada).
EDI Partner	Organisations that send or receive documents from each other based upon an agreement about the specific information to be transmitted and how it should be used.
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. [prEN27953 Human Pharmaceutical Reporting]
Interim reporter	A professional or public organisation who is monitoring, receiving and assessing ADR reports from health professionals and consumers and reporting significant ADRs to regulatory or statutory authority in its own region. [ISO/TS 22224:2007]
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 prEN 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]
National Pharmacovigilance Centre	A single, governmentally recognised centre (or integrated system) within a country with the clinical and scientific expertise to collect, collate, analyse and give advice on all information related to drug safety.

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	Generic transmission use case A thing or things produced by labour or effort for a specific use and marketed to satisfy a need or want. [HL7 Patient Safety]
Product Manufacturer	The organisation which is responsible for the manufacture of a medicinal product. This entity might or might not be the same as the marketing authorisation holder of the medicinal product. regulatory agency (or authorities)
Regulatory Agency or Regulatory Authorities	Geopolitical entities have established agencies/authority 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.
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. [EMEA]
Serious Adverse Reaction or Serious Adverse Drug Reaction	An adverse reaction which is fatal (results in death), is life threatening, requires hospitalisation or prolongation of a hospitalisation, results in persistent or significant disability/incapacity, results in a congenital anomaly/birth defect or is a medically important condition.
Sponsor	An individual, company, institution or organisation which takes responsibility for the initiation, management and/or financing of a clinical trial. [Article 2e; European Directive 2001/20/EC]
Spontaneous Reporting	An unsolicited communication to a company, regulatory authority or other organization 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.
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.

Term	Definition
Use Case	A description of a system's behaviour as it responds to a request that originates from outside of that system. [Objectory AB]

APPENDIX IV - EXAMPLES AND SAMPLE MESSAGES

Appendix IV (A) Sample ICSR Message Instance

The XML instance below is intended to assist tool developers by providing a reasonably complete representation of the content that would be contained in an ICSR message. It is not a complete message as the message header is missing. This instance does not contain every possible individual data element as some data elements can not logically be combined. The structure of the instance is technically sound and it can be used as a baseline going forward.

```
<?xml version="1.0" encoding="UTF-8"?>
<MCCI_IN200100UV01 ITSVersion="XML_1.0" xsi:schemaLocation="urn:hl7-org:v3
MCCI_IN200100UV01.xsd" xmlns="urn:hl7-org:v3" xmlns:mif="urn:hl7-org:v3/mif"
xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
  <id extension="M.1.4" root="sender-identifier-value"/>
  <!-- M.1.4: Batch Number -->
  <creationTime value="20101214151617"/>
  <!-- M.1.7: Date of Batch Transmission -->
  <responseModeCode code="D"/>
  <interactionId extension="MCCI_IN200100UV01" root="2.16.840.1.113883.1.6"/>
  <name code="M.1.1" codeSystem="ich-type-of-message-in-batch-oid"/>
  <!-- M.1.1: Type of Messages in Batch -->
  <!-- Message #1 -->
  <PORR_IN049016UV>
    <id extension="M.2.r.4" root="ich-senders-safety-report-identifier-oid"/>
    <!-- M.2.r.4: Message Identifier -->
    <creationTime value="20101214151617"/>
    <!-- M.2.r.7: Date of Message Creation -->
    <interactionId extension="MCCI_IN200100UV01" root="2.16.840.1.113883.1.6"/>
    <processingCode code="P"/>
    <processingModeCode code="T"/>
    <acceptAckCode code="AL"/>
    <receiver typeCode="RCV">
      <device classCode="DEV" determinerCode="INSTANCE">
        <id extension="M.2.r.6" root="ich-message-receiver-identifier-oid"/>
        <!-- M.2.r.6: Message Receiver Identifier -->
      </device>
    </receiver>
    <sender typeCode="SND">
      <device classCode="DEV" determinerCode="INSTANCE">
        <id extension="M.2.r.5" root="ich-message-sender-identifier-oid"/>
        <!-- M.2.r.5: Message Sender Identifier -->
      </device>
    </sender>
    <controlActProcess moodCode="EVN" classCode="CACT">
      <code code="PORR_TE049016UV" codeSystem="2.16.840.1.113883.1.18"/>
      <!-- HL7 Trigger Event ID -->
      <effectiveTime value="20101214"/>
      <!-- A1.3: Date of Creation -->
      <subject typeCode="SUBJ">
        <investigationEvent classCode="INVSTG" moodCode="EVN">
          <id extension="A.1.0.1" root="ich-senders-safety-report-identifier-oid"/>
          <!-- A.1.0.1: Sender's (case) Safety Report Unique Identifier -->
```

```
2262          <id extension="A.1.10.1" root="ich-worldwide-case-identifier-oid"/>
2263          <!-- A.1.10.1: Worldwide Unique Case Idntification number -->
2264          <code code="PAT_ADV_EVNT" codeSystem="2.16.840.1.113883.5.4"/>
2265          <text>B.5.1</text>
2266          <!-- B.5.1: Case Narrative Including Clinical Course, Therapeutic Measures, Outcome and Additional
2267    Relevant Information -->
2268          <statusCode code="active"/>
2269          <effectiveTime>
2270            <low value="20090101"/>
2271            <!-- A1.6: Date Report Was First Received from the Source -->
2272          </effectiveTime>
2273          <availabilityTime value="20090101"/>
2274          <!-- A1.7: Date of Most Recent Information for this report -->
2275          <reference typeCode="REFR">
2276            <document classCode="DOC" moodCode="EVN">
2277              <title>A.1.8.1.r.1 Documents Held by Sender</title>
2278              <!-- A.1.8.1.r.1: Documents Held by Sender -->
2279              <text mediaType="application/pdf" representation="B64">A.1.8.1.r.2</text>
2280              <!-- A.1.8.1.r.2: Included documents -->
2281            </document>
2282          </reference>
2283          <reference typeCode="REFR">
2284            <document classCode="DOC" moodCode="EVN">
2285              <title>A.1.8.1.r.1 Documents Held by Sender</title>
2286              <!-- A.1.8.1.r.1: Documents Held by Sender -->
2287              <text mediaType="image/jpeg" representation="B64" compression="DF">A.1.8.1.r.2</text>
2288              <!-- A.1.8.1.r.2: Included documents -->
2289            </document>
2290          </reference>
2291          <reference typeCode="REFR">
2292            <document classCode="DOC" moodCode="EVN">
2293              <text mediaType="application/pdf" representation="B64">A.4.r.2</text>
2294              <!-- A.4.r.2: Included documents -->
2295              <bibliographicDesignationText>A.4.r.1</bibliographicDesignationText>
2296              <!-- A.4.r.1: Literature Reference(s) -->
2297            </document>
2298          </reference>
2299          <component typeCode="COMP">
2300            <adverseEventAssessment classCode="INVSTG" moodCode="EVN">
2301              <subject1 typeCode="SBJ">
2302                <primaryRole classCode="INVSBJ">
2303                  <player1 classCode="PSN" determinerCode="INSTANCE">
2304                    <name>B.1.1</name>
2305                    <!-- B.1.1:  Patient (name or initials) -->
2306                    <administrativeGenderCode code="B.1.5" codeSystem="1.0.5218"/>
2307                    <!-- B.1.5 Sex [1] Male [2]Femail -->
2308                    <birthTime value="20090101"/>
2309                    <!-- B.1.2.1: Date of Birth -->
2310                    <deceasedTime value="20090101"/>
2311                    <!-- B.1.9.1: Date of Death -->
2312                    <asIdentifiedEntity classCode="IDENT">
2313                      <id extension="B.1.1.1a" root="ich-gp-medical-record-number-oid"/>
2314                      <!-- B.1.1.1a: Patient Medical Record Number(s) and the Source(s) of the Record Number (GP
2315    Medical Record Number) -->
2316                      <code code="gpmrn" codeSystem="ich-gp-medical-record-number-oid"/>
2317                    </asIdentifiedEntity>
2318                    <asIdentifiedEntity classCode="IDENT">
2319                      <id extension="B.1.1.1b" root="ich-specialist-record-number-oid"/>
```

```
<!-- B.1.1.1b: Patient Medical Record Number(s) and the Source(s) of the Record Number (Specialist Record Number) -->
<code code="specialistMrn" codeSystem="ich-specialist-medical-record-number-oid"/>
</asIdentifiedEntity>
<asIdentifiedEntity classCode="IDENT">
<id extension="B.1.1.1c" root="ich-hospital-record-number-oid"/>
<!-- B.1.1.1c: Patient Medical Record Number(s) and the Source(s) of the Record Number (Hospital Record Number) -->
<code code="hospitalMrn" codeSystem="ich-hospital-medical-record-number-oid"/>
</asIdentifiedEntity>
<asIdentifiedEntity classCode="IDENT">
<id extension="B.1.1.1d" root="ich-investigation-number-oid"/>
<!-- B.1.1.1d: Patient Medical Record Number(s) and the Source(s) of the Record Number (Investigation Number) -->
<code code="investigation" codeSystem="ch-investigation-medical-record-number-oid"/>
</asIdentifiedEntity>
<role classCode="PRS">
<code code="PRN" codeSystem="2.16.840.1.113883.5.111"/>
<associatedPerson determinerCode="INSTANCE" classCode="PSN">
<name>B.1.10.1</name>
<!-- B.1.10.1:  Parent Indentification -->
<administrativeGenderCode code="B.1.10.6" codeSystem="1.0.5218"/>
<!-- B.1.10.6: Sex of Parent [1]Male [2]Female-->
<birthTime value="20090101"/>
<!-- B.1.10.2.1: Date of Birth of Parent -->
</associatedPerson>
<subjectOf2 typeCode="SBJ">
<observation moodCode="EVN" classCode="OBS">
<code code="age" codeSystem="ich-observation-code-oid"/>
<value xsi:type="PQ" value="10" unit="B.1.10.2.2b"/>
<!-- B.1.10.2.2a: Age of Parent (age value) -->
<!-- B.1.10.2.2b: Age of Parent (age unit) -->
</observation>
</subjectOf2>
<subjectOf2 typeCode="SBJ">
<observation moodCode="EVN" classCode="OBS">
<code code="lastMenstrualPeriodDate" codeSystem="ich-observation-code-oid"/>
<value xsi:type="TS" value="20090101"/>
<!-- B.1.10.3: Last Menstrual Period Date of Parent -->
</observation>
</subjectOf2>
<subjectOf2 typeCode="SBJ">
<observation moodCode="EVN" classCode="OBS">
<code code="bodyweight" codeSystem="ich-observation-code-oid"/>
<value xsi:type="PQ" unit="kg" value="10"/>
<!-- B.1.10.4: Body Weight (kg) of Parent-->
</observation>
</subjectOf2>
<subjectOf2 typeCode="SBJ">
<observation moodCode="EVN" classCode="OBS">
<code code="height" codeSystem="ich-observation-code-oid"/>
<value xsi:type="PQ" unit="cm" value="10"/>
<!-- B.1.10.5: Height (cm) of Parent-->
</observation>
</subjectOf2>
<subjectOf2 typeCode="SBJ">
<organizer classCode="CATEGORY" moodCode="EVN">
<code code="relevantMedicalHistoryAndConcurrentConditions" codeSystem="TBD"/>
<component typeCode="COMP">
```

```
                    <observation moodCode="EVN" classCode="OBS">
                     <code code="B.1.10.7.1.r.a2" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.1.10.7.1.r.a.1"/>
                     <!-- B.1.10.7.1.r.a1: MedDRA Version for Parent Medical History -->
                     <!-- B.1.10.7.1.r.a2: Structured Information (disase / surgical procedure/ etc.) -->
                     <effectiveTime xsi:type="IVL_TS">
                      <low value="20090101"/>
                      <!-- B.1.10.7.1.r.c: Start Date -->
                      <high value="20090101"/>
                      <!-- B.1.10.7.1.r.f: End Date -->
                     </effectiveTime>
                     <outboundRelationship2 typeCode="COMP">
                      <observation moodCode="EVN" classCode="OBS">
                       <code code="comment" codeSystem="ich-observation-code-oid"/>
                       <value xsi:type="ED">B.1.10.7.1.r.g</value>
                       <!-- B.1.10.7.1.r.g: Comments -->
                      </observation>
                     </outboundRelationship2>
                     <inboundRelationship typeCode="REFR">
                      <observation moodCode="EVN" classCode="OBS">
                       <code code="continuing" codeSystem="ich-observation-code-oid"/>
                       <value xsi:type="BL" value="true"/>
                       <!-- B.1.10.7.1.r.d: Continuing -->
                      </observation>
                     </inboundRelationship>
                    </observation>
                   </component>
                   <component typeCode="COMP">
                    <observation moodCode="EVN" classCode="OBS">
                     <code code="historyAndConcurrentConditionText" codeSystem="ich-observation-code-
oid"/>
                     <value xsi:type="ED">B.1.10.7.2</value>
                     <!-- B.1.10.7.2: Text for Relevant Medical History and Concurrent Condition of Parent -->
                    </observation>
                   </component>
                  </organizer>
                 </subjectOf2>
                 <subjectOf2 typeCode="SBJ">
                  <organizer classCode="CATEGORY" moodCode="EVN">
                   <code code="drugHistory" codeSystem="TBD"/>
                   <component typeCode="COMP">
                    <substanceAdministration moodCode="EVN" classCode="SBADM">
                     <effectiveTime xsi:type="IVL_TS">
                      <low value="20090101"/>
                      <!-- B.1.10.8.r.c: Start Date -->
                      <high value="20090101"/>
                      <!-- B.1.10.8.r.e: End Date -->
                     </effectiveTime>
                     <consumable typeCode="CSM">
                      <instanceOfKind classCode="INST">
                       <kindOfProduct classCode="MMAT" determinerCode="KIND">
                        <code code="B.1.10.8.r.a1" codeSystem="TBD" codeSystemVersion="B.1.10.8.r.a2"/>
                        <!-- B.1.10.8.r.a1: Medicinal Products Identifier (MPID) -->
                        <!-- B.1.10.8.r.a2: MPID Version Date/Number -->
                        <name>B.1.10.8.r.a0</name>
                        <!-- B.1.10.8.r.a0: Name of Drug as Reported -->
                       </kindOfProduct>
                      </instanceOfKind>
                     </consumable>
```

```
                    <outboundRelationship2 typeCode="RSON">
                     <observation moodCode="EVN" classCode="OBS">
                      <code code="indication" codeSystem="ich-observation-code-oid"/>
                      <value xsi:type="CE" code="B.1.10.8.r.f.2" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.1.10.8.r.f.1"/>
                      <!-- B.1.10.8.r.f.1: MedDRA Version for Indication -->
                      <!-- B.1.10.8.r.f.2: Indication -->
                     </observation>
                    </outboundRelationship2>
                    <outboundRelationship2 typeCode="CAUS">
                     <observation moodCode="EVN" classCode="OBS">
                      <code code="reaction" codeSystem="ich-observation-code-oid"/>
                      <value xsi:type="CE" code="B.1.10.8.r.g.2" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.1.10.8.r.g.1"/>
                      <!-- B.1.10.8.r.g.1: MedDRA Version for Reaction -->
                      <!-- B.1.10.8.r.g.2: Reactions (if any and known) -->
                     </observation>
                    </outboundRelationship2>
                   </substanceAdministration>
                  </component>
                  <component typeCode="COMP">
                   <substanceAdministration moodCode="EVN" classCode="SBADM">
                    <effectiveTime xsi:type="IVL_TS">
                     <low value="20090101"/>
                     <!-- B.1.10.8.r.c: Start Date -->
                     <high value="20090101"/>
                     <!-- B.1.10.8.r.e: End Date -->
                    </effectiveTime>
                    <consumable typeCode="CSM">
                     <instanceOfKind classCode="INST">
                      <kindOfProduct classCode="MMAT" determinerCode="KIND">
                       <code code="B.1.10.8.r.a3" codeSystem="TBD" codeSystemVersion="B.1.10.8.r.a4"/>
                       <!-- B.1.10.8.r.a3: PhPID (PhPID) -->
                       <!-- B.1.10.8.r.a4: PhPID Version Date/Number -->
                       <name>B.1.10.8.r.a0</name>
                       <!-- B.1.10.8.r.a0: Name of Drug as Reported -->
                      </kindOfProduct>
                     </instanceOfKind>
                    </consumable>
                    <outboundRelationship2 typeCode="RSON">
                     <observation moodCode="EVN" classCode="OBS">
                      <code code="indication" codeSystem="ich-observation-code-oid"/>
                      <value xsi:type="CE" code="B.1.10.8.r.f.2" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.1.10.8.r.f.1"/>
                      <!-- B.1.10.8.r.f.1: MedDRA Version for Indication -->
                      <!-- B.1.10.8.r.f.2: Indication -->
                     </observation>
                    </outboundRelationship2>
                    <outboundRelationship2 typeCode="CAUS">
                     <observation moodCode="EVN" classCode="OBS">
                      <code code="reaction" codeSystem="ich-observation-code-oid"/>
                      <value xsi:type="CE" code="B.1.10.8.r.g.2" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.1.10.8.r.g.1"/>
                      <!-- B.1.10.8.r.g.1: MedDRA Version for Reaction -->
                      <!-- B.1.10.8.r.g.2: Reactions (if any and known) -->
                     </observation>
                    </outboundRelationship2>
                   </substanceAdministration>
                  </component>
```

```
                </organizer>
              </subjectOf2>
            </role>
          </player1>
          <subjectOf1 typeCode="SBJ">
            <researchStudy classCode="CLNTRL" moodCode="EVN">
              <id extension="A.5.3" root="oidSponsorStudyNumber"/>
              <!-- A.5.3: Sponsor Study Number -->
              <code code="A.5.4" codeSystem="ich-study-type-oid"/>
              <!-- A.5.4: Study Type Where Reaction(s) / Event(s) Were Observed [1] Clinical trials [2]
Individual patient use [3] Other studies-->
              <title>A.5.2</title>
              <!-- A.5.2: Study Name -->
              <authorization typeCode="AUTH">
                <studyRegistration classCode="ACT" moodCode="EVN">
                  <id extension="A.5.1.r.1" root="oidStudyRegistrationNumber"/>
                  <!-- A.5.1.r.1: Study Registration Number -->
                  <author typeCode="AUT">
                    <territorialAuthority classCode="TERR">
                      <governingPlace classCode="COUNTRY" determinerCode="INSTANCE">
                        <code code="A.5.1.r.2" codeSystem="1.0.3166.1.2.2"/>
                        <!-- A.5.1.r.2: Study Registration Country -->
                      </governingPlace>
                    </territorialAuthority>
                  </author>
                </studyRegistration>
              </authorization>
            </researchStudy>
          </subjectOf1>
          <subjectOf2 typeCode="SBJ">
            <observation moodCode="EVN" classCode="OBS">
              <code code="age" codeSystem="ich-observation-code-oid"/>
              <value xsi:type="PQ" value="10" unit="B.1.2.2b"/>
              <!-- B.1.2.2a: Age at Time of Onset of Reaction / Event (value) -->
              <!-- B.1.2.2b: Age at Time of Onset of Reaction / Event (unit) -->
            </observation>
          </subjectOf2>
          <subjectOf2 typeCode="SBJ">
            <observation moodCode="EVN" classCode="OBS">
              <code code="gestationPeriod" codeSystem="ich-observation-code-oid"/>
              <value xsi:type="PQ" value="10" unit="B.1.2.2.1b"/>
              <!-- B.1.2.2.1a: Gestation Period When Reaction / Event Was Observed in the Fetus (value) -->
              <!-- B.1.2.2.1b: Gestation Period When Reaction / Event Was Observed in the Fetus (unit) -->
            </observation>
          </subjectOf2>
          <subjectOf2 typeCode="SBJ">
            <observation moodCode="EVN" classCode="OBS">
              <code code="ageGroup" codeSystem="ich-observation-code-oid"/>
              <value xsi:type="CE" code="B.1.2.3" codeSystem="ich-patient-age-group-oid"/>
              <!-- B.1.2.3: Patient Age Group [0]Fetus [1]Neonate [2]Infant [3]Child [4]Adolescent [5]Adult
[6]Elderly -->
            </observation>
          </subjectOf2>
          <subjectOf2 typeCode="SBJ">
            <observation moodCode="EVN" classCode="OBS">
              <code code="bodyweight" codeSystem="ich-observation-code-oid"/>
              <value xsi:type="PQ" unit="kg" value="48.2"/>
              <!-- B.1.3: Body Weight (kg) -->
            </observation>
```

```
2556                </subjectOf2>
2557                <subjectOf2 typeCode="SBJ">
2558                  <observation moodCode="EVN" classCode="OBS">
2559                    <code code="height" codeSystem="ich-observation-code-oid"/>
2560                    <value xsi:type="PQ" unit="cm" value="152"/>
2561                    <!-- B.1.4: Height (cm) -->
2562                  </observation>
2563                </subjectOf2>
2564                <subjectOf2 typeCode="SBJ">
2565                  <observation moodCode="EVN" classCode="OBS">
2566                    <code code="lastMenstrualPeriodDate" codeSystem="ich-observation-code-oid"/>
2567                    <value xsi:type="TS" value="20090101"/>
2568                    <!-- B.1.6: Last Menstrual Period Date -->
2569                  </observation>
2570                </subjectOf2>
2571                <subjectOf2 typeCode="SBJ">
2572                  <organizer>
2573                    <code code="relevantMedicalHistoryAndConcurrentConditions" codeSystem="TBD"/>
2574                    <component typeCode="COMP">
2575                      <observation moodCode="EVN" classCode="OBS">
2576                        <code code="B.1.7.1.r.a.2" codeSystem="2.16.840.1.113883.6.163"
2577    codeSystemVersion="B.1.7.1.r.a.1"/>
2578                        <!-- B.1.7.1.r.a.1: MedDRA Version for Medical History -->
2579                        <!-- B.1.7.1.r.a.2: Structured Medical History Information (disease, surgical procedure, etc.) -->
2580                        <effectiveTime xsi:type="IVL_TS">
2581                          <low value="20090101"/>
2582                          <!-- B.1.7.1.r.c: Start Date -->
2583                          <high value="20090101"/>
2584                          <!-- B.1.7.1.r.f: End Date -->
2585                        </effectiveTime>
2586                        <outboundRelationship2 typeCode="COMP">
2587                          <observation moodCode="EVN" classCode="OBS">
2588                            <code code="comment" codeSystem="ich-observation-code-oid"/>
2589                            <value xsi:type="ED">B.1.7.1.r.g</value>
2590                            <!-- B.1.7.1.r.g: Comments -->
2591                          </observation>
2592                        </outboundRelationship2>
2593                        <!--B.1.7.1.r.h (Family History of the disease/surgical procedure) is in the message because it is
2594    true, if false the following snippet would not appear -->
2595                        <outboundRelationship2 typeCode="EXPL">
2596                          <observation moodCode="EVN" classCode="OBS">
2597                            <code code="10157-6" codeSystem="2.16.840.1.113883.6.12"/>
2598                            <!-- B.1.7.1.r.h Family History -->
2599                          </observation>
2600                        </outboundRelationship2>
2601                        <inboundRelationship typeCode="REFR">
2602                          <observation moodCode="EVN" classCode="OBS">
2603                            <code code="continuing" codeSystem="ich-observation-code-oid"/>
2604                            <value xsi:type="BL" value="true"/>
2605                            <!-- B.1.7.1.r.d: Continuing -->
2606                          </observation>
2607                        </inboundRelationship>
2608                      </observation>
2609                    </component>
2610                    <component typeCode="COMP">
2611                      <observation moodCode="EVN" classCode="OBS">
2612                        <code code="historyAndConcurrentConditionText" codeSystem="ich-observation-code-oid"/>
2613                        <value xsi:type="ED">B.1.7.2</value>
```

```
                    <!-- B.1.7.2: Text for Relevant medical History and Concurrent Conditions (not including
reaction / event) -->
                  </observation>
                 </component>
                 <component typeCode="COMP">
                  <observation moodCode="EVN" classCode="OBS">
                   <code code="concommitantTherapy" codeSystem="ich-observation-code-oid"/>
                   <value xsi:type="BL" value="true"/>
                   <!-- B.1.7.3:  Concomitant therapies-->
                  </observation>
                 </component>
                </organizer>
               </subjectOf2>
               <subjectOf2 typeCode="SBJ">
                <organizer>
                 <code code="drugHistory" codeSystem="TBD"/>
                 <component typeCode="COMP">
                  <substanceAdministration moodCode="EVN" classCode="SBADM">
                   <effectiveTime xsi:type="IVL_TS">
                    <low value="20090101"/>
                    <!-- B.1.8.r.c: Start Date -->
                    <high value="20090101"/>
                    <!-- B.1.8.r.e: End Date -->
                   </effectiveTime>
                   <consumable>
                    <instanceOfKind classCode="INST">
                     <kindOfProduct classCode="MMAT" determinerCode="KIND">
                      <code code="B.1.8.r.a1" codeSystem="TBD" codeSystemVersion="B.1.8.r.a2"/>
                      <!-- B.1.8.r.a1: Medicinal Product Identifier (MPID) -->
                      <!-- B.1.8.r.a2: MPID Version Date/Number -->
                      <name>B.1.8.r.a0</name>
                      <!-- B.1.8.r.a0: Name of Drug as Reported -->
                     </kindOfProduct>
                    </instanceOfKind>
                   </consumable>
                   <outboundRelationship2 typeCode="RSON">
                    <observation moodCode="EVN" classCode="OBS">
                     <code code="indication" codeSystem="ich-observation-code-oid"/>
                     <value xsi:type="CE" code="B.1.8.r.f.2" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.1.8.r.f.1"/>
                     <!-- B.1.8.r.f.1: MedDRA Version for Indication -->
                     <!-- B.1.8.r.f.2: Indication -->
                    </observation>
                   </outboundRelationship2>
                   <outboundRelationship2 typeCode="CAUS">
                    <observation moodCode="EVN" classCode="OBS">
                     <code code="reaction" codeSystem="ich-observation-code-oid"/>
                     <value xsi:type="CE" code="B.1.8.r.g.2" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.1.8.r.g.1"/>
                     <!-- B.1.8.r.g.1: MedDRA Version for Reaction -->
                     <!-- B.1.8.r.g.2: Reaction -->
                    </observation>
                   </outboundRelationship2>
                  </substanceAdministration>
                 </component>
                 <component typeCode="COMP">
                  <substanceAdministration moodCode="EVN" classCode="SBADM">
                   <effectiveTime xsi:type="IVL_TS">
                    <low value="20090101"/>
```

```
                    <!-- B.1.8.r.c: Start Date -->
                    <high value="20090101"/>
                    <!-- B.1.8.r.e: End Date -->
                  </effectiveTime>
                  <consumable>
                    <instanceOfKind classCode="INST">
                      <kindOfProduct classCode="MMAT" determinerCode="KIND">
                        <code code="B.1.8.r.a3" codeSystem="TBD" codeSystemVersion="B.1.8.r.a4"/>
                        <!-- B.1.8.r.a3: Pharmaceutical product Identifier (PhPID) -->
                        <!-- B.1.8.r.a4: PhPID Version Date/Number -->
                        <name>B.1.8.r.a0</name>
                        <!-- B.1.8.r.a0: Name of Drug as Reported -->
                      </kindOfProduct>
                    </instanceOfKind>
                  </consumable>
                  <outboundRelationship2 typeCode="RSON">
                    <observation moodCode="EVN" classCode="OBS">
                      <code code="indication" codeSystem="ich-observation-code-oid"/>
                      <value xsi:type="CE" code="B.1.8.r.f.2" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.1.8.r.f.1"/>
                      <!-- B.1.8.r.f.1: MedDRA Version for Indication -->
                      <!-- B.1.8.r.f.2: Indication -->
                    </observation>
                  </outboundRelationship2>
                  <outboundRelationship2 typeCode="CAUS">
                    <observation moodCode="EVN" classCode="OBS">
                      <code code="reaction" codeSystem="ich-observation-code-oid"/>
                      <value xsi:type="CE" code="B.1.8.r.g.2" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.1.8.r.g.1"/>
                      <!-- B.1.8.r.g.1: MedDRA Version for Reaction -->
                      <!-- B.1.8.r.g.2: Reaction -->
                    </observation>
                  </outboundRelationship2>
                </substanceAdministration>
              </component>
            </organizer>
          </subjectOf2>
          <subjectOf2 typeCode="SBJ">
            <observation moodCode="EVN" classCode="OBS">
              <code code="reportedCauseOfDeath" codeSystem="ich-observation-code-oid"/>
              <value xsi:type="CE" code="B.1.9.2.r.b1" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.1.9.2.r.a">
                <!-- B.1.9.2.r.a: MedDRA Version for Reported Cause(s) of Death -->
                <!-- B.1.9.2.r.b1: Reported Cause(s) of Death -->
                <originalText>B.1.9.2.r.b2</originalText>
                <!-- B.1.9.2.r.b2: Reported Cause(s) of Death -->
              </value>
            </observation>
          </subjectOf2>
          <subjectOf2 typeCode="SBJ">
            <observation moodCode="EVN" classCode="OBS">
              <code code="autopsy" codeSystem="ich-observation-code-oid"/>
              <value xsi:type="BL" value="true"/>
              <!-- B.1.9.3  Was autopsy done -->
              <outboundRelationship2 typeCode="DRIV">
                <observation moodCode="EVN" classCode="OBS">
                  <code code="causeOfDeath" codeSystem="ich-observation-code-oid"/>
                  <value xsi:type="CE" code="B.1.9.4.r.b1" codeSystemVersion="B.1.9.4.r.a">
                    <!-- B.1.9.4.r.a: MedDRA Version for Autopsy-determined Cause(s) of Death -->
```

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                    <!-- B.1.9.4.r.b1 Autopsy-determined Cause(s) of Death -->
                    <originalText>B.1.9.4.r.b2</originalText>
                    <!-- B.1.9.4.r.b2: Autopsy-determined Cause(s) of Death -->
                   </value>
                  </observation>
                 </outboundRelationship2>
                </observation>
               </subjectOf2>
               <subjectOf2 typeCode="SBJ">
                <observation moodCode="EVN" classCode="OBS">
                 <id extension="1" root="oidInternalReferencesToReaction"/>
                 <code code="reaction" codeSystem="ich-observation-code-oid"/>
                 <effectiveTime xsi:type="IVL_TS">
                  <low value="20090101"/>
                  <!-- B.2.i.3 Date of Start of Reaction / Event -->
                  <high value="20090102"/>
                  <!-- B.2.i.4: Date of End of Reaction / Event -->
                 </effectiveTime>
                 <value xsi:type="CE" code="B.2.i.1.b" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.2.i.1.a">
                  <!-- B.2.i.1.a: MedDRA Version for Reaction / Event -->
                  <!-- B.2.i.1.b: Reaction / Event in MedDRA Terminology-->
                  <originalText language="B.2.i.0.a2">B.2.i.0.a1</originalText>
                  <!-- B.2.i.0.a1: Reaction / Event as Reported by the Primary Source in Native Language -->
                  <!-- B.2.i.0.a2: Reaction / Event as Reported by the Primary Source Language -->
                 </value>
                 <location typeCode="LOC">
                  <locatedEntity classCode="LOCE">
                   <locatedPlace classCode="COUNTRY" determinerCode="INSTANCE">
                    <code code="B.2.i.8" codeSystem="1.0.3166.1.2.2"/>
                    <!-- B.2.i.8: Identification of the Country Where the Reaction / Event Occurred -->
                   </locatedPlace>
                  </locatedEntity>
                 </location>
                 <outboundRelationship2 typeCode="PERT">
                  <observation moodCode="EVN">
                   <code code="reactionForTranslation" codeSystem="ich-observation-code-oid"/>
                   <value xsi:type="ED">B.2.i.0.b</value>
                   <!-- B.2.i.0.b: Reaction / Event as Reported by the Primary Source for Translation -->
                  </observation>
                 </outboundRelationship2>
                 <outboundRelationship2 typeCode="PERT">
                  <observation moodCode="EVN" classCode="OBS">
                   <code code="termHighlightedByReporter" codeSystem="ich-observation-code-oid"/>
                   <value xsi:type="CE" code="B.2.i.2.1" codeSystem="ich-term-hilighted-oid"/>
                   <!-- B.2.i.2.1: Term Highlighted by the Reporter [1]no, serious [2]yes, serious [3]no, non seious
[4]yes, no serious -->
                  </observation>
                 </outboundRelationship2>
                 <outboundRelationship2 typeCode="PERT">
                  <observation moodCode="EVN" classCode="OBS">
                   <code code="resultsInDeath" codeSystem="ich-observation-code-oid"/>
                   <value xsi:type="BL" value="true"/>
                   <!-- B.2.i.2.2: Seriousness Criteria at Event Level (Results in Death) -->
                  </observation>
                 </outboundRelationship2>
                 <outboundRelationship2 typeCode="PERT">
                  <observation moodCode="EVN" classCode="OBS">
                   <code code="isLifeThreatening" codeSystem="ich-observation-code-oid"/>
```

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2791                    <value xsi:type="BL" nullFlavor="NI"/>
2792                    <!-- B.2.i.2.2: Seriousness Criteria at Event Level (Life Threatening) -->
2793                   </observation>
2794                  </outboundRelationship2>
2795                  <outboundRelationship2 typeCode="PERT">
2796                   <observation moodCode="EVN" classCode="OBS">
2797                    <code code="requiresInpatientHospitalization" codeSystem="ich-observation-code-oid"/>
2798                    <value xsi:type="BL" value="true"/>
2799                    <!-- B.2.i.2.2: Seriousness Criteria at Event Level (Caused / Prolonged Hospitalisation) -->
2800                   </observation>
2801                  </outboundRelationship2>
2802                  <outboundRelationship2 typeCode="PERT">
2803                   <observation moodCode="EVN" classCode="OBS">
2804                    <code code="resultsInPersistentOrSignificantDisability" codeSystem="ich-observation-code-
2805    oid"/>
2806                    <value xsi:type="BL" nullFlavor="NI"/>
2807                    <!-- B.2.i.2.2: Seriousness Criteria at Event Level (Disabling / Incapacitating)  -->
2808                   </observation>
2809                  </outboundRelationship2>
2810                  <outboundRelationship2 typeCode="PERT">
2811                   <observation moodCode="EVN" classCode="OBS">
2812                    <code code="congenitalAnomalyBirthDefect" codeSystem="ich-observation-code-oid"/>
2813                    <value xsi:type="BL" nullFlavor="NI"/>
2814                    <!-- B.2.i.2.2: Seriousness Criteria at Event Level (Congenital Anomaly / Birth Defect) -->
2815                   </observation>
2816                  </outboundRelationship2>
2817                  <outboundRelationship2 typeCode="PERT">
2818                   <observation moodCode="EVN" classCode="OBS">
2819                    <code code="otherMedicallyImportantCondition" codeSystem="ich-observation-code-oid"/>
2820                    <value xsi:type="BL" value="true"/>
2821                    <!-- B.2.i.2.2: Seriousness Criteria at Event Level (Other Medically Important Condition) -->
2822                   </observation>
2823                  </outboundRelationship2>
2824                  <outboundRelationship2 typeCode="PERT">
2825                   <observation moodCode="EVN" classCode="OBS">
2826                    <code code="outcome" codeSystem="ich-observation-code-oid"/>
2827                    <value xsi:type="CE" code="1" codeSystem="ich-outcome-of-reaction-event-oid"/>
2828                    <!-- B.2.i.6: Outcome of Reaction / Event at the Time of Last Observation
2829    [1]recovered/resolved [2]recovering/resolving [3]not recovered/not resolved/ongoing
2830                     [4]recovered/resolved with sequelae [5]fatal [6]unknown -->
2831                   </observation>
2832                  </outboundRelationship2>
2833                  <outboundRelationship2 typeCode="PERT">
2834                   <observation moodCode="EVN" classCode="OBS">
2835                    <code code="medicalConfirmationByHealthProfessional" codeSystem="ich-observation-code-
2836    oid"/>
2837                    <value xsi:type="BL" value="true"/>
2838                    <!-- B.2.i.7: Medical Confirmation by Healthcare Professional -->
2839                   </observation>
2840                  </outboundRelationship2>
2841                 </observation>
2842                </subjectOf2>
2843                <subjectOf2 typeCode="SBJ">
2844                 <observation moodCode="EVN" classCode="OBS">
2845                  <id extension="2" root="oidInternalReferencesToReaction"/>
2846                  <code code="reaction" codeSystem="ich-observation-code-oid"/>
2847                  <effectiveTime xsi:type="IVL_TS">
2848                   <low value="20090101"/>
2849                   <!-- B.2.i.3 Date of Start of Reaction / Event -->
```

```
                    <width value="24" unit="B.2.i.5b"/>
                    <!-- B.2.i.5a: Duration of Reaction / Event -->
                    <!-- B.2.i.5b: Duration of Reaction / Event (Duration Unit) -->
                   </effectiveTime>
                   <value xsi:type="CE" code="B.2.i.1.b" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.2.i.1.a">
                    <!-- B.2.i.1.a: MedDRA Version for Reaction / Event -->
                    <!-- B.2.i.1.b: Reaction / Event in MedDRA Terminology-->
                    <originalText language="B.2.i.0.a2">B.2.i.0.a1</originalText>
                    <!-- B.2.i.0.a1: Reaction / Event as Reported by the Primary Source in Native Language -->
                    <!-- B.2.i.0.a2: Reaction / Event as Reported by the Primary Source Language -->
                   </value>
                   <location typeCode="LOC">
                    <locatedEntity classCode="LOCE">
                     <locatedPlace classCode="COUNTRY" determinerCode="INSTANCE">
                      <code code="B.2.i.8" codeSystem="1.0.3166.1.2.2"/>
                      <!-- B.2.i.8: Identification of the Country Where the Reaction / Event Occurred -->
                     </locatedPlace>
                    </locatedEntity>
                   </location>
                   <outboundRelationship2 typeCode="PERT">
                    <observation moodCode="EVN">
                     <code code="reactionForTranslation" codeSystem="ich-observation-code-oid"/>
                     <value xsi:type="ED">B.2.i.0.b</value>
                     <!-- B.2.i.0.b: Reaction / Event as Reported by the Primary Source for Translation -->
                    </observation>
                   </outboundRelationship2>
                   <outboundRelationship2 typeCode="PERT">
                    <observation moodCode="EVN" classCode="OBS">
                     <code code="termHighlightedByReporter" codeSystem="ich-observation-code-oid"/>
                     <value xsi:type="CE" code="B.2.i.2.1" codeSystem="ich-term-hilighted-oid"/>
                     <!-- B.2.i.2.1: Term Highlighted by the Reporter [1]no, serious [2]yes, serious [3]no, non seious
[4]yes, no serious -->
                    </observation>
                   </outboundRelationship2>
                   <outboundRelationship2 typeCode="PERT">
                    <observation moodCode="EVN" classCode="OBS">
                     <code code="resultsInDeath" codeSystem="ich-observation-code-oid"/>
                     <value xsi:type="BL" value="true"/>
                     <!-- B.2.i.2.2: Seriousness Criteria at Event Level (Results in Death) -->
                    </observation>
                   </outboundRelationship2>
                   <outboundRelationship2 typeCode="PERT">
                    <observation moodCode="EVN" classCode="OBS">
                     <code code="isLifeThreatening" codeSystem="ich-observation-code-oid"/>
                     <value xsi:type="BL" nullFlavor="NI"/>
                     <!-- B.2.i.2.2: Seriousness Criteria at Event Level (Life Threatening) -->
                    </observation>
                   </outboundRelationship2>
                   <outboundRelationship2 typeCode="PERT">
                    <observation moodCode="EVN" classCode="OBS">
                     <code code="requiresInpatientHospitalization" codeSystem="ich-observation-code-oid"/>
                     <value xsi:type="BL" value="true"/>
                     <!-- B.2.i.2.2: Seriousness Criteria at Event Level (Caused / Prolonged Hospitalisation) -->
                    </observation>
                   </outboundRelationship2>
                   <outboundRelationship2 typeCode="PERT">
                    <observation moodCode="EVN" classCode="OBS">
```

```
                    <code code="resultsInPersistentOrSignificantDisability" codeSystem="ich-observation-code-
oid"/>
                    <value xsi:type="BL" nullFlavor="NI"/>
                    <!-- B.2.i.2.2: Seriousness Criteria at Event Level (Disabling / Incapacitating)  -->
                   </observation>
                  </outboundRelationship2>
                  <outboundRelationship2 typeCode="PERT">
                   <observation moodCode="EVN" classCode="OBS">
                    <code code="congenitalAnomalyBirthDefect" codeSystem="ich-observation-code-oid"/>
                    <value xsi:type="BL" nullFlavor="NI"/>
                    <!-- B.2.i.2.2: Seriousness Criteria at Event Level (Congenital Anomaly / Birth Defect) -->
                   </observation>
                  </outboundRelationship2>
                  <outboundRelationship2 typeCode="PERT">
                   <observation moodCode="EVN" classCode="OBS">
                    <code code="otherMedicallyImportantCondition" codeSystem="ich-observation-code-oid"/>
                    <value xsi:type="BL" value="true"/>
                    <!-- B.2.i.2.2: Seriousness Criteria at Event Level (Other Medically Important Condition) -->
                   </observation>
                  </outboundRelationship2>
                  <outboundRelationship2 typeCode="PERT">
                   <observation moodCode="EVN" classCode="OBS">
                    <code code="outcome" codeSystem="ich-observation-code-oid"/>
                    <value xsi:type="CE" code="B.2.i.6" codeSystem="ich-outcome-of-reaction-event-oid"/>
                    <!-- B.2.i.6: Outcome of Reaction / Event at the Time of Last Observation
[1]recovered/resolved [2]recovering/resolving [3]not recovered/not resolved/ongoing
                     [4]recovered/resolved with sequelae [5]fatal [6]unknown -->
                   </observation>
                  </outboundRelationship2>
                  <outboundRelationship2 typeCode="PERT">
                   <observation moodCode="EVN" classCode="OBS">
                    <code code="medicalConfirmationByHealthProfessional" codeSystem="ich-observation-code-
oid"/>
                    <value xsi:type="BL" value="true"/>
                    <!-- B.2.i.7: Medical Confirmation by Healthcare Professional -->
                   </observation>
                  </outboundRelationship2>
                 </observation>
                </subjectOf2>
                <subjectOf2 typeCode="SBJ">
                 <organizer classCode="CATEGORY">
                  <code code="testsAndProceduresRelevantToTheInvestigation" codeSystem="TBD"/>
                  <component typeCode="COMP">
                   <observation moodCode="EVN" classCode="OBS">
                    <code code="B.3.r.c2" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.3.r.c3">
                     <!-- B.3.r.c2: Test Name (MedDRA code) -->
                     <!-- B.3.r.c3: Test Name (MedDRA version) -->
                     <originalText>B.3.r.c1</originalText>
                     <!-- B.3.r.c1: Test Name (free text) -->
                    </code>
                    <effectiveTime xsi:type="SXCM_TS" value="20090101"/>
                    <!-- B.3.r.b: Test Date -->
                    <value xsi:type="IVL_PQ">
                     <center value="10" unit="mg/dl"/>
                     <!-- B.3.r.d2: Test Result (Value and Qualifier) -->
                     <!-- B.3.r.e: Unit -->
                    </value>
                    <interpretationCode code="B.3.r.d1" codeSystem="ich-test-result-code-oid"/>
```

```
                    <!-- B.3.r.d1: Test Result (Code) -->
                    <referenceRange>
                      <observationRange classCode="OBS" moodCode="EVN.CRT">
                        <value xsi:type="PQ" value="40" unit="mg/dl"/>
                        <!-- B.3.r.1: Normal Low Value -->
                        <interpretationCode code="L" codeSystem="2.16.840.1.113883.5.83"/>
                      </observationRange>
                    </referenceRange>
                    <referenceRange>
                      <observationRange classCode="OBS" moodCode="EVN.CRT">
                        <value xsi:type="PQ" value="110" unit="mg/dl"/>
                        <!-- B.3.r.2:  Normal High Value -->
                        <interpretationCode code="H" codeSystem="2.16.840.1.113883.5.83"/>
                      </observationRange>
                    </referenceRange>
                    <outboundRelationship2 typeCode="PERT">
                      <observation moodCode="EVN" classCode="OBS">
                        <code code="comment" codeSystem="ich-observation-code-oid"/>
                        <value xsi:type="ED">B.3.r.3</value>
                        <!-- B.3.r.3: Comments (free text) -->
                      </observation>
                    </outboundRelationship2>
                    <outboundRelationship2 typeCode="REFR">
                      <observation moodCode="EVN" classCode="OBS">
                        <code code="moreInformationAvailable" codeSystem="ich-observation-code-oid"/>
                        <value xsi:type="BL" value="true"/>
                        <!-- B.3.r.4: More Information Available -->
                      </observation>
                    </outboundRelationship2>
                  </observation>
                </component>
                <component typeCode="COMP">
                  <observation moodCode="EVN" classCode="OBS">
                    <code code="B.3.r.c2" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.3.r.c3">
                      <!-- B.3.r.c2: Test Name (MedDRA code) -->
                      <!-- B.3.r.c3: Test Name (MedDRA version) -->
                      <originalText>B.3.r.c1</originalText>
                      <!-- B.3.r.c1: Test Name (free text) -->
                    </code>
                    <effectiveTime xsi:type="SXCM_TS" value="20090101"/>
                    <!-- B.3.r.b - Test Date -->
                    <value xsi:type="IVL_PQ">
                      <low nullFlavor="NINF"/>
                      <high value="10" unit="mg/dl" inclusive="false"/>
                    </value>
                    <!-- B.3.r.d2: Test Result (Value and Qualifier) -->
                    <!-- LT 10 mg/dl -->
                  </observation>
                </component>
                <component typeCode="COMP">
                  <observation moodCode="EVN" classCode="OBS">
                    <code code="B.3.r.c2" codeSystem="2.16.840.1.113883.6.163"
codeSystemVersion="B.3.r.c3">
                      <!-- B.3.r.c2: Test Name (MedDRA code) -->
                      <!-- B.3.r.c3: Test Name (MedDRA version) -->
                      <originalText>B.3.r.c1</originalText>
                      <!-- B.3.r.c1: Test Name (free text) -->
                    </code>
```

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3026                    <effectiveTime xsi:type="SXCM_TS" value="20090101"/>
3027                    <!-- B.3.r.b - Test Date -->
3028                    <value xsi:type="IVL_PQ">
3029                      <low nullFlavor="NINF"/>
3030                      <high value="10" unit="mg/dl" inclusive="true"/>
3031                    </value>
3032                    <!-- B.3.r.d2: Test Result (Value and Qualifier) -->
3033                    <!-- LE 10 mg/dl -->
3034                  </observation>
3035                </component>
3036                <component typeCode="COMP">
3037                  <observation moodCode="EVN" classCode="OBS">
3038                    <code code="B.3.r.c2" codeSystem="2.16.840.1.113883.6.163"
3039    codeSystemVersion="B.3.r.c3">
3040                      <!-- B.3.r.c2: Test Name (MedDRA code) -->
3041                      <!-- B.3.r.c3: Test Name (MedDRA version) -->
3042                      <originalText>B.3.r.c1</originalText>
3043                      <!-- B.3.r.c1: Test Name (free text) -->
3044                    </code>
3045                    <effectiveTime xsi:type="SXCM_TS" value="20090101"/>
3046                    <!-- B.3.r.b - Test Date -->
3047                    <value xsi:type="IVL_PQ">
3048                      <low value="10" unit="mg/dl" inclusive="false"/>
3049                      <high nullFlavor="PINF"/>
3050                    </value>
3051                    <!-- B.3.r.d2: Test Result (Value and Qualifier) -->
3052                    <!-- GT 10 mg/dl -->
3053                  </observation>
3054                </component>
3055                <component typeCode="COMP">
3056                  <observation moodCode="EVN" classCode="OBS">
3057                    <code code="B.3.r.c2" codeSystem="2.16.840.1.113883.6.163"
3058    codeSystemVersion="B.3.r.c3">
3059                      <!-- B.3.r.c2: Test Name (MedDRA code) -->
3060                      <!-- B.3.r.c3: Test Name (MedDRA version) -->
3061                      <originalText>B.3.r.c1</originalText>
3062                      <!-- B.3.r.c1: Test Name (free text) -->
3063                    </code>
3064                    <effectiveTime xsi:type="SXCM_TS" value="20090101"/>
3065                    <!-- B.3.r.b - Test Date -->
3066                    <value xsi:type="IVL_PQ">
3067                      <low value="10" unit="mg/dl" inclusive="true"/>
3068                      <high nullFlavor="PINF"/>
3069                    </value>
3070                    <!-- B.3.r.d2: Test Result (Value and Qualifier) -->
3071                    <!-- GE 10 mg/dl -->
3072                  </observation>
3073                </component>
3074                <component typeCode="COMP">
3075                  <observation moodCode="EVN" classCode="OBS">
3076                    <code code="B.3.r.c2" codeSystem="2.16.840.1.113883.6.163"
3077    codeSystemVersion="B.3.r.c3">
3078                      <!-- B.3.r.c2: Test Name (MedDRA code) -->
3079                      <!-- B.3.r.c3: Test Name (MedDRA version) -->
3080                      <originalText>B.3.r.c1</originalText>
3081                      <!-- B.3.r.c1: Test Name (free text) -->
3082                    </code>
3083                    <effectiveTime xsi:type="SXCM_TS" value="20090101"/>
3084                    <!-- B.3.r.b - Test Date -->
```

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3085                    <value xsi:type="ED">B.3.r.f</value>
3086                    <!-- B.3.r.f: Result Unstructured Data (free text) -->
3087                  </observation>
3088                </component>
3089              </organizer>
3090            </subjectOf2>
3091            <subjectOf2 typeCode="SBJ">
3092              <organizer>
3093                <code code="drugInformation" codeSystem="TBD"/>
3094                <component typeCode="COMP">
3095                  <substanceAdministration moodCode="EVN" classCode="SBADM">
3096                    <id extension="1" root="oidInternalReferencesToSubstanceAdministration"/>
3097                    <consumable>
3098                      <instanceOfKind classCode="INST">
3099                        <kindOfProduct classCode="MMAT" determinerCode="KIND">
3100                          <code code="B.4.k.2.1.1a" codeSystem="TBD" codeSystemVersion="B.4.k.2.1.1b"/>
3101                          <!-- B.4.k.2.1.1a: MPID -->
3102                          <!-- B.4.k.2.1.1b: MPID Version Date / Number -->
3103                          <name>B.4.k.2.2</name>
3104                          <!--B.4.k.2.2: Medicinal Product Name as Reported by the Primary Source  -->
3105                          <asManufacturedProduct classCode="MANU">
3106                            <subjectOf typeCode="SBJ">
3107                              <approval classCode="CNTRCT" moodCode="EVN">
3108                                <id extension="B.4.k.3.1" root="oidAuthorisationNumber"/>
3109                                <!-- B.4.k.3.1: Authorisation / Application Number -->
3110                                <holder typeCode="HLD">
3111                                  <role classCode="HLD">
3112                                    <playingOrganization classCode="ORG" determinerCode="INSTANCE">
3113                                      <name>B.4.k.3.3</name>
3114                                      <!-- B.4.k.3.3: Name of Holder / Applicant -->
3115                                    </playingOrganization>
3116                                  </role>
3117                                </holder>
3118                                <author typeCode="AUT">
3119                                  <territorialAuthority classCode="TERR">
3120                                    <territory classCode="NAT" determinerCode="INSTANCE">
3121                                      <code code="B.4.k.3.2" codeSystem="1.0.3166.1.2.2"/>
3122                                      <!-- B.4.k.3.2: Country of Authorisation / Application -->
3123                                    </territory>
3124                                  </territorialAuthority>
3125                                </author>
3126                              </approval>
3127                            </subjectOf>
3128                          </asManufacturedProduct>
3129                          <ingredient classCode="ACTI">
3130                            <quantity>
3131                              <numerator value="10" unit="B.4.k.2.3.r.4"/>
3132                              <!-- B.4.k.2.3.r.3: Strength -->
3133                              <!-- B.4.k.2.3.r.4: Strength Unit -->
3134                              <denominator value="1"/>
3135                            </quantity>
3136                            <ingredientSubstance classCode="MMAT" determinerCode="KIND">
3137                              <code code="B.4.k.2.3.r.2a" codeSystem="TBD" codeSystemVersion="B.4.k.2.3.r.2b"/>
3138                              <!-- B.4.k.2.3.r.2a: Substance / Specified Substance TermID -->
3139                              <!-- B.4.k.2.3.r.2b: Substance / Specified Substance TermID Version Date/Number -->
3140                              <name>B.4.k.2.3.r.1</name>
3141                              <!-- B.4.k.2.3.r.1: Substance / Specified Substance Name -->
3142                            </ingredientSubstance>
3143                          </ingredient>
```

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                    </kindOfProduct>
                    <subjectOf typeCode="SBJ">
                      <productEvent classCode="ACT" moodCode="EVN">
                        <code code="retailSupply" codeSystem="TBD"/>
                        <performer typeCode="PRF">
                          <assignedEntity classCode="ASSIGNED">
                            <representedOrganization classCode="ORG" determinerCode="INSTANCE">
                              <addr>
                                <country>B.4.k.2.4</country>
                                <!-- B.4.k.2.4: Identification of the Country Where the Drug Was Obtained -->
                              </addr>
                            </representedOrganization>
                          </assignedEntity>
                        </performer>
                      </productEvent>
                    </subjectOf>
                  </instanceOfKind>
                </consumable>
                <outboundRelationship1 typeCode="SAS">
                  <pauseQuantity value="10" unit="B.4.k.9.i.3.1b"/>
                  <!-- B.4.k.9.i.3.1a: Time Interval between Beginning of Drug Administration and Start of
Reaction / Event (number) -->
                  <!-- B.4.k.9.i.3.1b: Time Interval between Beginning of Drug Administration and Start of
Reaction / Event (unit) -->
                  <actReference classCode="OBS" moodCode="EVN">
                    <id extension="1" root="oidInternalReferencesToReaction"/>
                  </actReference>
                </outboundRelationship1>
                <outboundRelationship1 typeCode="SAE">
                  <pauseQuantity value="10" unit="B.4.k.9.i.3.2b"/>
                  <!-- B.4.k.9.i.3.2a: Time Interval between Last Dose of Drug and Start of Reaction / Event
(number) -->
                  <!-- B.4.k.9.i.3.2b: Time Interval between Last Dose of Drug and Start of Reaction / Event
(unit) -->
                  <actReference classCode="OBS" moodCode="EVN">
                    <id extension="1" root="oidInternalReferencesToReaction"/>
                  </actReference>
                </outboundRelationship1>
                <outboundRelationship2 typeCode="PERT">
                  <observation moodCode="EVN" classCode="OBS">
                    <code code="blinded" codeSystem="ich-observation-code-oid"/>
                    <value xsi:type="BL" nullFlavor="NI"/>
                    <!-- B.4.k.2.5: Investigational Product Status -->
                  </observation>
                </outboundRelationship2>
                <!-- dose #1 -->
                <outboundRelationship2 typeCode="COMP">
                  <!-- B.4.k.4.r: Dosage Information -->
                  <substanceAdministration classCode="SBADM" moodCode="EVN">
                    <text>B.4.k.4.r.10</text>
                    <!-- B.4.k.4.r.10: Dosage Text -->
                    <effectiveTime xsi:type="SXPR_TS">
                      <comp xsi:type="PIVL_TS">
                        <period value="10" unit="B.4.k.4.r.5"/>
                        <!-- B.4.k.4.r.4: Number of Units in the Interval -->
                        <!-- B.4.k.4.r.5: Definition of the Time Interval Unit -->
                      </comp>
                      <comp xsi:type="IVL_TS" operator="A">
                        <low value="20090101"/>
```

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3203                        <!-- B.4.k.4.r.6: Date and Time of Start of Drug-->
3204                        <high value="20090101"/>
3205                        <!-- B.4.k.4.r.7: Date and Time of Last Administration-->
3206                       </comp>
3207                      </effectiveTime>
3208                      <routeCode code="B.4.k.4.r.12.2a" codeSystem="ich-route-of-administration-oid"
3209 codeSystemVersion="B.4.k.4.r.12.2b">
3210                       <!-- B.4.k.4.r.12.2a: Route of Administration TermID -->
3211                       <!-- B.4.k.4.r.12.2b: Route of Administration TermID Version Date -->
3212                       <originalText>B.4.k.4.r.12.1</originalText>
3213                       <!-- B.4.k.4.r.12.1: Route of Administration -->
3214                      </routeCode>
3215                      <doseQuantity value="10" unit="B.4.k.4.r.2"/>
3216                      <!-- B.4.k.4.r.1: Dose (number) -->
3217                      <!-- B.4.k.4.r.2: Dose (unit) -->
3218                      <consumable typeCode="CSM">
3219                       <instanceOfKind classCode="INST">
3220                        <productInstanceInstance classCode="MMAT" determinerCode="INSTANCE">
3221                         <id nullFlavor="NI"/>
3222                         <lotNumberText>B.4.k.4.r.9</lotNumberText>
3223                         <!-- B.4.k.4.r.9: Batch / Lot Number -->
3224                        </productInstanceInstance>
3225                        <kindOfProduct classCode="MMAT" determinerCode="KIND">
3226                         <formCode code="B.4.k.4.4.11.2a" codeSystem="TBD"
3227 codeSystemVersion="B.4.k.4.4.11.2b">
3228                          <!-- B.4.k.4.r.11.2a: Pharmaceutical Dose Form TermID -->
3229                          <!-- B.4.k.4.r.11.2b: Pharmaceutical Dose Form TermID Version Date/Number -->
3230                          <originalText>B.4.k.4.r.11.1</originalText>
3231                          <!-- B.4.k.4.r.11.1: Pharmaceutical Dose Form Text -->
3232                         </formCode>
3233                        </kindOfProduct>
3234                       </instanceOfKind>
3235                      </consumable>
3236                      <inboundRelationship typeCode="REFR">
3237                       <observation moodCode="EVN" classCode="OBS">
3238                        <code code="parentRouteOfAdministration" codeSystem="ich-observation-code-oid"/>
3239                        <value xsi:type="CE" code="B.4.k.4.r.13.2a" codeSystem="ich-route-of-administration-
3240 oid" codeSystemVersion="B.4.k.4.r.13.2b">
3241                         <!-- B.4.k.4.r.13.2a: Parent Route of Administration TermID -->
3242                         <!-- B.4.k.4.r.13.2b: Parent Route of Administration TermID Version Date -->
3243                         <originalText>B.4.k.4.r.13.1</originalText>
3244                         <!-- B.4.k.4.r.13.1: Parent Route of Administration -->
3245                        </value>
3246                       </observation>
3247                      </inboundRelationship>
3248                     </substanceAdministration>
3249                    </outboundRelationship2>
3250                    <!-- dose #2 -->
3251                    <outboundRelationship2 typeCode="COMP">
3252                     <!-- B.4.k.4.r: Dosage Information -->
3253                     <substanceAdministration classCode="SBADM" moodCode="EVN">
3254                      <text>B.4.k.4.r.10</text>
3255                      <!-- B.4.k.4.r.10: Dosage Text -->
3256                      <effectiveTime xsi:type="SXPR_TS">
3257                       <comp xsi:type="PIVL_TS">
3258                        <period value="10" unit="B.4.k.4.r.5"/>
3259                        <!-- B.4.k.4.r.4: Number of Units in the Interval -->
3260                        <!-- B.4.k.4.r.5: Definition of the Time Interval Unit -->
3261                       </comp>
```

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3262                        <comp xsi:type="IVL_TS" operator="A">
3263                          <low value="20090101"/>
3264                          <!-- B.4.k.4.r.6: Date and Time of Start of Drug-->
3265                          <width value="4" unit="B.4.k.4.r.8b"/>
3266                          <!-- B.4.k.4.r.8a: Duration of Drug Administration (number) -->
3267                          <!-- B.4.k.4.r.8b: Duration of Drug Administration (unit) -->
3268                        </comp>
3269                      </effectiveTime>
3270                      <routeCode code="B.4.k.4.r.12.2a" codeSystem="ich-route-of-administration-oid"
3271    codeSystemVersion="B.4.k.4.r.12.2b">
3272                        <!-- B.4.k.4.r.12.2a: Route of Administration TermID -->
3273                        <!-- B.4.k.4.r.12.2b: Route of Administration TermID Version Date -->
3274                        <originalText>B.4.k.4.r.12.1</originalText>
3275                        <!-- B.4.k.4.r.12.1: Route of Administration -->
3276                      </routeCode>
3277                      <doseQuantity value="10" unit="B.4.k.4.r.2"/>
3278                      <!-- B.4.k.4.r.1: Dose (number) -->
3279                      <!-- B.4.k.4.r.2: Dose (unit) -->
3280                      <consumable typeCode="CSM">
3281                        <instanceOfKind classCode="INST">
3282                          <productInstanceInstance classCode="MMAT" determinerCode="INSTANCE">
3283                            <id nullFlavor="NI"/>
3284                            <lotNumberText>B.4.k.4.r.9</lotNumberText>
3285                            <!-- B.4.k.4.r.9: Batch / Lot Number -->
3286                          </productInstanceInstance>
3287                          <kindOfProduct classCode="MMAT" determinerCode="KIND">
3288                            <formCode code="B.4.k.4.r.11.2a" codeSystem="TBD"
3289    codeSystemVersion="B.4.k.4.r.11.2b">
3290                              <!-- B.4.k.4.r.11.2a: Pharmaceutical Dose Form TermID -->
3291                              <!-- B.4.k.4.r.11.2b: Pharmaceutical Dose Form TermID Version Date/Number -->
3292                              <originalText>B.4.k.4.r.11.1</originalText>
3293                              <!-- B.4.k.4.r.11.1: Pharmaceutical Dose Form Text -->
3294                            </formCode>
3295                          </kindOfProduct>
3296                        </instanceOfKind>
3297                      </consumable>
3298                      <inboundRelationship typeCode="REFR">
3299                        <observation moodCode="EVN" classCode="OBS">
3300                          <code code="parentRouteOfAdministration" codeSystem="ich-observation-code-oid"/>
3301                          <value xsi:type="CE" code="B.4.k.4.r.13.2a" codeSystem="ich-route-of-administration-
3302    oid" codeSystemVersion="B.4.k.4.r.13.2b">
3303                            <!-- B.4.k.4.r.13.2a: Parent Route of Administration TermID -->
3304                            <!-- B.4.k.4.r.13.2b: Parent Route of Administration TermID Version Date -->
3305                            <originalText>B.4.k.4.r.13.1</originalText>
3306                            <!-- B.4.k.4.r.13.1: Parent Route of Administration -->
3307                          </value>
3308                        </observation>
3309                      </inboundRelationship>
3310                    </substanceAdministration>
3311                  </outboundRelationship2>
3312                  <outboundRelationship2 typeCode="SUMM">
3313                    <observation moodCode="EVN" classCode="OBS">
3314                      <code code="cumulativeDoseToReaction" codeSystem="ich-observation-code-oid"/>
3315                      <value xsi:type="PQ" value="10" unit="B.4.k.5.2"/>
3316                      <!-- B.4.k.5.1: Cumulative Dose to First Reaction (number) -->
3317                      <!-- B.4.k.5.2: Cumulative Dose to First Reaction (unit) -->
3318                    </observation>
3319                  </outboundRelationship2>
3320                  <outboundRelationship2 typeCode="PERT">
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3321                    <observation moodCode="EVN" classCode="OBS">
3322                     <code code="gestationPeriod" codeSystem="ich-observation-code-oid"/>
3323                     <value xsi:type="PQ" value="10" unit="B.4.k.6b"/>
3324                     <!-- B.4.k.6a: Gestation Peirod at Time of Exposure (number) -->
3325                     <!-- B.4.k.6b: Gestation Peirod at Time of Exposure (unit) -->
3326                    </observation>
3327                   </outboundRelationship2>
3328                   <outboundRelationship2 typeCode="PERT">
3329                    <observation moodCode="EVN" classCode="OBS">
3330                     <code code="recurranceOfReaction" codeSystem="ich-observation-code-oid"/>
3331                     <value xsi:type="CE" code="B.4.k.9.i.4" codeSystem="ich-recur-on-readministration-oid"/>
3332                     <!-- B.4.k.9.i.4: Did Reaction Recur on Re-administration?  -->
3333                     <outboundRelationship1 typeCode="REFR">
3334                      <actReference moodCode="EVN" classCode="ACT">
3335                       <id extension="1" root="oidInternalReferencesToReaction"/>
3336                      </actReference>
3337                     </outboundRelationship1>
3338                    </observation>
3339                   </outboundRelationship2>
3340                   <outboundRelationship2 typeCode="PERT">
3341                    <observation moodCode="EVN" classCode="OBS">
3342                     <code code="recurranceOfReaction" codeSystem="ich-observation-code-oid"/>
3343                     <value xsi:type="CE" code="B.4.k.9.i.4" codeSystem="ich-recur-on-readministration-oid"/>
3344                     <!-- B.4.k.9.i.4: Did Reaction Recur on Re-administration? -->
3345                     <outboundRelationship1 typeCode="REFR">
3346                      <actReference moodCode="EVN" classCode="ACT">
3347                       <id extension="2" root="oidInternalReferencesToReaction"/>
3348                      </actReference>
3349                     </outboundRelationship1>
3350                    </observation>
3351                   </outboundRelationship2>
3352                   <outboundRelationship2 typeCode="REFR">
3353                    <observation moodCode="EVN" classCode="OBS">
3354                     <code code="codedDrugInformation" codeSystem="ich-observation-code-oid"/>
3355                     <value xsi:type="CE" code="B.4.k.10.r" codeSystem="ich-additional-info-on-drug-code-
3356 oid"/>
3357                     <!-- B.4.k.10.r: Additional Information on Drug (Coded) -->
3358                    </observation>
3359                   </outboundRelationship2>
3360                   <outboundRelationship2 typeCode="REFR">
3361                    <observation moodCode="EVN" classCode="OBS">
3362                     <code code="additionalInformation" codeSystem="ich-observation-code-oid"/>
3363                     <value xsi:type="ST">B.4.k.11</value>
3364                     <!-- B.4.k.11: Additional Information on Drug (free text) -->
3365                    </observation>
3366                   </outboundRelationship2>
3367                   <inboundRelationship typeCode="RSON">
3368                    <observation moodCode="EVN" classCode="OBS">
3369                     <code code="indication" codeSystem="ich-observation-code-oid"/>
3370                     <value xsi:type="CE" code="B.4.k.7.r.2b" codeSystem="2.16.840.1.113883.6.163"
3371 codeSystemVersion="B.4.k.7.r.2a">
3372                      <!-- B.4.k.7.r.2a: Indication in MedDRA Terminology (version) -->
3373                      <!-- B.4.k.7.r.2b: Indication in MedDRA Terminology (LLT code) -->
3374                      <originalText>B.4.k.7.r.1</originalText>
3375                      <!-- B.4.k.7.r.1: Indication as Reported by the Primary Source-->
3376                     </value>
3377                     <performer>
3378                      <assignedEntity>
3379                       <code code="sourceReporter" codeSystem="TBD"/>
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                    </assignedEntity>
                  </performer>
                  <outboundRelationship1 typeCode="REFR">
                    <actReference classCode="SBADM" moodCode="EVN">
                      <id extension="2" root="oidInternalReferencesToSubstanceAdministration"/>
                    </actReference>
                  </outboundRelationship1>
                </observation>
              </inboundRelationship>
              <inboundRelationship typeCode="CAUS">
                <act moodCode="EVN" classCode="ACT">
                  <code code="B.4.k.8" codeSystem="ich-action-taken-with-drug-oid"/>
                  <!-- B.4.k.8: Action(s) Taken with Drug [1]Drug withdrawn [2]Dose reduced [3]Dose
increased [4]Dose not changed
                    [5]Unknown [6]Not applicable -->
                </act>
              </inboundRelationship>
            </substanceAdministration>
          </component>
        </organizer>
      </subjectOf2>
    </primaryRole>
  </subject1>
  <component typeCode="COMP">
    <causalityAssessment classCode="OBS" moodCode="EVN">
      <code code="interventionCharacterization" codeSystem="TBD"/>
      <value xsi:type="CE" code="B.4.k.1" codeSystem="ich-characterisation-of-drug-role-oid"/>
      <!-- B.4.k.1: Characterisation of Drug Role [1]Suspect [2]Concomitant [3]Interacting [4]Drug Not
Administered -->
      <subject2 typeCode="SUBJ">
        <productUseReference classCode="ACT" moodCode="EVN">
          <id extension="1" root="oidInternalReferencesToSubstanceAdministration"/>
        </productUseReference>
      </subject2>
    </causalityAssessment>
  </component>
  <component typeCode="COMP">
    <causalityAssessment classCode="OBS" moodCode="EVN">
      <code code="causality" codeSystem="TBD"/>
      <value xsi:type="ST">B.4.k.9.i.2.r.3</value>
      <!-- B.4.k.9.i.2.r.3: Result of Assessment -->
      <methodCode>
        <originalText>B.4.k.9.i.2.r.2</originalText>
        <!-- B.4.k.9.i.2.r.2: Method of Assessment -->
      </methodCode>
      <author typeCode="AUT">
        <assignedEntity classCode="ASSIGNED">
          <code>
            <originalText>B.4.k.9.i.2.r.1</originalText>
            <!-- B.4.k.9.i.2.r.1: Source of Assessment -->
          </code>
        </assignedEntity>
      </author>
      <subject1 typeCode="SUBJ">
        <adverseEffectReference classCode="ACT" moodCode="EVN">
          <id extension="1" root="oidInternalReferencesToReaction"/>
        </adverseEffectReference>
      </subject1>
      <subject2 typeCode="SUBJ">
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3439                <productUseReference classCode="ACT" moodCode="EVN">
3440                  <id extension="1" root="oidInternalReferencesToSubstanceAdministration"/>
3441                </productUseReference>
3442              </subject2>
3443            </causalityAssessment>
3444          </component>
3445          <component1 typeCode="COMP">
3446            <observationEvent classCode="OBS" moodCode="EVN">
3447              <code code="comment" codeSystem="ich-observation-code-oid"/>
3448              <value xsi:type="ED">B.5.2</value>
3449              <!-- B.5.2: Reporter's Comments -->
3450              <author typeCode="AUT">
3451                <assignedEntity classCode="ASSIGNED">
3452                  <code code="sourceReporter" codeSystem="TBD"/>
3453                </assignedEntity>
3454              </author>
3455            </observationEvent>
3456          </component1>
3457          <component1 typeCode="COMP">
3458            <observationEvent moodCode="EVN" classCode="OBS">
3459              <code code="diagnosis" codeSystem="ich-observation-code-oid"/>
3460              <value xsi:type="CE" code="B.5.3.r.2" codeSystem="2.16.840.1.113883.6.163"
3461  codeSystemVersion="B.5.3.r.1"/>
3462              <!-- B.5.3.r.1: MedDRA Version for Sender's Diagnosis / Syndrome and / or Reclassification of
3463  Reaction / Event -->
3464              <!-- B.5.3.r.2: Sender's Diagnosis / Syndrome and / or Reclassification of Reaction / Event -->
3465              <author typeCode="AUT">
3466                <assignedEntity classCode="ASSIGNED">
3467                  <code code="sender" codeSystem="TBD"/>
3468                </assignedEntity>
3469              </author>
3470            </observationEvent>
3471          </component1>
3472          <component1 typeCode="COMP">
3473            <observationEvent classCode="OBS" moodCode="EVN">
3474              <code code="comment" codeSystem="ich-observation-code-oid"/>
3475              <value xsi:type="ED">B.5.4</value>
3476              <!--B.5.4: Sender's Comments -->
3477              <author typeCode="AUT">
3478                <assignedEntity classCode="ASSIGNED">
3479                  <code code="sender" codeSystem="TBD"/>
3480                </assignedEntity>
3481              </author>
3482            </observationEvent>
3483          </component1>
3484        </adverseEventAssessment>
3485      </component>
3486      <component typeCode="COMP">
3487        <observationEvent classCode="OBS" moodCode="EVN">
3488          <code code="additionalDocumentsAvailable" codeSystem="ich-observation-code-oid"/>
3489          <value xsi:type="BL" value="true"/>
3490          <!-- A.1.8.1: Are Additional Documents Available? -->
3491        </observationEvent>
3492      </component>
3493      <component typeCode="COMP">
3494        <observationEvent classCode="OBS" moodCode="EVN">
3495          <code code="localCriteriaForExpedited" codeSystem="ich-observation-code-oid"/>
3496          <value xsi:type="BL" value="true"/>
3497          <!-- A.1.9: Does this Case Fulfil the Local Criteria for an Expedited Report?-->
```

```
3498            </observationEvent>
3499          </component>
3500          <component typeCode="COMP">
3501            <observationEvent classCode="OBS" moodCode="EVN">
3502              <code code="summaryAndComment" codeSystem="ich-observation-code-oid"/>
3503              <value xsi:type="ED" language="B.5.5.r.2">B.5.5.r.1</value>
3504              <!-- B.5.5.r.1: Case Summary and Reporter's Comments Text  -->
3505              <!-- B.5.5.r.2: Case Summary and Reporter's Comments Text Language -->
3506              <author typeCode="AUT">
3507                <assignedEntity classCode="ASSIGNED">
3508                  <code code="reporter" codeSystem="TBD"/>
3509                </assignedEntity>
3510              </author>
3511            </observationEvent>
3512          </component>
3513          <outboundRelationship typeCode="SPRT">
3514            <relatedInvestigation classCode="INVSTG" moodCode="EVN">
3515              <code code="initialReport" codeSystem="TBD"/>
3516              <subjectOf2 typeCode="SUBJ">
3517                <controlActEvent classCode="CACT" moodCode="EVN">
3518                  <author typeCode="AUT">
3519                    <assignedEntity classCode="ASSIGNED">
3520                      <code code="A.1.10.2" codeSystem="ich-first-sender-of-this-case-oid"/>
3521                      <!-- A.1.10.2: First Sender of this Case [1]:Regulator [2]:Other -->
3522                    </assignedEntity>
3523                  </author>
3524                </controlActEvent>
3525              </subjectOf2>
3526            </relatedInvestigation>
3527          </outboundRelationship>
3528          <outboundRelationship typeCode="SPRT">
3529            <relatedInvestigation classCode="INVSTG" moodCode="EVN">
3530              <code nullFlavor="NA"/>
3531              <subjectOf2 typeCode="SUBJ">
3532                <controlActEvent classCode="CACT" moodCode="EVN">
3533                  <id extension="A.1.12.r" root="worldWideCaseIdOid"/>
3534                  <!-- A.1.12.r: Identification Number of the Report Which Is Linked to this Report  -->
3535                </controlActEvent>
3536              </subjectOf2>
3537            </relatedInvestigation>
3538          </outboundRelationship>
3539          <outboundRelationship typeCode="SPRT">
3540            <priorityNumber value="1"/>
3541            <!-- A.2.r.1.5: Primary source for regulatory purposes -->
3542            <relatedInvestigation classCode="INVSTG" moodCode="EVN">
3543              <code code="sourceReport" codeSystem="TBD"/>
3544              <subjectOf2 typeCode="SUBJ">
3545                <controlActEvent classCode="CACT" moodCode="EVN">
3546                  <author typeCode="AUT">
3547                    <assignedEntity classCode="ASSIGNED">
3548                      <addr>
3549                        <streetAddressLine>A.2.r.1.2c</streetAddressLine>
3550                        <!-- A.2.r.1.2c: Reporter's Address and Telephone (Reporter street) -->
3551                        <city>A.2.r.1.2d</city>
3552                        <!-- A.2.r.1.2d: Reporter's Address and Telpehone (Reporter city) -->
3553                        <state>A.2.r.1.2e</state>
3554                        <!-- A.2.r.1.2e:  Reporter's Address and Telephone (Reporter state or province) -->
3555                        <postalCode>A.2.r.1.2f</postalCode>
3556                        <!-- A.2.r.1.2f:  Reporter's Address and Telephone (Reporter postcode) -->
```

```
                </addr>
                <telecom value="A.2.r.1.2g"/>
                <!-- A.2.r.1.2g Reporter's Address and Telephone (Telephone) -->
                <assignedPerson classCode="PSN" determinerCode="INSTANCE">
                  <name>
                    <prefix>A.2.r.1.1a</prefix>
                    <!-- A.2.r.1.1a: Reporter Identifier (Reporter title) -->
                    <given>A.2.r.1.1b</given>
                    <!-- A.2.r.1.1b: Reporter Identifier (Reporter given name) -->
                    <given>A.2.r.1c</given>
                    <!-- A.2.r.1.1c: Reporter Identifire (Reporter middle name) -->
                    <family>A.2.r.1.1d</family>
                    <!-- A.2.r.1.1d: Reporter Identifier (Reporter family name) -->
                  </name>
                  <asQualifiedEntity classCode="QUAL">
                    <code code="A.2.r.1.4" codeSystem="ich-qualification-oid"/>
                    <!-- A.2.r.1.4: Qualification [1] Physician [2]Pharmacist -->
                  </asQualifiedEntity>
                  <asLocatedEntity classCode="LOCE">
                    <location determinerCode="INSTANCE" classCode="COUNTRY">
                      <code code="A.2.r.1.3" codeSystem="1.0.3166.1.2.2"/>
                      <!-- A.2.r.1.3: Country (Reporter country code) -->
                    </location>
                  </asLocatedEntity>
                </assignedPerson>
                <representedOrganization classCode="ORG" determinerCode="INSTANCE">
                  <name>A.2.r.1.2b</name>
                  <!-- A.2.r.1.2b: Reporter's Address and Telephone (Reporter department) -->
                  <assignedEntity classCode="ASSIGNED">
                    <representedOrganization classCode="ORG" determinerCode="INSTANCE">
                      <name>A.2.r.1.2a</name>
                      <!-- A.2.r.1.2a: Reporter's Address and Telephone (Reporter organisation) -->
                    </representedOrganization>
                  </assignedEntity>
                </representedOrganization>
              </assignedEntity>
            </author>
          </controlActEvent>
        </subjectOf2>
      </relatedInvestigation>
    </outboundRelationship>
    <subjectOf1 typeCode="SUBJ">
      <controlActEvent classCode="CACT" moodCode="EVN">
        <author typeCode="AUT">
          <assignedEntity classCode="ASSIGNED">
            <code code="A.3.1" codeSystem="ich-sender-type-oid"/>
            <!-- A.3.1: Sender Type [1] Pharmaceutical Company [2]Regulatory Authority [3]Health
Professional [4] Regional Pharmacovigilance Center
            [5] WHO collaborating center for international drug monitoring [6] Other [7] Patient / Consumer -->
            <addr>
              <streetAddressLine>A.3.4a</streetAddressLine>
              <!-- A.3.4a: Sender's Street Address -->
              <city>A.3.4b</city>
              <!-- A.3.4b: Sender's City -->
              <state>A.3.4c</state>
              <!-- A.3.4c: Sender's State or Province -->
              <postalCode>A.3.4d</postalCode>
              <!-- A.3.4d: Sender's Postcode -->
            </addr>
```

```
3616                <telecom value="tel:A.3.4f"/>
3617                <!-- A.3.4f: Sender's Telephone -->
3618                <telecom value="fax:A.3.4i"/>
3619                <!-- A.3.4i: Sender's Fax -->
3620                <telecom value="mailto:A.3.4l"/>
3621                <!-- A.3.4l : Sender's E-mail Address -->
3622                <!-- A.3.4.f,i,l Sender's address, fax, telephone and E-mail address -->
3623                <assignedPerson classCode="PSN" determinerCode="INSTANCE">
3624                  <name>
3625                    <prefix>A.3.3b</prefix>
3626                    <!-- A.3.3b: Sender's Title -->
3627                    <given>A.3.3c</given>
3628                    <!-- A.3.3c: Sender's Given Name -->
3629                    <given>A.3.3d</given>
3630                    <!-- A.3.3d: Sender's Middle Name -->
3631                    <family>A.3.3e</family>
3632                    <!-- A.3.3e: Sender's Family Name -->
3633                  </name>
3634                  <asLocatedEntity classCode="LOCE">
3635                    <location classCode="COUNTRY" determinerCode="INSTANCE">
3636                      <code code="A.3.4e" codeSystem="1.0.3166.1.2.2"/>
3637                      <!-- A.3.4e: Sender's Country Code -->
3638                    </location>
3639                  </asLocatedEntity>
3640                </assignedPerson>
3641                <representedOrganization classCode="ORG" determinerCode="INSTANCE">
3642                  <name>A.3.3a</name>
3643                  <!-- A.3.3a: Sender's Department -->
3644                  <assignedEntity classCode="ASSIGNED">
3645                    <representedOrganization classCode="ORG" determinerCode="INSTANCE">
3646                      <name>A.3.2</name>
3647                      <!-- A.3.2: Sender's Organization -->
3648                    </representedOrganization>
3649                  </assignedEntity>
3650                </representedOrganization>
3651              </assignedEntity>
3652            </author>
3653          </controlActEvent>
3654        </subjectOf1>
3655        <subjectOf1 typeCode="SUBJ">
3656          <controlActEvent classCode="CACT" moodCode="EVN">
3657            <id assigningAuthorityName="A.1.11.r.1" extension="A.1.11.r.2" root="caseIdentifierOid"/>
3658            <!-- A.1.11.r.1: Source(s) of the Case Identifier -->
3659            <!-- A.1.11.r.2 Case Identifiers(s) -->
3660          </controlActEvent>
3661        </subjectOf1>
3662        <subjectOf2 typeCode="SUBJ">
3663          <investigationCharacteristic classCode="OBS" moodCode="EVN">
3664            <code code="ichReportType" codeSystem="TBD"/>
3665            <value xsi:type="CE" code="A.1.4" codeSystem="ich-type-of-report-oid"/>
3666            <!-- A.1.4 Type of Report [1] Spontaneous report [2] Report from study [3] Other [4] Not available to
3667 sender (unknown) -->
3668          </investigationCharacteristic>
3669        </subjectOf2>
3670        <subjectOf2 typeCode="SUBJ">
3671          <investigationCharacteristic classCode="OBS" moodCode="EVN">
3672            <code code="otherCaseIds" codeSystem="TBD"/>
3673            <value xsi:type="BL" value="true"/>
3674            <!-- A.1.11 Other case identifiers in previous transmissions-->
```

```
        </investigationCharacteristic>
      </subjectOf2>
      <subjectOf2 typeCode="SUBJ">
        <investigationCharacteristic classCode="OBS" moodCode="EVN">
          <code code="nullificationAmendmentCode" codeSystem="TBD"/>
          <value xsi:type="CE" code="A.1.13" codeSystem="ich-report-nullification-amendment-oid"/>
          <!-- A.1.13: Report Nullification / Amendment [1]:Nullification [2]:Amendment  -->
        </investigationCharacteristic>
      </subjectOf2>
      <subjectOf2 typeCode="SUBJ">
        <investigationCharacteristic classCode="OBS" moodCode="EVN">
          <code code="nullificationAmendmentReason" codeSystem="TBD"/>
          <value xsi:type="CE">
            <originalText>A.1.13.1</originalText>
            <!-- A.1.13.1: Reason for Nullification / Amendment -->
          </value>
        </investigationCharacteristic>
      </subjectOf2>
    </investigationEvent>
  </subject>
 </controlActProcess>
</PORR_IN049016UV>
<!-- Message #2 -->
<!-- PORR_IN049016UV -->
<!-- /PORR_IN049016UV -->
<!-- Message #2 -->
<receiver>
 <device classCode="DEV" determinerCode="INSTANCE">
  <id extension="M.1.6" root="ich-batch-receiver-identifier-oid"/>
  <!-- M.1.6: Batch Receiver Identifier -->
 </device>
</receiver>
<sender>
 <device classCode="DEV" determinerCode="INSTANCE">
  <id extension="M.1.5" root="ich-batch-sender-identifier-oid"/>
  <!-- M.1.5: Batch Sender Identifier -->
 </device>
</sender>
</MCCI_IN200100UV01>
```

Appendix IV (B) - Start date, End date, and Duration

Two of three elements should be populated as indicated in business rules in section 3.4.

1 B.2.i.3 Start Date and B.2.i.4 End date are populated, but B.2.i.5 Duration is not populated

```
    <observation moodCode="EVN" classCode="OBS">
        <id extension="1" root="oidInternalReferencesToReaction"/>
            <code code="reaction" codeSystem="TBD"/>
          <effectiveTime xsi:type="IVL_TS">
            <low value="20090101"/>
            <!-- B.2.i.3 Date of Start of Reaction / Event -->
            <high value="20090102"/>
            <!-- B.2.i.4: Date of End of Reaction / Event -->
          </effectiveTime>
          <value xsi:type="CE" code="B.2.i.1.b" codeSystem="2.16.840.1.113883.6.163"
                               codeSystemVersion="B.2.i.1.a">
            <!-- B.2.i.1.a: MedDRA Version for Reaction / Event -->
            <!-- B.2.i.1.b: Reaction / Event in MedDRA Terminology-->
```

```
                    <originalText>B.2.i.0.a</originalText>
                    <!-- B.2.i.0.a: Reaction / Event as Reported by the Primary Source in Native Language -->
                </value>

2   B.2.i.3 Start Date (or B.2.i.4 End Date) and B.2.i.5 Duration are populated

    <observation moodCode="EVN" classCode="OBS">
        <id extension="1" root="oidInternalReferencesToReaction"/>
            <code code="reaction" codeSystem="TBD"/>
                <effectiveTime xsi:type="IVL_TS">
                 <low value="20090101"/>
                <!-- B.2.i.3 Date of Start of Reaction / Event -->
                <width value="24" unit="B.2.i.5b"/>
                <!-- B.2.i.5a: Duration of Reaction / Event -->
                <!-- B.2.i.5b: Duration of Reaction / Event (Duration Unit) -->
                </effectiveTime>
                <value xsi:type="CE" code="B.2.i.1.b" codeSystem="2.16.840.1.113883.6.163"
                                    codeSystemVersion="B.2.i.1.a">
                <!-- B.2.i.1.a: MedDRA Version for Reaction / Event -->
                <!-- B.2.i.1.b: Reaction / Event in MedDRA Terminology-->
                <originalText>B.2.i.0.a</originalText>
                <!-- B.2.i.0.a: Reaction / Event as Reported by the Primary Source in Native Language -->
                </value>

3   B.2.i.3 Start date, B.2.i.4 End date, and B.2.i.5 Duration are populated

    <observation moodCode="EVN" classCode="OBS">
        <id extension="1" root="oidInternalReferencesToReaction"/>
            <code code="reaction" codeSystem="TBD"/>
            <effectiveTime xsi:type="SXPR_TS">
                <comp xsi:type="IVL_TS">
                    <low value="20090101"/>
                    <!-- B.2.i.3 Date of Start of Reaction / Event -->
                    <high value="20090102"/>
                    <!-- B.2.i.4: Date of End of Reaction / Event -->
                </comp>
                <comp xsi:type="IVL_TS" operator="A">
                    <width value="24" unit="h"/>
                    <!-- B.2.i.5a: Duration of Reaction / Event -->
                    <!-- B.2.i.5b: Duration of Reaction / Event (Duration Unit) -->
                </comp>
            </effectiveTime>
            <value xsi:type="CE" code="B.2.i.1.b"
                                codeSystem="2.16.840.1.113883.6.163" codeSystemVersion="B.2.i.1.a">
                    <!-- B.2.i.1.a: MedDRA Version for Reaction / Event -->
                <!-- B.2.i.1.b: Reaction / Event in MedDRA Terminology-->
                <originalText language="B.2.i.0.a2">B.2.i.0.a1</originalText>
                <!-- B.2.i.0.a1: Reaction / Event as Reported by the Primary Source in Native Language -->
                <!-- B.2.i.0.a2: Reaction / Event as Reported by the Primary Source Language -->
            </value>

4   B.4.k.4.r.6 Start Date and B.4.k.4.r.7 End Date are populated, but B.4.k.4.r.8 is not populated

    <substanceAdministration classCode="SBADM" moodCode="EVN">
        <text>B.4.k.4.r.10</text>
        <!-- B.4.k.4.r.10: Dosage Text -->
        <effectiveTime xsi:type="SXPR_TS">
            <comp xsi:type="PIVL_TS">
                <period value="10" unit="B.4.k.4.r.5"/>
```

```
                    <!-- B.4.k.4.r.4: Number of Units in the Interval -->
                    <!-- B.4.k.4.r.5: Definition of the Time Interval Unit -->
                </comp>
                  <comp xsi:type="IVL_TS" operator="A">
                    <low value="20090101"/>
                    <!-- B.4.k.4.r.6: Date and Time of Start of Drug-->
                    <high value="20090101"/>
                     <!-- B.4.k.4.r.7: Date and Time of Last Administration-->
                  </comp>
               </effectiveTime>
```

5 B.4.k.4.r.6 Start Date (or B.4.k.4.r.7 End Date) and B.4.k.4.r.8 are populated

```
      <substanceAdministration classCode="SBADM" moodCode="EVN">
            <text>B.4.k.4.r.10</text>
          <!-- B.4.k.4.r.10: Dosage Text -->
            <effectiveTime xsi:type="SXPR_TS">
               <comp xsi:type="PIVL_TS">
                    <period value="10" unit="B.4.k.4.r.5"/>
                  <!-- B.4.k.4.r.4: Number of Units in the Interval -->
                   <!-- B.4.k.4.r.5: Definition of the Time Interval Unit -->
                </comp>
                  <comp xsi:type="IVL_TS" operator="A">
                    <low value="20090101"/>
                    <!-- B.4.k.4.r.6: Date and Time of Start of Drug -->
                    <width value ="4" unit ="B.4.k.4.8b“/>
                     <!-- B.4.k.4.8a: Duration of Drug Administration (number) -->
                     <!-- B.4.k.4.8b: D\\uration of Drug Administration (unit) -->
                  </comp>
               </effectiveTime>
```

6 B.4.k.4.r.4 and B.4.k.4.r.5 are NOT populated, but one of the element from B.4.k.4.r.6, B.4.k.4.7, or B.4.k.4.r.8 is populated

In this case, data type should be IVL_TS or PIVL_TS to avoid schema error. SXPR_TS is not permitted.

An example with IVL_TS:

```
      <substanceAdministration classCode="SBADM" moodCode="EVN">
            <text>B.4.k.4.r.10</text>
          <!-- B.4.k.4.r.10: Dosage Text -->
            <effectiveTime xsi:type=“IVL_TS">
                <low value="20090101"/>
                    <!-- B.4.k.4.r.6: Date and Time of Start of Drug -->
              <width value ="4" unit ="B.4.k.4.8b“/>
                    <!-- B.4.k.4.r.8a: Duration of Drug Administration (number) -->
                    <!-- B.4.k.4.r.8b: Duration of Drug Administration (unit) -->
            </effectiveTime>
```

Another example with PIVL_TS:

```
      <substanceAdministration classCode="SBADM" moodCode="EVN">
            <text>B.4.k.4.r.10</text>
          <!-- B.4.k.4.r.10: Dosage Text -->
            <effectiveTime xsi:type="PIVL_TS">
              <period value="10" unit="B.4.k.4.r.5"/>
               <!-- B.4.k.4.r.4: Number of Units in the Interval -->
               <!-- B.4.k.4.r.5: Definition of the Time Interval Unit -->
            </effectiveTime>
```

7 B.4.k.4.r.6 Start date, B.4.k.4.r.7 End date, and B.4.k.4.r.8 Duration are populated

```
<substanceAdministration classCode="SBADM" moodCode="EVN">
    <text>B.4.k.4.r.10</text>
    <!-- B.4.k.4.r.10: Dosage Text -->
    <effectiveTime xsi:type="SXPR_TS">
        <comp xsi:type="PIVL_TS">
            <period value="10" unit="B.4.k.4.r.5"/>
            <!-- B.4.k.4.r.4: Number of Units in the Interval -->
            <!-- B.4.k.4.r.5: Definition of the Time Interval Unit -->
        </comp>
        <comp xsi:type="IVL_TS" operator="A">
            <low value="20090101"/>
            <!-- B.4.k.4.r.6: Date and Time of Start of Drug-->
            <high value="20090101"/>
            <!-- B.4.k.4.r.7: Date and Time of Last Administration -->
        </comp>
        <comp xsi:type="IVL_TS" operator="A">
            <width value="20090101"/>
            <!-- B.4.k.4.r.8a: Duration of Drug Administration (number) -->
            <!-- B.4.k.4.r.8b: Duration of Drug Administration (unit) -->
        </comp>
    </effectiveTime>
```

Appendix IV (C) - B.3 Test Result

1 B.3.r.d2 Value and Qualifier

- A value (e.g., “10 mg/dl”)
  In such case, the HL7 “value” element is composed of a single “center” element:

```
<value xsi:type="IVL_PQ" >
        <center value="10" unit="mg/dl" />
</value>
```

- Greater than a value (e.g. “ > 10 mg/dl”)
  In such case, the HL7 “value” element is composed of a range with “low” and “high” values. The “greater than” qualifier is represented with a positive infinite high value (i.e., using the “PINF” null flavour). The attribute “inclusive” is set to “false” to state that the qualifier is strict (i.e., with the equality):

```
<value xsi:type="IVL_PQ" >
        <low value="10" unit="mg/dl" inclusive="false"/>
        <high nullFlavor="PINF"/>
</value>
```

- Less than a value (e.g. “ < 10 mg/dl”)
  In such case, the HL7 “value” element is composed of a range with “low” and “high” values. The “less than” qualifier is represented with a negative infinite low value (i.e., using the “NINF” null flavour). The attribute “inclusive” is set to “false” to state that the qualifier is strict (i.e., with the equality):

```
<value xsi:type="IVL_PQ" >
        <low nullFlavor="NINF"/>
        <high value="10" unit="mg/dl" inclusive="false"/>
</value>
```

- Greater than or equal to a value (e.g. “ >= 10 mg/dl”)

In such case, the HL7 “value” element is composed of a range with “low” and “high” values. The “greater than or equal to” qualifier is represented with a positive infinite high value (i.e., using the “PINF” null flavour). The attribute “inclusive” is set to “true” to represent the equality:

```
<value xsi:type="IVL_PQ" >
        <low value="10" unit="mg/dl" inclusive="true"/>
        <high nullFlavor="PINF"/>
 </value
```

- Less than or equal to a value (e.g. “ <= 10 mg/dl”)
  In such case, the HL7 “value” element is composed of a range with “low” and “high” values. The “less than” qualifier is represented with a negative infinite low value (i.e., using the “NINF” null flavour). The attribute “inclusive” is set to “true” to represent the equality:

```
<value xsi:type="IVL_PQ" >
        <low nullFlavor="NINF"/>
        <high value="10" unit="mg/dl" inclusive="true"/>
 </value>
```

2 B.3.r.d.2 and B.3.r.e is populated

```
<observation moodCode="EVN" classCode="OBS">
     <code code="B.3.r.c2" codeSystem="2.16.840.1.113883.6.163"
     codeSystemVersion="B.3.r.c3">
        <!-- B.3.r.c2: Test Name (MedDRA code) -->
        <!-- B.3.r.c3: Test Name (MedDRA version) -->
       <originalText>B.3.r.c1</originalText>
        <!-- B.3.r.c1: Test Name (free text) -->
     </code>
     <effectiveTime xsi:type="SXCM_TS" value="20090101"/>
     <!-- B.3.r.b: Test Date -->
     <value xsi:type="IVL_PQ">
       <center value="10" unit="mg/dl"/>
        <!-- B.3.r.d2: Test Result (Value) -->
        <!-- B.3.r.e: Unit -->
      </value>
```

3 B.3.r.d.1 is populated

```
<observation moodCode="EVN" classCode="OBS">
      <code code="B.3.r.c2" codeSystem="2.16.840.1.113883.6.163"
      codeSystemVersion="B.3.r.c3">
       <originalText>B.3.r.c1</originalText>
      </code>
      <effectiveTime xsi:type="SXCM_TS" value="20090101"/>
      <!-- B.3.r.b: Test Date -->
      <interpretationCode code="Positive" codeSystem="TBD"/>
      <!-- B.3.r.d1: Test Result (Code) -->
```

4 B.3.r.f is populated

```
<observation moodCode="EVN" classCode="OBS">
      <code code="B.3.r.c2" codeSystem="2.16.840.1.113883.6.163"
     codeSystemVersion="B.3.r.c3">
      <originalText>B.3.r.c1</originalText>
      </code>
```

```
<effectiveTime xsi:type="SXCM_TS" value="20090101"/>
<!-- B.3.r.b: Test Date -->
<value xsi:type="ED">B.3.r.f</value>
 <!-- B.3.r.f: Result Unstructured Data (free text) -->
```

Appendix IV (D) – B.4.k.4.r Dosing Examples

1. 1 per day

```
<sourceOf2 typeCode="COMP" contextConductionInd="true">
    <substanceAdministration classCode="SBADM" moodCode="EVN">
        <text>1 per day</text>
        <statusCode code="active"/>
        <effectiveTime xsi:type="PIVL_TS">
            <period value="1" unit="d"/>
        </effectiveTime>
    </substanceAdministration>
</sourceOf2>
```

—2. 1 tablet per day

```
<sourceOf2 typeCode="COMP" contextConductionInd="true">
    <substanceAdministration classCode="SBADM" moodCode="EVN">
        <text>1 tablet per day</text>
        <statusCode code="active"/>
        <effectiveTime xsi:type="PIVL_TS">
            <period value="1" unit="d"/>
        </effectiveTime>
        <doseQuantity value="1" unit="1"/>
        <consumable>
            <instanceOfKind classCode="INST">
            <kindOfProduct classCode="MMAT" determinerCode="KIND">
                    <code code="drugTypeCode"/>
                    <formCode code="123" codeSystem="1.2.3"
                    displayName="tablet"/>
                </kindOfProduct>
            </instanceOfKind>
        </consumable>
    </substanceAdministration>
</sourceOf2>
```

—3. One time daily, 1/4 tablet

```
<sourceOf2 typeCode="COMP" contextConductionInd="true">
    <substanceAdministration classCode="SBADM" moodCode="EVN">
        <text>One time daily, 1/4 tablet</text>
        <statusCode code="active"/>
        <effectiveTime xsi:type="PIVL_TS">
            <period value="1" unit="d"/>
        </effectiveTime>
        <doseQuantity value="0.25" unit="1"/>
        <consumable>
            <instanceOfKind classCode="INST">
                <kindOfProduct classCode="MMAT"
                determinerCode="KIND">
                    <code code="drugTypeCode"/>
                    <formCode code="123" codeSystem="1.2.3"
                    displayName="tablet"/>
                </kindOfProduct>
            </instanceOfKind>
        </consumable>
    </substanceAdministration>
</sourceOf2>
```

—4. Once per week, 6 tablets

```
<sourceOf2 typeCode="COMP" contextConductionInd="true">
    <substanceAdministration classCode="SBADM" moodCode="EVN">
        <text>Once per week, 6 tablets</text>
        <statusCode code="active"/>
        <effectiveTime xsi:type="PIVL_TS">
```

```
                                    <period value="1" unit="wk"/>
                                </effectiveTime>
                                <doseQuantity value="6" unit="1"/>
                                <consumable>
                                    <instanceOfKind classCode="INST">
                                        <kindOfProduct classCode="MMAT"
                                        determinerCode="KIND">
                                            <code code="drugTypeCode"/>
                                            <formCode code="123" codeSystem="1.2.3"
                                            displayName="tablet"/>
                                        </kindOfProduct>
                                    </instanceOfKind>
                                </consumable>
                            </substanceAdministration>
                        </sourceOf2>
7. Two times a day, 1 tablet
                        <sourceOf2 typeCode="COMP" contextConductionInd="true">
                            <substanceAdministration classCode="SBADM" moodCode="EVN">
                                <text>Two times a day, 1 tablet</text>
                                <statusCode code="active"/>
                                <effectiveTime xsi:type="PIVL_TS">
                                    <period value="0.5" unit="d"/>
                                </effectiveTime>
                                <doseQuantity value="1" unit="1"/>
                                <consumable>
                                    <instanceOfKind classCode="INST">
                                        <kindOfProduct classCode="MMAT"
                                        determinerCode="KIND">
                                            <code code="drugTypeCode"/>
                                            <formCode code="123" codeSystem="1.2.3"
                                            displayName="tablet"/>
                                        </kindOfProduct>
                                    </instanceOfKind>
                                </consumable>
                            </substanceAdministration>
                        </sourceOf2>
—8. Four times a day, 7.5 milligrams
                        <sourceOf2 typeCode="COMP" contextConductionInd="true">
                            <substanceAdministration classCode="SBADM" moodCode="EVN">
                                <text>Four times a day, 7.5 milligrams</text>
                                <statusCode code="active"/>
                                <effectiveTime xsi:type="PIVL_TS">
                                    <period value="0.25" unit="d"/>
                                </effectiveTime>
                                <doseQuantity value="7.5" unit="mg"/>
                            </substanceAdministration>
                        </sourceOf2>
9. One time daily in a spoon (=15 ml)
                        <sourceOf2 typeCode="COMP" contextConductionInd="true">
                            <substanceAdministration classCode="SBADM" moodCode="EVN">
                                <text>One time daily in a spoon (=15 ml)</text>
                                <statusCode code="active"/>
                                <effectiveTime xsi:type="PIVL_TS">
                                    <period value="1" unit="d"/>
                                </effectiveTime>
                                <doseQuantity value="15" unit="ml">
                                <translation code="SP" codeSystem="1.2.3" displayName="spoon
                                full"/>
                                </doseQuantity>
                            </substanceAdministration>
                        </sourceOf2>
<!-- xxxxxxxxxx 1 tablet every other day xxxxxxxxxxxxxxxxxxxxx -->
                        <sourceOf2 typeCode="COMP" contextConductionInd="true">
                            <substanceAdministration classCode="SBADM" moodCode="EVN">
                                <text>1 tablet every other day</text>
                                <statusCode code="active"/>
```

```
                    <effectiveTime xsi:type="PIVL_TS">
                        <period value="2" unit="d"/>
                    </effectiveTime>
                    <doseQuantity value="1" unit="1"/>
                    <consumable>
                        <instanceOfKind classCode="INST">
                            <kindOfProduct classCode="MMAT"
                            determinerCode="KIND">
                                <code code="drugTypeCode"/>
                                <formCode code="123" codeSystem="1.2.3"
                                displayName="tablet"/>
                            </kindOfProduct>
                        </instanceOfKind>
                    </consumable>
                </substanceAdministration>
            </sourceOf2>
```

APPENDIX V - ABBREVIATIONS

Abbreviations	Definition
A	Alpha
AA	Application Acknowledgement Accept
AAE	Application Acknowledgement Error
ADR	Adverse Drug Reaction
AE	Adverse Event
AN	Alphanumeric
APEC	Asia-Pacific Economic Cooperation
ASEAN	Association of Southeast Asian Nations
BAG	An HL7 data type that refers to an unordered collection of values where each value can be contained more than once
BL	Boolean
CD	Concept Descriptor*
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
DA	Document Available
DSTU	Draft Standard for Trial Use
DTD	Document Type Definition
ECG	electrocardiogram
ED	Encapsulated Data*
EDIFACT	Electronic Data Interchange for Administration, Commerce and Transport
EEA	European Economic Area
EFPIA	European Federation of Pharmaceutical Industries and Associations
EFTA	European Free Trade Association
EN	Entity Name
ESTRI	Electronic Standards for the Transmission of Regulatory Information
EU	European Union
FDA	United States Food and Drug Administration
GCC	Gulf Cooperation Countries
GCG	Global Cooperation Group
GTS	General Timing Specifications
HCP	Healthcare Professionals
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 3.3.1)
IFPMA	International Federation of Pharmaceutical Manufacturers Associations
II	Instance Identifier

Abbreviations	Definition
ISO	International Organisation for Standardisation
ITS	Implementable Technology Specification
IVL_TS	Interval of time*
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
PQ	physical quantity
prEN ISO 27953	Reference number for working document prepared by ISO Technical Committee TC 215 on Health informatics jointly with HL7 and CEN.
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
SET	An HL7 data type that refers to a data element that contains other distinct values in no particular order
SGML	Standard Generalised Markup Language. An ISO standard for describing structured information in a platform independent manner
SNOMED	The Systematized Nomenclature of Human and Veterinary Medicine
SNOMED-CT	Systematized Nomenclature of Medicine-Clinical Terms
ST	Character String*
TC215	International Organisation of Standards Technical Committee 215, Health Informatics
TN	Trivial Name*
TS	Point in Time*
UCUM	UCUM (Unified Code for Units of Measure)
UML	Unified Modeling Language
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 VI - ROUTES OF ADMINISTRATION (E2B(R2) ATTACHMENT 2)

The three digit numeric codes provided below should be used to populate fields that require the routes of administration documented in this Implementation Guide until such a time as prEN ISO 11239 becomes an International Standard. The M2 numeric codes below represent various pre-defined routes of administration.

Please use the ICH M2 numeric codes below to populate fields that require the E2B(R3) routes of administration.

Description	ICH M2 Numeric Codes
Auricular (otic)	001
Buccal	002
Cutaneous	003
Dental	004
Endocervical	005
Endosinusial	006
Endotracheal	007
Epidural	008
Extra-amniotic	009
Hemodialysis	010
Intra corpus cavernosum	011
Intra-amniotic	012
Intra-arterial	013
Intra-articular	014
Intra-uterine	015
Intracardiac	016
Intracavernous	017
Intracerebral	018
Intracervical	019
Intracisternal	020
Intracorneal	021
Intracoronary	022
Intradermal	023
Intradiscal (intraspinal)	024
Intrahepatic	025
Intralesional	026
Intralymphatic	027
Intramedullar (bone marrow)	028
Intrameningeal	029
Intramuscular	030
Intraocular	031
Intrapericardial	032
Intraperitoneal	033
Intrapleural	034
Intrasynovial	035
Intratumor	036
Intrathecal	037
Intrathoracic	038
Intratracheal	039
Intravenous bolus	040
Intravenous drip	041

Description	ICH M2 Numeric Codes
Intravenous (not otherwise specified)	042
Intravesical	043
Iontophoresis	044
Nasal	045
Occlusive dressing technique	046
Ophthalmic	047
Oral	048
Oropharingeal	049
Other	050
Parenteral	051
Periarticular	052
Perineural	053
Rectal	054
Respiratory (inhalation)	055
Retrobulbar	056
Sunconjunctival	057
Subcutaneous	058
Subdermal	059
Sublingual	060
Topical	061
Transdermal	062
Transmammary	063
Transplacental	064
Unknown	065
Urethral	066
Vaginal	067

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