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

ICH M2 EWG

Electronic Transmission of Individual Case Safety Reports Message Specification

(ICH ICSR DTD Version 2.1)

Final Version 2.3 Document Revision February 1, 2001

Rapporteur

Greg Brolund
Associate Director for Technology
Policy and Standards
Office of Information Technology

Center for Drug Evaluation and Research (CDER)
U.S. Food and Drug Administration
5600 Fishers Lane, Room 12A43
Rockville, MD 20857

This Specification has been developed by the ICH M2 Expert Working Group in accordance with the ICH Process as it pertains to the M2 EWG.

ICH M2 Expert Working Group Members

Name	Organization
Greg Brolund - *Rapporteur*	FDA
Melissa R. Chapman	FDA
Robin Jones	FDA
George P. George	FDA
Esteban G. Juarros	EU
Antonia Rana	EU
Takahisa Murakami	MHW
Mihoko Okada	MHW
Shigekoto Kaihara	MHW
Daisuke Koide	MHW
Kenichi Tamiya	MHW
Krishan Arora	PhRMA
Robert Hizer	PhRMA
Rick Bowen	PhRMA
Mervyn Mitchard	EFPIA
Gabriele Disselhoff	EFPIA
Marc Elbet	EFPIA
Tohru Uwoi	JPMA
Keiji Sawamukai	JPMA
Yuichi Nagoshi	JPMA
Hitoshi Asano	JPMA
Tadao Akiyama	JPMA
Harv Martens	JPMA
Robert Kapitany	HC

TABLE OF CONTENTS

1.0 PURPOSE

This document describes the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) M2 Document Type Definition (DTD) of the electronic message for the transmission of Individual Case Safety Reports (ICSRs) based on the ICH E2BM step 4 document version 4.4, Data Elements for Transmission of Individual Case Safety Reports.

The only source of ICH official information is the ICH website: http://www.ifpma.org/m2-main.html.

2.0 BACKGROUND

The ICH was organized to provide an opportunity for tripartite harmonization initiatives to be developed with input from both regulatory and industry representatives. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products among three regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission-European Union (EU), the European Federation of Pharmaceutical Industries' Associations (EFPIA), the Japan Ministry of Health and Welfare (MHW), the Japan Pharmaceutical Manufacturers Association (JPMA), the US Food and Drug Administration (FDA), and the Pharmaceutical Research and Manufacturers of America (PhRMA). The ICH Secretariat, which co-ordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization (WHO), the Canadian Health Protection Branch, and the European Free Trade Area.

To facilitate the standardization of the data elements for the transmission of ICSRs for both pre-approval and post-approval reporting periods, the ICH E2BM Expert Working Group prepared the guideline "Data Elements for Transmission of Individual Case Safety Reports."

The guideline standardizes the data elements for the transmission of ICSRs by identifying and defining the data elements for the transmission of all types of ICSRs, regardless of source and destination. This includes case safety reports for both pre- and post-approval periods and covers both adverse drug reaction and adverse event (AE) reports.

The guideline states that because of national and international agreements, rules, and regulations, ICSRs of adverse drug reactions and AE should be transmitted (e.g., US 21CFR314.80):

- From identified reporting sources to regulatory authorities and pharmaceutical companies
- Between regulatory authorities
- Between pharmaceutical companies and regulatory authorities
- Within authorities or pharmaceutical companies

- From clinical investigators, via the sponsor, to ethics committees

- From authorities to the WHO Collaborating Centre for International Drug Monitoring.

The transmission of ICSRs currently relies on paper-based formats (e.g., yellow cards, Council for International Organizations of Medical Sciences (CIOMS) forms, MedWatch) or electronic media (e.g., within pharmaceutical companies, or with WHO), usually via online access, tape, or file transfer.

Considering the high volume of data and the large number of potential participants in a world-wide exchange of information, there is a need for an electronic format capable of accommodating the electronic transmission of the Safety Reports that can be directly generated and processed by a database application.

Successful electronic transmission of ICSRs relies on the agreement of common data elements and on the syntactical definition of the electronic message.

The definition of the common data elements is provided in the E2BM step 4 document version 4.4. The syntactical definition of the electronic message is provided in the ICH M2 Expert Working Group (EWG) recommendations and specifications.

This document describes the specification of the message definition for the electronic transmission of ICSRs agreed by ICH M2.

This document also reflects modifications agreed to by the E2BM EWG during meetings from February 2000 through November 2000.

2.1 Representation of the Electronic ICSR

The ICH community agreed that the ICSRs, including pre-marketing and post-marketing adverse drug reactions and adverse drug events, should be gathered, managed, and distributed electronically, but there was a need to find consensus on how this should be done.

The objective was to represent the document in a way that would make possible transfer of its contents from one database to another. In addition, the representation should use an international standard that is platform, application and vendor independent.

This initiative relied on the previous work done by the EuroScape consortium that had defined the MEDADR safety report in EDIFACT (Electronic Data Interchange for Administration, Commerce and Transport). There was also a large tradition of standardization of health related messages in HL7 (Health Level Seven), a specification used for electronic data exchange of healthcare information. As a result, both EDIFACT and HL7 syntax were originally considered for the formal specification of the electronic message for the transmission of safety reports of adverse drug reactions and adverse drug events. However, the need to support multi-lingual characters and the time it takes to get a new message approved for use by the standards organizations made Standard Generalized Markup Language (SGML, ISO 8879:1986) a better alternative.

SGML is an international standard for documents and it is also useful for the interchange of structured data. It presents some advantages:

- Validation of the message with available off-the-shelf software
- Creation and processing of messages on current document technology.

In addition SGML document types facilitate the implementation of relevant functions:

- Interchange of data among different databases with heterogeneous data types
- Transformation of the data structure into relational databases
- Portability of data.

Information for electronic submission in SGML is prepared by inserting data appropriately between the start and end tags so the information maintains the relationships specified by the DTD. Typically, SGML editing tools can be used to prepare a data set that is specific to the SGML DTD.

In November 1996, in London, the ICH M2 EWG decided to concentrate the efforts to produce a DTD[1] of the message for the electronic transmission of ICSRs: the ICH_ICSR.DTD.

At the following meeting of the ICH M2 EWG in March 1997 in Narita, the six parties agreed on the relational data model to be used for the definition of the electronic message based on the ICH E2B document Step 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, and 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 E2BM and the ICH ICSR specifications were completed in November 2000. The official guidelines,

---

[1] An SGML conformant document consists of an SGML prologue and a document instance. The prologue contains an SGML declaration and a document type definition, which contains element and entity declarations. Different software applications may provide different ways of associating the document instance with the prologue and in some cases the prologue may be inserted into the software used, so that it is transparent to the user.

The SGML declaration specifies basic facts about the dialect of SGML being used, such as the character set, the codes used for SGML delimiters, and the length of identifiers.

The document type definition specifies the DTD against which the document instance is to be validated. Like the SGML declaration, it may be held in the form of compiled tables within the SGML processor, or associated with it in some way that is invisible to the user, or require only that the name of the document type be specified before the document is validated.

The data instance is the content of the data itself. It may contain text, mark-up, and general entity references.

recommendations and specifications for the ICH ICSR message definition can be obtained only from the ICH M2 website, http://www.ifpma.org/m2-main.html. Detailed instructions for preparing SGML data are also available from the manuals section of the website.

As a result of this activity, AE data can be extracted, populated, and electronically transmitted in the manner specified by the ICH ICSR message from safety and surveillance databases.

3.0 ESSENTIAL COMPONENTS

Developing software specifications to meet requirements, such as those specified in the E2BM step 4 document version 4.4, requires an approach where the functional and procedural requirements are well understood and reflected accurately in the electronic message. The electronic message must constitute not only the definition of the data elements, but also maintain the required relationships between the elements for efficient information exchange. The development of the relational diagrams, an attribute list, numeric codes, and the ICH ICSR SGML DTD is a result of efforts to define software specifications to facilitate electronic submissions of ICSRs. The ICH ICSR message allows for the preparation of AE data sets that can accurately maintain and represent the intended purpose of the E2BM document. Section 3 of this ICSR specification document lists the essential components required to develop usable ICH ICSR messages.

3.1 ICSR Relational Diagrams

The following ICSR relational diagrams illustrate the relationship between the various sections and data elements defined in the E2BM step 4 document version 4.4 and the field attributes for the ICH ICSR message and DTD descriptors. A box in the relational view diagram represents the entire related section of the E2BM document and all the data elements in the related block of the attribute list. For example, box A.1 in the diagram, Identification of the Case Safety Report, represents the complete A.1 section of the E2BM document and the A.1 block of elements listed in the attribute list. To maintain the intent of the E2BM specifications and to represent the various mandatory, optional, single, and repeatable sections or fields, the relationships between the boxes also vary from as much as a 1 to 1 relationship, a 1 to 0 or 1 relationship, a 1 to 1 or many relationship, or a 1 to 0 or many relationship. These diagrams are particularly useful for database administrators and application developers in understanding how the ICSR SGML DTD was designed and developed per the E2BM specification document.

3.1.1 M2 Relational View of E2B Data Elements

The ICH M2 relational view of the E2B data elements shows the order and relationship between the various sections of the E2B document. This diagram (Figure 1) is useful in understanding how the various sections in the E2B document are organized and related to one another.

M2 Relational View of E2B Data Elements

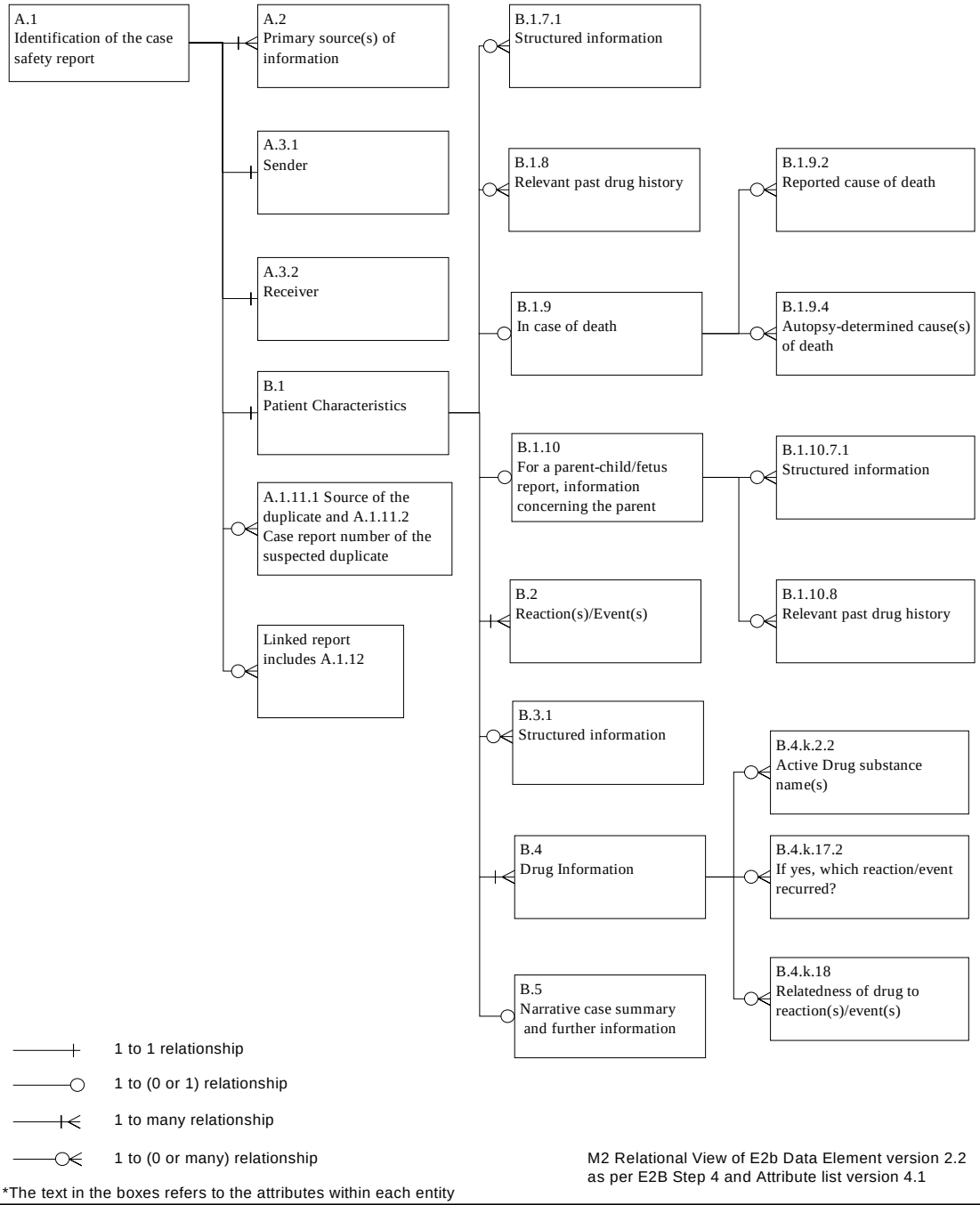

Figure 1 Note: The element names of A.1.11.1 and A.1.11.2 changed in E2BM step 4 document version 4.4 changed to A.1.11.1 Source(s) of the case identifier and A.1.11.2 Case Identifier(s).

3.1.2 M2 Entities and Relationships Diagram

The M2 Entities and Relationships diagram (Figure 2) depicts the M2 defined entities and their relationships to the E2B data elements. The field names are found in the description column of the ICSR attributes list for the ICH ICSR message and DTD.

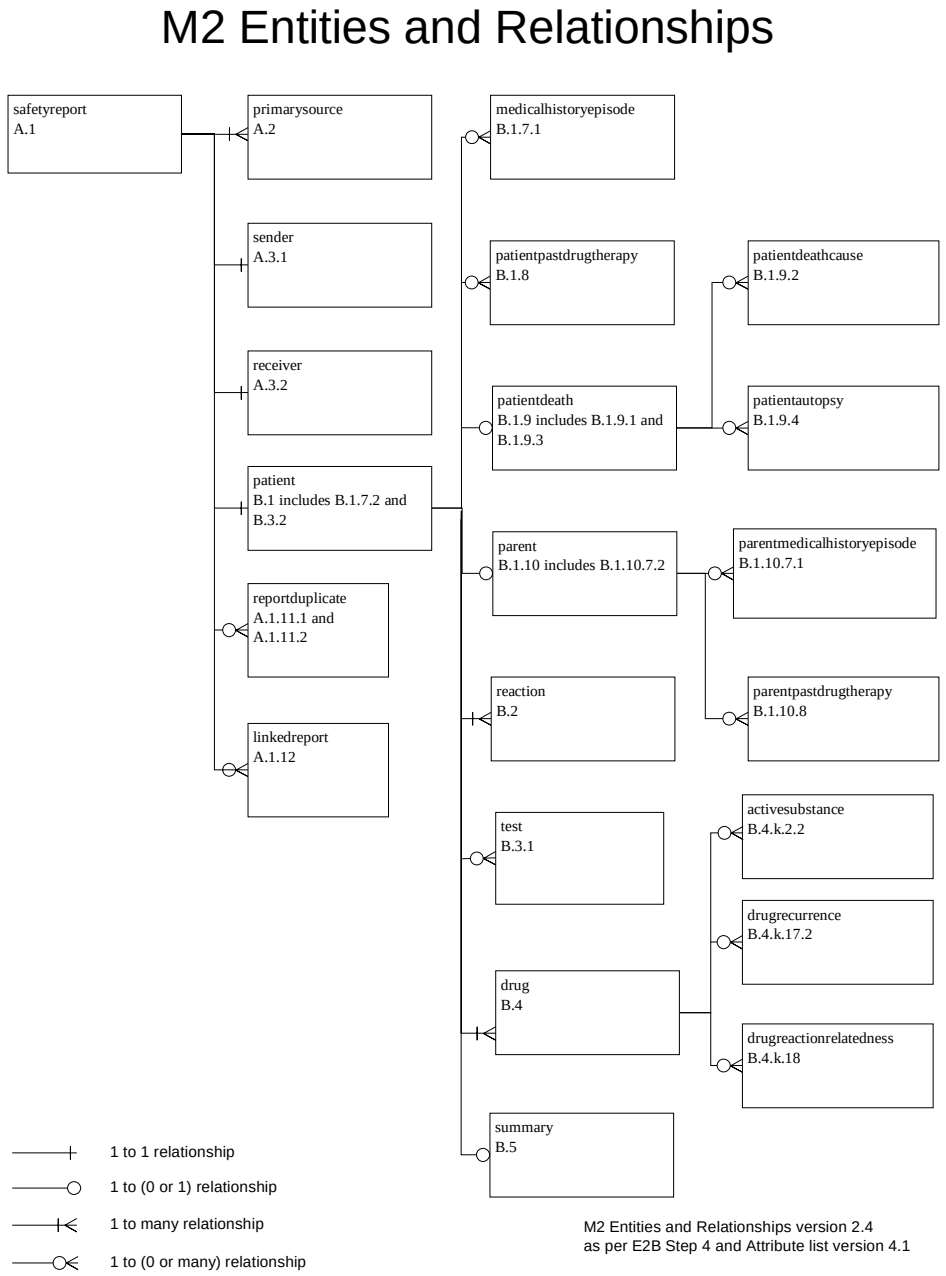

Figure 2

The entities and relationships diagram is similar to the relational view diagram, but it is particularly helpful to bridge the gap from the M2 relational view diagram to the ICSR attribute list, and eventually to the ICSR SGML DTD.

3.2 ICH ICSR Attribute List

This ICSR specification document contains the ICH M2 attribute list with SGML descriptor names per the E2BM step 4 document version 4.4 in Attachment1. This ICSR attribute list contains the data element number, title, description, field length, field value, and DTD descriptor for each data element. The various elements are also grouped and numbered to match with the organization of the E2BM document. The attribute list has three types of blocks, depicted as a regular single line border, bold lined border, and double lined border. Fields within the single line border can occur once or not at all, while fields or blocks with a bold border might be repeated, and fields or blocks with a double line border might also be repeated, within the containing block. The ICH M2 field attribute list should be used to verify the accuracy and compliance of data entered when preparing an ICSR SGML 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 M2 group has also defined the following elements for a message header section. The detailed specifications of these elements are mentioned in Appendix A.1.

ICH ICSR Message Header

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

Message Type

The message type contains information on the type of information being transmitted. It is specified in the M2 Recommendation 5.3. When creating an ICH ICSR message, the value of this field should be “ichicsr”.

Message Format Version

The message format version contains the version number of the DTD and it is specified in M2 Recommendation 5.3. The value of the version number can be obtained from the documentation section of the ICH ICSR DTD.

Message Format Release

The message format release contains the release number of the message format version number of the DTD and it is specified in M2 Recommendation 5.3. The value of the release number can be obtained from the documentation section of the ICH ICSR DTD.

Message Number, Sender defined message number (unique to the sender)

The message number is a unique tracking number assigned to a specific ICH ICSR message file transmitted by the sender. This message number is unique to the sender.

Message Sender Identifier

This field identifies the sender of the ICSR reports, e.g., company name or regulatory authority name (ICSR Attribute List A.3.1.2).

Message Receiver Identifier

This field identifies the intented recipient of the transmission of ICSR reports, e.g., company name or regulatory authority name (ICSR Attribute List A.3.2.2a).

Message Date and Format

The message date is the date on which the ICH ICSR message was initiated.

The diagram on the next page illustrates the specified relationship where each ICH ICSR message will have one message header section, and one or more ICSRs.

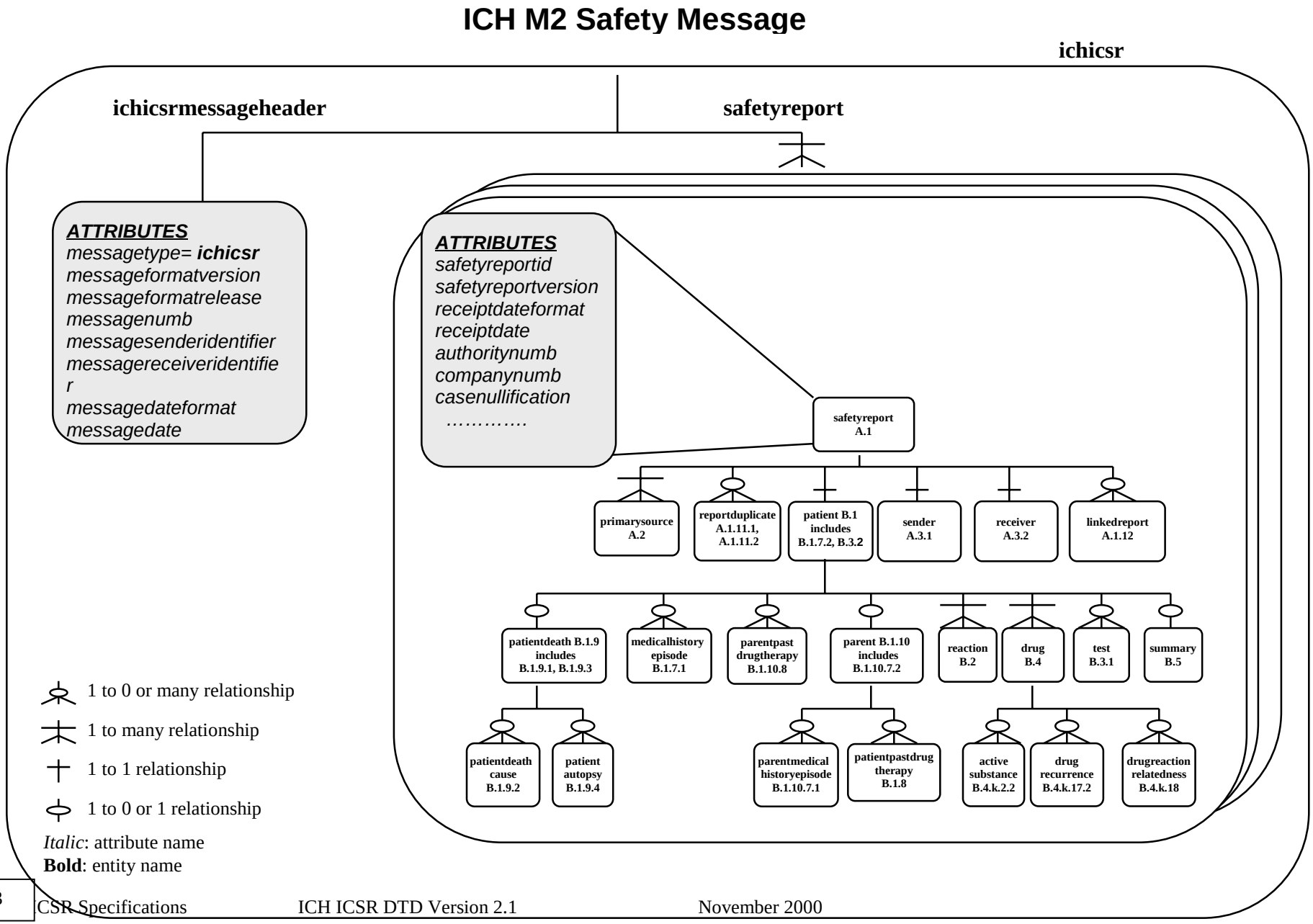
ICH M2 Safety Message
ichicsr
ichicsrmessageheader
safetyreport
ATTRIBUTES
messagetype= ichicsr
messageformatversion
messageformatrelease
messagenumb
messagesenderidentifier
messagereceiveridentifier
messagedateformat
messagedate
ATTRIBUTES
safetyreportid
safetyreportversion
receiptdateformat
receiptdate
authoritynumb
companynumb
casenullification
……
safetyreport A.1
primarysource A.2
reportduplicate A.1.11.1, A.1.11.2
patient B.1 includes B.1.7.2, B.3.2
sender A.3.1
receiver A.3.2
linkedreport A.1.12
patientdeath B.1.9 includes B.1.9.1, B.1.9.3
medicalhistory episode B.1.7.1
parentpast drugtherapy B.1.10.8
parent B.1.10 includes B.1.10.7.2
reaction B.2
drug B.4
test B.3.1
summary B.5
patientdeath cause B.1.9.2
patient autopsy B.1.9.4
parentmedical historyepisode B.1.10.7.1
patientpastdrug therapy B.1.8
active substance B.4.k.2.2
drug recurrence B.4.k.17.2
drugreaction relatedness B.4.k.18
1 to 0 or many relationship
1 to many relationship
1 to 1 relationship
1 to 0 or 1 relationship
Italic: attribute name
Bold: entity name

Figure 3

3.3 ICH ICSR DTD

The DTD describes each element of the ICSR being transmitted and shows how the various elements relate to each other. Within the encoded text, the DTD specifies which elements are required and the order in which they should appear. According to the model specified in the DTD, each ICSR consists of one message header, followed by one or more ICSRs. Please refer to Appendix A.2 for a full text definition of this document. The original document can be obtained from the M2 website at the following URL: http://www.ifpma.org/m2-main.html.

To make improvements to version 1.0 of the ICH ICSR DTD, the M2 Expert Working Group has made the following modifications that are reflected in ICH ICSR DTD, Version 2.0. The documentation section of version 2.0 contains the complete list of changes.

- The ICH ICSR DTD, version 2.0 is now designed to support multiple language character sets to meet the diverse and complex reporting requirements of all the ICH regions. The details on the use of multiple language character sets are described in section 6.0 of this document.

- To help manage, route, identify, and track ICH ICSR messages, new elements have been added to the message header section of the ICH ICSR DTD.

- Data prepared for the ICH ICSR, version 1.0 required that no carriage returns be inserted after end tags. This was because version 1.0 of the ICH ICSR DTD was sensitive to carriage returns. Often, inserting carriage returns, after end tags caused SGML errors when the file was parsed. This was caused by the use of "mixed content models" within the DTD, and in particular with the way sequence numbers were represented. It is not necessary to understand the details of the SGML concept of a mixed content model, other than to point out that using it within the ICH ICSR DTD version 1.0 caused unpredictable parsing errors, when carriage returns were inserted after the end tags. This absence of carriage returns in turn made the SGML documents difficult to read.

  To make the SGML data more readable, by permitting insertion of carriage returns after end tags and to eliminate the mixed content model problem, the sequence number elements (all XXXXsq elements) were removed. However, to maintain compliance with the relational model, the SGML specification had to be modified so that the higher level entities were specified as (+) for 1 or more or (*) for 0 or more.

  The following table illustrates how data is prepared without the use of sequence numbers. In version 1.0, repeating elements had a sequence number, such as <reportduplicatesq> for <reportduplicate>. The elements related to the sequence number, such as <duplicatesource> and <duplicatenumb> were repeated within a sequence. For version 2.0 of the ICH ICSR DTD, the data elements that required multiple occurrences are repeated, such as <duplicatesource> and <duplicatenumb> within <reportduplicate>.

	ICSR DTD	**ICSR SGML Data**
Specification for ICH ICSR, Version 1.0	Medicallyconfirm? & (**reportduplicate?** & linkedreport? & …….. <!ELEMENT reportduplicate - - (**reportduplicatesq***) > <!ELEMENT reportduplicatesq - - (#PCDATA, (**duplicatesource?** & **duplicatenumb?**)) > <!ATTLIST reportduplicatesq %ope.rec; >	<medicallyconfirm>1</medicallyconfirm> <**reportduplicate**><**reportduplicatesq**>**001**<**duplicatesource**> smith, coopers, barnies, and young pharmaceuticals</duplicatesource>**><duplicatenumb**>nmbr123456789101112131415161718920</duplicatenumb>**</**reportduplicatesq><**reportduplicatesq**>**002<duplicatesource>** smith, coopers, barnies, and young pharmaceuticals</duplicatesource><**duplicatenumb>**number123456789101112131415161718l9</duplicatenumb></reportduplicatesq></reportduplicate>
Specification for ICH ICSR, Version 2.0	Medicallyconfirm? , (**reportduplicate*** , linkedreport* , primarysource+ , ……. <!ELEMENT **reportduplicate** (**duplicatesource?,** **duplicatenumb**?)> <!ATTLIST reportduplicate %lang.att; >	<medicallyconfirm>1</medicallyconfirm> **<reportduplicate>** <**duplicatesource**>smith, coopers, barnies, and young pharmaceuticals</duplicatesource> <**duplicatenumb**>nmbr12345678910111213 14151617181920</duplicatenumb> </reportduplicate> **<reportduplicate>** <**duplicatesource**>smith, coopers, barnies, and young pharmaceuticals</duplicatesource> <**duplicatenumb**>number1234567891011121 3141516171819</duplicatenumb> </reportduplicate>

- The data elements in the ICH ICSR DTD version 1.0 could occur in any order. Now the specifications are tighter, specifying a particular order.

- APP/REP/DEL was removed in version 2.0 to ensure that each ICSR submission will contain as much information as is available at the time of submission (i.e., “complete submission”). The %act.rec; and %ope.rec; internal entities, were removed, thus removing all support for the "(app | rep | del)" construct. This also removes all support for "old" attribute.

- References to “old” attribute were removed from version 2.0 of the DTD to ensure that new or changed information will not be electronically “highlighted” on electronic ICSR submissions.

- The “lang” attribute was added to all the elements of the ICH ICSR DTD to ensure that data in multiple languages can be supported.

- To cover all of the languages necessary to support the use of the ICH ICSR message, five declaration (DCL) files, including one for ISO 10646 (UNICODE), are distributed with the DTD. Additional information on the DCL files is provided in section 3.4 of this document.

- Special characters, such as "<" or "&", are represented according to the SGML standard. Specifications have been added to allow for standard character entities to escape SGML special characters. When "<", ">", and "&" occurred in text, they can be replaced by "<", ">", and "&" respectively.

- The relationship between Drug and Active Substance was changed from a 1 to 1 or many relationship to a 1 to 0 or many relationship, in version 2.0 of the ICH ICSR DTD.

- The data model of the ICH ICSR message has been modified so that the root element of DTD is now "ichicsr" which is related to one "ichicsrmessageheader" and multiple (1 or more) "safetyreport" (See Figure 3).

- A tag, safetyreportversion, has been added to go with safetyreportid to enable the recording of the version number of the safetyreportid. A sender of an ICH ICSR message might assign a number to the safetyreportid, to identify each ICSR, and assign a number to safetyreportversion to differenciate the different versions of an ICSR.

- The field resultstestsprocedures (E2B – B.3.2 Results of test and procedures relevant to the investigation of the patient) is now an optional field.

- The lengths of certain fields have been changed to meet the business requirements.

Improvements in version 2.0 of the DTD and version 2.24 of the ICSR specification document made by the E2BM EWG. The changes, resulting in version 2.1 of the DTD and version 2.3 of the ICSR specification document, are summarized as follows:

- A new data element was added to allow for reporting of events/reactions as reported, and as MedDRA Lowest Level Terms (LLT) and Preferred Terms (PT). The "as reported" and reaction term elements existed in the previous version. A new element was added allowing inclusion of both LLT and PT in the ICSR. The ICSR attribute list and the DTD were changed to reflect these modifications.

- There are several data elements that are MedDRA controlled fields. MedDRA version should be included for each term used. A data element for each MedDRA controlled field has been added to accommodate MedDRA version number. The ICSR attribute list and the DTD were changed to reflect these modifications.

- The use of report identification and sender identification elements has been clarified. The previous description of unique identifier was removed from the ICSR specification and is now described in detail in the E2BM revised Step 4 document (version 4.4).

- The valid field lengths for several data elements were extended to allow for more information to be submitted. These new lengths are detailed in the ICSR Attribute List.

- The DCL (declaration) file for supporting the Shift JIS character set for encoding Japanese has been modified.

- Safety Report Version (ICH ICSR M2 Data Processing element) is not an E2BM data element, but rather should be used for technical transmission purposes.

3.4 DCL Files for Multi-Language Character Sets

The DCL (declaration) file describes the capabilities of an SGML system. It includes the following information: the character encoding used in the DTD and the document, the amount of system resources required by the DTD, the delimiters used in marking up the document, the SGML features used by the document markup, and other information specific to the application.

The SGML declaration provides several critical pieces of information to the SGML parser that allow it to correctly interpret an SGML document. Relevant to the use of the ICH ICSR message is the SGML declaration's function to tell the SGML parser which character set has been used to encode an SGML document. Because ICH ICSR messages may be interchanged in several languages, and because each language may require a different character set, the SGML declaration becomes critical in documenting which character set is being used in an ICH ICSR message.

SGML was designed with the assumption that only one character set would be used within any one document. As such, an SGML declaration documents a single character set, and expects that any one SGML document will be encoded with a single character set. A single character set may be able to represent more than one language. The ASCII character set can only represent English, however the ISO 8858-1 character set can represent most of the Western European languages, and ISO 10646 (UNICODE) can represent almost all of the world's currently written languages.

To meet the multi-language capabilities of the three regions, five different DCL files have been provided for use with the ICH ICSR, version 2.0 and the ICSR Acknowledgment Message DTDs. The receiver of the SGML message needs to know which of the five DCL files were used for the reports. For example, one way might be to use the trading partnership agreement to specify the type of DCL file that can be used for the submission.

The DCL files along with brief descriptions of their purpose are provided in Appendix A.3. The ICH ICSR and ICSR Acknowledgment DTDs also have a technical note with instructions on appropriate use and brief descriptions of the five DCL files.

3.5 ICH M2 Numeric Codes for E2BM Unit Codes and Routes of Administration

E2BM has specified various unit codes and routes of administration codes for population of certain fields. To facilitate efficient data transport, validation, and information exchange, the M2 EWG has provided numeric codes for both the unit codes and the routes of administration.

3.5.1 ICH M2 Numeric Codes for Unit List (E2BM Attachment 1)

The ICH M2 numeric codes, listed in Appendix A.4, must be used to populate fields that require the E2BM unit list, documented in Attachment 1 of the E2BM document. The three

digit ICH M2 numeric codes represent unit measurements for mass, volume, radioactivity, other units, and unit intervals.

3.5.2 Routes of Administration (E2BM Attachment 2)

The three digit numeric codes provided in Appendix A.5 must be used to populate fields that require the E2BM routes of administration, documented in Attachment 2 of the E2BM document. The M2 numeric codes represent various pre-defined routes of administration. For example, the fields B.4.k.8 - drugadministrationroute and B.4.k.9 - drugparadministration require to be populated with the codes for the E2BM routes of administration.

3.6 E2BM Document on Data Elements for the Transmission of Individual Case Safety Reports

The E2BM document provides a detailed breakdown of the data elements for the ICSR, as well as notes on transmission and user guidance information. The E2BM document provides the appropriate background, scope, and detailed specifications on the data elements for the transmission of all types of ICSRs. In order to comply with the standardized data elements for the successful electronic transmission of information, it is vital for the user to understand the E2BM document. A copy of this document can be obtained from the ICH Web Site, hosted on the IFPMA server, URL: http://www.ifpma.org/ich1.

4.0 APPROACH TO PREPARING ICSR SGML DATA FILES

Extracting, translating, populating, and packaging adverse events (AE) data from heterogeneous AE databases can be complex. The M2 specifications, such as the relational view diagram, entity relationship diagram, attribute list, codes for E2BM route of administration list and unit list, and the ICH ICSR DTD have to be used to develop an electronic ICSR that complies with the E2BM document. This section is provided to help users understand the relationship between these products to develop valid electronic ICSRs that can be transported and loaded into receiving databases.

This section does not provide guidance on the interpretation of the E2BM field specifications. The E2BM document must be referenced and thoroughly understood to derive the intent of each field and the ICSR.

4.1 Organization Required for Preparing ICSR SGML Data Sets

Using the ICH ICSR DTD to prepare electronic ICSRs requires an organized approach and an understanding of the content and intended use of the ICH E2BM document and the various M2 products. As shown in Figure 4, the process should begin with an in-depth study of the E2BM document, to understand the intent of the report and interpret the content and appropriate use of the data definitions. The E2BM data elements should then be mapped to corresponding data elements in the AE databases, with the help of the M2 relational view diagram, entity relationship diagram, and attribute list. This is an important step and all measures must be taken to ensure that the correct data values are extracted from existing AE databases to populate the SGML data file. Once the AE data has been mapped to the ICSR schema, internal procedures and software routines must be used to extract, translate, populate, and prepare the SGML data file. The figure below shows the process for the electronic submission of ICSRs.

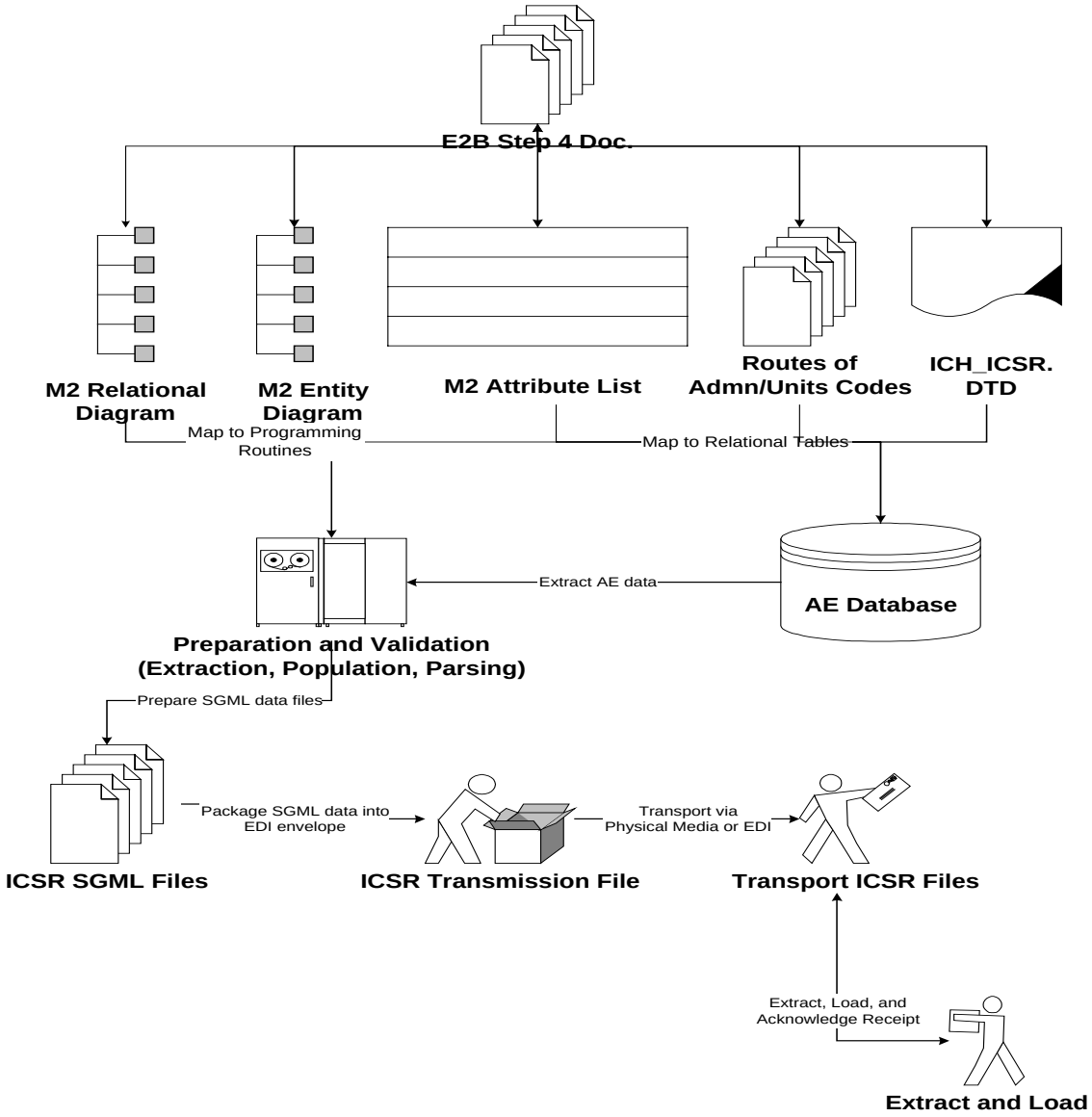

Figure 4

The following section provides step-by-step instructions for creating an SGML data file. Please refer to the ICH M2 website for additional information: http://www.ifpma.org/m2-main.html.

4.2 Step-By-Step Instructions on How to Prepare a Data File

This section explains some basic steps to help prepare a SGML data set that is compliant with the ICH ICSR DTD and can be used for the electronic transmission of structured individual case safety data.

The E2BM document, the M2 relational view diagram, the ICSR attribute list, and the DTD descriptors must be used as a reference while entering data to verify the accuracy of the DTD descriptor and E2BM field definitions. AE data must be extracted from safety and

surveillance databases in a manner specified by the ICH ICSR message. Information for electronic submission is prepared by inserting data appropriately between the start and end tags so the information maintains the relationships specified by the DTD. Typically, SGML editing tools can be used to prepare a data set that is specific to an SGML DTD. The SGML tools check for valid SGML rules and provide efficient features, like automatic insertion of start and end tags to make the task of preparing data easier. However, in the absence of SGML editing tools, a word processor or simple text editor can also be used in the following manner:

- Open ICH_ICSR.DTD.

- Define the appropriate tags for each DTD element.

  For example, in the new document, define tag as <ichicsr> for element defined in DTD as <!ELEMENT ichicsr - - (ichicsrmessageheader, safetyreport+) >.

- AE data must be placed after the open tag of the appropriate descriptors defined in the new text file. To verify that data are populated appropriately, check the E2BM document and M2 field attribute spreadsheet (Appendix A.1) for field definitions, titles, field lengths, field values, and descriptor names.

  For example, in the populated SGML file – ich-icsr-v2.0-19981018-test-english.sgm, the value "US" is entered after the field descriptor <primarysourcecountry>, as <primarysourcecountry>**US**. This value was entered after verifying that the tag <primarysourcecountry> referred to the E2BM field A 1.1, identification of the country where the reaction/event, with DTD descriptor <primarysourcecountry>, field length of 2AN, and a country code compliant with ISO3166, US.

- Make sure that there is an end tag for every start tag.

  For example, <tagname> must be followed by </tagname>

  <primarysourcecountry>US</primarysourcecountry>

- Between the start and end tag of a large text field, such as 200AN or longer, you can have carriage returns to make the data more readable.

  For example,

  <nullificationreason>invalid information regarding…
  …..
  the drug reaction
  </nullificationreason>

- The repeatable fields and sections (designated by a double line box in the M2 field attribute list) are populated by copying and pasting the DTD descriptors as necessary, then populating them with data.

  Note: Each section that is repeated, must begin with the section name (e.g. <reportduplicate> and end with the corresponding end tag (back slash before the same title (e.g. </reportduplicate>)).

  For example:
  `<reportduplicate>`

```
<duplicatesource>smith, coopers, barnies, and young
pharmaceuticals</duplicatesource>
<duplicatenumb>nmbr12345678910111213141516171819 20</duplicatenumb>
</reportduplicate>
<reportduplicate>
<duplicatesource>smith, coopers, barnies, and young
pharmaceuticals</duplicatesource>
<duplicatenumb>number123456789101112131415161718 19</duplicatenumb>
</reportduplicate>
<linkedreport>
<linkreportnumb>12345678910111213141516171819202122</linkreportnumb>
</linkedreport>
<linkedreport>
<linkreportnumb>report number 123456789101234567891</linkreportnumb>
</linkedreport>
```

- However, if there is no data for an optional block, then the complete block must be omitted. For example, since reportduplicate is an optional block and if there is no report duplicate information, then the complete block shown above, beginning with <reportduplicate> and ending with the </reportduplicate> must be omitted.

- For further illustration, the following scripts are provided as an example of a DTD definition and the corresponding syntax of a populated SGML file. Appendices A.2 and A.7 provide the definitions of the ICH ICSR and ICSR Acknowledgment DTDs. Appendix A.8 provides the definition of a sample ICSR Acknowledgment SGML data file.

  Part of the ICH_ICSR.DTD:

```
<!ELEMENT safetyreport        - -
        (safetyreportversion?,
      safetyreportid?,

      primarysourcecountry?         ,
      occurcountry?                   ,
      transmissiondateformat?         ,
      transmissiondate?               ,
      reporttype?                     ,
      serious?                        ,
      seriousnessdeath?               ,
      seriousnesslifethreatening?     ,
      seriousnesshospitalization?     ,
      seriousnessdisabling?           ,
      seriousnesscongenitalanomali?   ,
      seriousnessother?               ,
      receivedateformat?              ,
      receivedate?                    ,
      receiptdateformat?              ,
      receiptdate?                    ,
      additionaldocument?             ,
```

  Sample SGML data file:

```
<safetyreport>
      <safetyreportversion>1</safetyreportversion>
      <safetyreportid>US-XYZ-12345</safetyreportid>

      <primarysourcecountry>US</primarysourcecountry>
```

```
<occurcountry>US</occurcountry>
<transmissiondateformat>102</transmissiondateformat>
<transmissiondate>19980101</transmissiondate>
<reporttype>1</reporttype>
<serious>1</serious>
<seriousnessdeath>1</seriousnessdeath>
<seriousnesslifethreatening>1</seriousnesslifethreatening>
<seriousnesshospitalization>1</seriousnesshospitalization>
<seriousnessdisabling>2</seriousnessdisabling>
<seriousnesscongenitalanomali>2</seriousnesscongenitalanomali>
<seriousnessother>2</seriousnessother>
<receivedateformat>102</receivedateformat>
<receivedate>19980102</receivedate>
<receiptdateformat>102</receiptdateformat>
<receiptdate>19970103</receiptdate>
<additionaldocument>1</additionaldocument>
```

Once all the E2BM compliant information is entered in the appropriate sections, the document must be saved as, “filename.SGM”. The SGML data file must then be parsed by an SGML parser, such as the James Clark SP parser, with reference to the ICH ICSR DTD, to ensure the file is syntactically error free. To parse the data file by using the James Clark SP parser, assuming that all of the files (DCL, DTD, and SGML) are in the same directory, the following command may be executed:

nsgmls -s declaration-file.dcl dtd-file.dtd sgml-file.sgm.

The "-s" is a flag that suppresses the normal output of "nsgmls". Only errors in the SGML files will be reported with the "-s" flag set and there shouldn't be any. The SGML data can be transmitted via physical media, such as CD-ROM, or via secure EDI. In the case of transmitting data via secure EDI over the Internet, the SGML data generally must be packaged by inserting it into an EDI envelope to facilitate the data transmission. The details of packaging data for EDI transmissions can be obtained from other sources, such as user manuals for EDI application software.

4.3 The Information Requirements for the Tracking and Routing of ICSRs

Multiple ICSRs can be sent in a single transmission, via physical media or secure EDI over the Internet. It is also important to correctly populate specific data elements to provide a link that will help uniquely identify an ICSR and the transmission message that contains the single or multiple ICSRs. To accomplish this unique identification of each ICSR, it will be useful to adopt the following approach:

- For each electronic transmission of an ICH ICSR message, the following information must be provided in the M2 message header section, when submitting via physical media or via secure EDI over the Internet.

  Message Number, sender defined transmission number – specify a transmission number that is unique to the sender. This number can also be incremental.

  Message Sender Identifier – specify the identification of the sender of the ICSR message, e.g., company name or regulatory authority name (ICSR Attribute List A.3.1.2).

Message Receiver Identifier – specify the identification of the receiver of the ICSR message, e.g., company name or regulatory authority name (ICSR Attribute List A.3.2.2a).

Message Date – specify the date and time on which the transmission of the message was initiated in the format CCYYMMDDHHMMSS.

Additionally, each ICSR should be uniquely identified. This is critical for message and report transmission. The data elements and their definitions for unique identification are described in the E2BM revised Step 4 document, version 4.4. The pertinent data elements include Sender's (Case) Safety Report Unique Identifier (A.1.0.1), Date of receipt of the most recent information (A.1.7), Worldwide unique case identification number (A.1.10), and Other case identifiers in previous transmissions (A.1.11).

5.0 THE ICSR ACKNOWLEDGMENT MESSAGE

The ICH M2 group has realized that to facilitate electronic submissions of ICSRs and to help pharmaceutical companies send useable data in a timely fashion, there is a need to provide feedback in an appropriate manner. The required feedback acknowledges receipt of the transmitted message as well as validating that each ICSR is syntactically correct and that data for all mandatory fields are provided.

To provide the required feedback for the ICH ICSR message, M2 has developed a specification for an ICSR Acknowledgment Message and corresponding SGML DTD, with appropriate validation and acknowledgment procedures, to support the requirements. The overall objective of developing an ICSR Acknowledgment Message is to help automate the status tracking of the electronic submission of ICSRs.

The following sections provide descriptions of the ICSR Acknowledgment Message. The data element specifications and message structure are contained in Appendix A.6. The ICSR Acknowledgment DTD is contained in Appendix A.7.

Typically a receiver of ICH ICSR messages will validate the incoming messages as described in the section below and create an SGML message to comply with the ICSR Acknowledgment DTD, specified in Appendix A.7. The details for creating the SGML message will be similar to the steps described in section 4.2. The sender of the ICSR message can then extract the data from this ICSR Acknowledgment Message to determine the status of each ICSR.

5.1 Validation and Automated Acknowledgments of EDI Submissions

The ICSR Acknowledgment allows receivers of the SGML data, such as regulatory authorities, to provide valuable feedback about the usability of the data in the transmission message. The ICSR Acknowledgment allows senders, typically pharmaceutical companies, to track and correct SGML syntax errors prior to re-transmission.

Transmission file validation

Once an EDI gateway decrypts and passes the file to the AE databases, an application parses the SGML data file to extract the structured information. If there is an SGML parsing error, the whole file is rejected and no further processing occurs. The sender must then re-transmit

the same data file, after correcting the SGML file for syntactical or structural errors. The application software may be able to provide information about parsing errors and the acknowledgment message is used to convey information on such errors.

ICSR Database Load Validation

Once the data has been parsed without any errors from the SGML file, each report is loaded into the target AE database system. As each report is loaded into the data tables, each field is validated for:

- Data type
- Data length
- Field value
- Required data.

The AE application will perform limited validations and will reject reports that don't have the required database fields. The system reports the status of each report as “loadable” or “not loadable” and requests re-transmission of only those reports that are not loadable into the database.

Once the reports are loaded into the application database, it becomes the responsibility of the regulatory authority to assess the reports.

5.2 Acknowledgment Message Format

According to the model specified for the acknowledgment DTD, the ICSR Acknowledgment Message is comprised of two sections, each occurring once; the message header section and the acknowledgment section. The acknowledgment section is comprised of two portions, a message acknowledgment portion which occurs once, and a report acknowledgment portion which can occur one time, many times, or not at all.

Message Acknowledgment

This section of the DTD specifies the required elements to indicate whether or not the SGML parser was able to extract the transmitted data. To help in tracking and identifying the transmission, this section includes the sender defined ICH ICSR message number, identifier of sender of the ICH ICSR message, identifier of receiver of the ICH ICSR message, message date, and a transmission acknowledgment code. The transmission acknowledgment code notifies the sender that one of the following is true:

- Parsing was successful and all ICSRs could be loaded into the target database
- Parsing was successful but not all ICSRs could be loaded into the target database
- The SGML file failed validation by an SGML parser.

The details of this specification are documented in Appendix A.7 of this document.

ICSR Report Acknowledgment

The ICSR report acknowledgment is a repeatable section for acknowledging each report included in the SGML file. This section provides information to help identify each ICSR, such as the safety report id, safety report version number, local report number, worldwide unique case identification number, and date of receipt of the most recent information. This section will also provide information on the errors encountered while loading the data into the relevant tables. This information will be particularly helpful for companies to improve the quality of the data, prior to re-transmission. The details of this specification are also documented in Appendix A.7 of this document.

The diagram on the next page illustrates the specified relationship, where each ICSR acknowledgment message includes the message header section, one message acknowledgment section and multiple acknowledgments for each safety report.

ICH M2 Acknowledgment Message

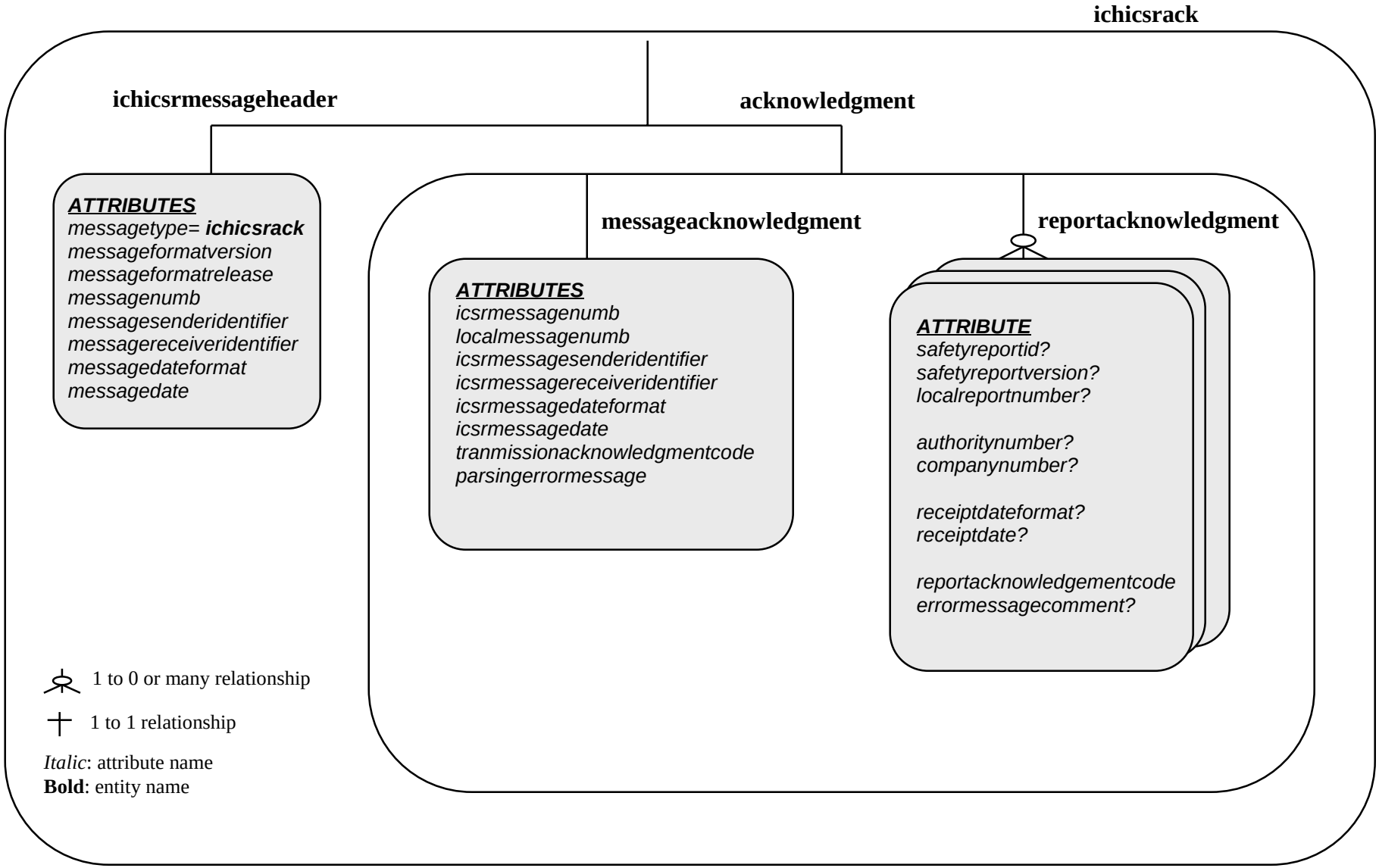

Figure 5

6.0 MULTILINGUAL SUPPORT IN ICH ICSR MESSAGES

There are two important features in version 2.0 that allow the development of an SGML data set that contains multi-language characters in a single SGML file. The first feature is that five different DCL files are distributed along with the ICH ICSR DTD, version 2.0. Correctly parsing an ICH ICSR message requires the selection of the correct SGML declaration, along with this DTD, and the ICH ICSR SGML instance. Depending upon the character sets being transmitted, a reference should be made to a specific DCL file. The specifics on the DCL files with brief descriptions of their purpose are provided in Appendix A.3. The ICH ICSR and the ICSR Acknowledgment DTDs also have a technical note with instructions on appropriate use of the five DCL files.

The second feature is to know how to label the language being used in each field of an ICH ICSR message. This section describes the method to be used.

To accommodate the incorporation of multiple languages and to identify the various languages of the text within the various tags of an ICH ICSR message, a method of labeling the tags with a language attribute is used. This method is a common requirement in SGML applications and is a widely accepted technique for Hypertext Markup Language (HTML), SGML, and eXtensible Markup Language (XML). The method involves four rules:

- Rule 1: When an SGML element contains only character data, (as opposed to other SGML elements), that character data can only be in one language.

- Rule 2: An SGML attribute may be added to any SGML element to indicate the language of that element's content. This attribute is called "lang", and its value is one of the ISO 639 language digraphs. These digraphs are always entered in lower case.

- Rule 3: If a "lang" attribute is not set, then the content of the element is assumed to be in the same language as the nearest containing element that does have a language attribute.

- Rule 4: The root element of the document is required to have a language attribute.

6.1 Directions on How to Use DTD to Support Multi-Language Characters

To understand how these rules apply, it is first necessary to review a basic principle of SGML, namely that in SGML, documents consist of a collection of tagged elements that are nested within each other to form a hierarchy or tree. In the ICH ICSR message format the first, or root element of the tree is indicated in SGML by the tag <ichicsr>. The tag </ichicsr> indicates the end of the root element, and the end of the ICH ICSR message. Inside of these two tags all other ICH ICSR elements occur, each indicated by a tag that contains other tags, actual data, or a combination of the two. Graphically, a portion of the ICH ICSR document tree would look like Figure 6. In actuality, it would be represented in SGML as shown in Example 1, where indentation is used to highlight the nesting hierarchical structure of the SGML document.

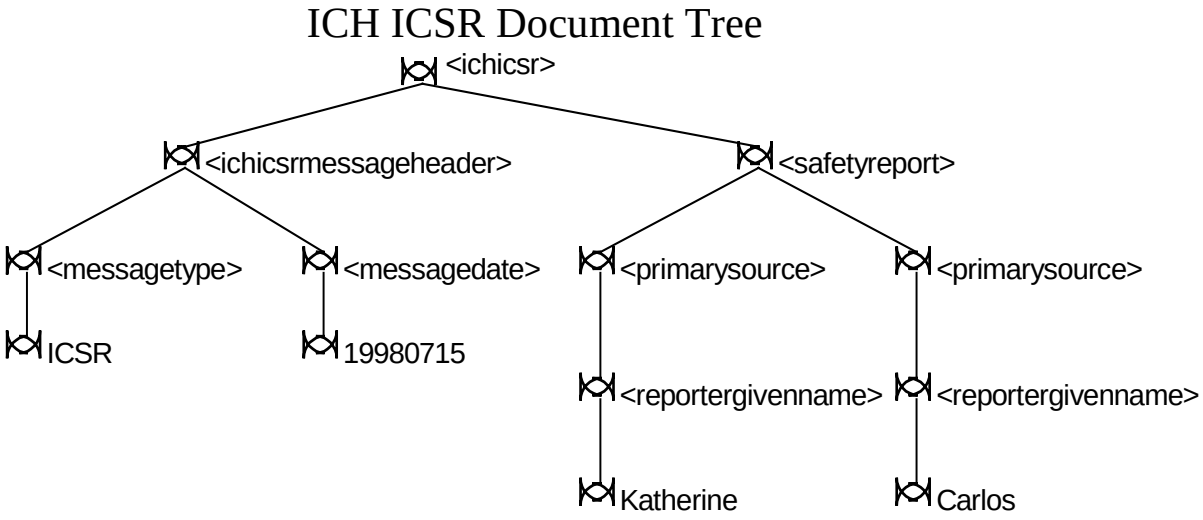

Figure 6

Sample SGML Data Set

```
<ichicsr>
  <ichicsrmessageheader>
     <messagetype>ICSR</messagetype>
     <messagedate>19980715</messagedate>
…
  </ichicsrmessageheader>
  <safetyreport>
     <primarysource>
        <reportergivenname>Katherine</reportergivenname>
     </primarysource>
     <primarysource>
        <reportergivenname>Carlos</reportergivenname>
     </primarysource>
  </safetyreport>
</ichicsr>
```

Example 1

A new SGML message will now be constructed following the four rules outlined above. First, rule four states that the root element of the SGML document must have a lang attribute. For example, if the document will contain English, this would be indicated with the SGML attribute “lang” being set to the value “en” on the root element <ichicsr>, as illustrated in Example 2. Because of rule three, if no other language attributes, are set on any element, all document content is assumed to be in English, because <ichicsr> “contains” all other elements in the document tree.

Now assume that all of the information under <ichicsrmessageheader> should be in French. This would be accomplished by adding the attribute lang=”fr” to the <ichicsrmessageheader> element. Now, all SGML elements subordinate to <ichicsrmessageheader> would be assumed to contain French. Finally look at <reportergivenname>Katherine</reportergivenname>. Indicate that this should be in Spanish by adding the now familiar lang attribute. It is important to note that <reportergivenname>Carlos</reportergivenname> is still assumed to be in English because its ancestor in the tree with a lang attribute is the root element <ichicsr>. The complete example is given below, both in the graphical representation, and SGML syntax.

ICH ICSR Document Tree Using the Language Attribute

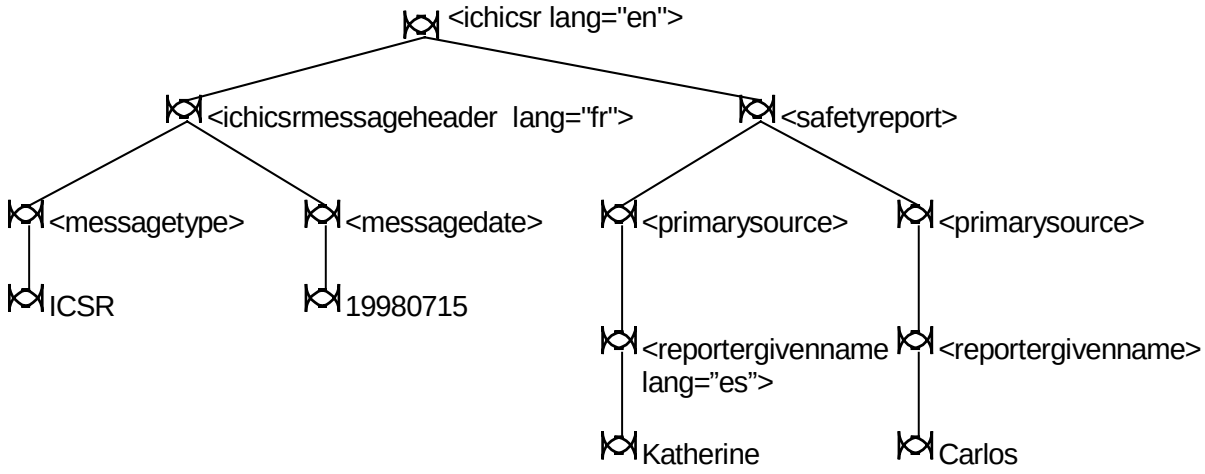

Figure 7

Sample SGML Data Set Using the Language Attribute

```
<ichicsr lang=”en”>
  <ichicsrmessageheader lang=”fr”>
     <messagetype>ICSR</messagetype>
     <messagedate>19980715</messagedate>
…
  </ichicsrmessageheader>
  <safetyreport>
     <primarysource>
        <reportergivenname lang=”es”>Katherine</reportergivenname>
     </primarysource>
     <primarysource>
        <reportergivenname>Carlos</reportergivenname>
     </primarysource>
  </safetyreport>
</ichicsr>
```

Example 2

In summary, by following the four rules outlined in this section, multiple languages can be supported

by the ICH ICSR message formats, with minimal impact on the complexity or size of the messages. **If the entire, ICH ICSR message is only in one language, then placing the "lang" attribute on the very first SGML tag <ichicsr> in the document is all that is required.** Moreover, because of the hierarchical structure of the SGML document itself, and the fact that a given use of the "lang" attribute effects all elements subordinate to it, the use of the "lang" attributes can be minimized. It is incumbent on applications that process this data to know what language can be expected in each element. This can be accomplished by implementing a simple stack data structure to keep track of language information.

A.0 APPENDIX

The following appendices contain specifications of the various components that have been referenced throughout the Electronic Transmission of ICSRs Message Specification document. These appendices provide the necessary details required to aid in the preparation of a valid ICH ICSR message, as well as ICSR Acknowledgment Message, for electronic submission. The appropriate appendices should be referenced along with the instructions provided in the specification document to understand the data requirements and the process for preparing a usable SGML message. The ICH M2 website (http://www.ifpma.org/m2-main.html) is the only source for obtaining the ICH ICSR DTD, ICSR Acknowledgment DTD, and the SGML DCL files for multi-language support.

The following references are for those preparing and sending ICH ICSRs:

- **Appendix A.1 - ICSR Attribute List**, used to verify the title, description, field length, field value, and DTD descriptor for each data element. The various elements are also grouped and numbered to match the organization of the E2BM document. The attribute list has three types of blocks, depicted as a regular single line border, bold lined border, and double lined border. Fields within the single line border can occur once or not at all, while fields or blocks with a bold border might be repeated, and fields or blocks with a double line border might also be repeated, within the containing block. This attribute list must be used to verify the accuracy and compliance of data entered when preparing an ICSR SGML data file.

- **Appendix A.2 - ICH ICSR DTD**, used to describe the elements of the ICSR being transmitted. The DTD describes each element of the ICSR being transmitted and shows how the various elements relate to each other. Within the encoded text, the DTD specifies which elements are required and where they may appear, as well as their order of appearance.

- **Appendix A.3 - Declaration Files for Multi-language Character Sets**, used to describe the capabilities of an SGML system and is intended for human interpretation. The DCL files provide information on character encoding used in the DTD and the document, the amount of system resources required by the DTD, the delimiters used in marking up the document, the SGML features used by the document markup, and other application-specific information.

  To support the multi-language character set capability and to allow for the population of data in multiple languages in a single SGML message, several SGML declaration files are included in the distribution of the ICH ICSR DTD. The correct SGML declaration file must be selected along with the ICH ICSR DTD and the ICH ICSR SGML instance, to correctly parse an ICH ICSR message. The method by which an SGML parser is told to use a specific declaration is parser specific. Appendix A.3 lists the five DCL files that have been included in the distribution of ICH ICSR version 2.0. These DCL files are also to be used in a similar manner when preparing the ICSR Acknowledgment Messages.

- **Appendix A.4 - ICH M2 Numeric Codes for Unit List**, used to populate fields that require the E2BM unit list, documented in Attachment 1 of the E2BM document. The three digit ICH M2 numeric codes represent unit measurements for mass, volume, radioactivity, other units, and unit intervals.

- **Appendix A.5 - ICH M2 Numeric Codes for Routes of Administration**, used to populate fields that require the E2BM Routes of Administration, documented in Attachment 2 of the E2BM document. The M2 numeric codes represent various pre-defined routes of administration.

The references below help those receiving, validating, and acknowledging ICH ICSRs prepare ICSR Acknowledgment Messages:

- **Appendix A.6 - Requirements for the ICSR Acknowledgment Message**, used to verify the field name, description, DTD descriptor, field length, and field value for each data element of the ICSR Acknowledgment Message. In addition, this document is used to verify repeatable blocks and communicate to the sender of the ICSR message the results of the validation of the transmitted data set. This list of data element requirements must be used to verify the accuracy and compliance of data entered when preparing an ICSR Acknowledgment Message.

- **Appendix A.7 - ICH ICSR Acknowledgment DTD**, used to describe the SGML specifications of the elements and relationships of the acknowledgment message being transmitted. Within the encoded text, the DTD specifies which elements are required and where they may appear, as well as their order of appearance.

- **Appendix A.8 - Sample SGML Data File for the ICH ICSR Acknowledgment DTD,** used to provide an example of a valid SGML data file. This example represents a usable ICSR Acknowledgment SGML message that complies with ICSR Acknowledgment DTD, as well as the requirements specified for an acknowledgment message.

A.1 ICSR Attribute List (Ver 4.5, November 9, 2000 , E2bs4v44.doc)

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
		ICH ICSR Message Header Specifications			
M.1	ICH ICSR Message Header	Header/Entity			**ichicsrmessageheader**
M.1.1	Message Type	Type of information being transmitted	16AN	ichicsr	messagetype
M.1.2	Message Format Version	Version number of Message Format	3AN		messageformatversion
M.1.3	Message Format Release	Release number of the Message Format	3AN		messageformatrelease
M.1.4	Message Number	Message Number	100AN		messagenumb
M.1.5	Message Sender Identifier	Message Sender Identifier	60AN		messagesenderidentifier
M.1.6	Message Receiver Identifier	Message Receiver Identifier	60AN		messagereceiveridentifier
M.1.7a	Message Date	Message Date Format (include as an attribute)	3N	204 – Format CCYYMMDDHHMMSS	messagedateformat
M.1.7b	Message Date	Message Date	14N	CCYYMMDDHHMMSS	messagedate
		ICH ICSR M2 Data Processing Specifications			
	Safety Report Version Number	Safety Report Version Number	2AN		safetyreportversion
		E2B Step 4 Specifications			
A.1	Identification of the case safety report	Header/entity			**safetyreport**
A.1.0.1	Sender's (Case) Safety Report Unique Identifier	Safety Report Identifier	100 AN		safetyreportid
A.1.1	Identification of the country of the primary		2A	ISO3166	primarysourcecountry
A.1.2	Identification of the country where the reaction/event occurred		2A	ISO3166	occurcountry

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
A.1.3a	Date of this transmission	Date format	3N	102 - Format CCYYMMDD	transmissiondateformat
A.1.3b	Date of this transmission		8N	CCYYMMDD	transmissiondate
A.1.4	Type of report		1N	1=Spontaneous 2=Report from study 3=Other 4=Not available to sender (unknown)	reporttype
A 1.5	Seriousness	Header			
A.1.5.1	Serious		1N	1=Yes 2=No	serious
A.1.5.2	Seriousness criteria	Results in death	1N	1=Yes 2=No	seriousnessdeath
		Life threatening	1N	1=Yes 2=No	seriousnesslifethreatening
		Caused/prolonged hospitalization	1N	1=Yes 2=No	seriousnesshospitalization
		Disabling/Incapacitating	1N	1=Yes 2=No	seriousnessdisabling
		Congenital anomaly/birth defect	1N	1=Yes 2=No	seriousnesscongenitalanomali
		Other medically important condition	1N	1=Yes 2=No	seriousnessother
A.1.6a	Date report was first received from source	Date format	3N	102 - Format CCYYMMDD	receivedateformat
A.1.6b	Date report was first received from source		8N	CCYYMMDD	receivedate
A.1.7a	Date of receipt of the most recent information for this report	Date format	3N	102 - Format CCYYMMDD	receiptdateformat
A.1.7b	Date of receipt of the most recent information for this report		8N	CCYYMMDD	receiptdate
A.1.8	Additional available documents held by sender	Header			
A.1.8.1	Are additional documents available		1N	1=Yes 2=No	additionaldocument
A.1.8.2	List of documents held by sender		100AN		documentlist

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
A.1.9	Does this case fulfill the local criteria for an expedited report?		1N	1=Yes 2=No	fulfillexpeditecriteria
A.1.10	Worldwide unique case identification number	Header			
A.1.10.1	Regulatory authority's case report number		100AN		authoritynumb
A.1.10.2	Other sender's case report number		100AN		companynumb
A.1.11	Other case identifiers in previous transmissions		1N	1=Yes	duplicate
		entity			**reportduplicate**
A.1.11.1	Source(s) of the case identifier		50AN	Should be a repeatable block	duplicatesource
A.1.11.2	Case identifiers		100AN	Should be a repeatable block	duplicatenumb
		entity			**linkedreport**
A.1.12	Identification number of the report which is linked to this report		100AN	Should be a repeatable field	linkreportnumb
		entity			**(safetyreport)**
A.1.13	Report nullification		1N	1=Yes	casenullification
A.1.13.1	Reason for nullification		200AN		nullificationreason
A.1.14	Was the case medically confirmed, if not initially from health professional?		1N	1=Yes 2=No	medicallyconfirm
A.2	Primary source(s) of information	Header/entity		Area below should be a repeatable block	**primarysource**
A.2.1	Primary source(s)	Header			
A.2.1.1a	Reporter identifier	Reporter title	50AN		reportertitle
A.2.1.1b	Reporter identifier	Reporter given name	35AN		reportergivename
A.2.1.1c	Reporter identifier	Reporter middle name	15AN		reportermiddlename
A.2.1.1d	Reporter identifier	Reporter family name	50AN		reporterfamilyname

For Japan, field length must be two times the current length when AN or A.

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
A.2.1.2a	Reporter identifier	Reporter organization	60AN		reporterorganization
A.2.1.2b	Reporter identifier	Reporter department	60AN		reporterdepartment
A.2.1.2c	Reporter's address	Reporter street	100AN		reporterstreet
A.2.1.2d	Reporter's address	Reporter city	35AN		reportercity
A.2.1.2e	Reporter's address	Reporter state or province	40AN		reporterstate
A.2.1.2f	Reporter's address	Reporter postcode	15AN		reporterpostcode
A.2.1.3	Country	Reporter country code	2A	ISO3166	reportercountry
A.2.1.4	Qualification		1N	1=Physician 2=Pharmacist 3=Other Health Professional 4=Lawyer 5=Consumer or other non health professional	qualification
A.2.2	Literature reference(s)		500 AN		literaturereference
A.2.3	Study identification	Header			
A.2.3.1	Study name		100AN		studyname
A.2.3.2	Sponsor study number		35AN		sponsorstudynumb
A.2.3.3	Study type in which the reaction(s)/event(s) were observed		1N	1=Clinical trials 2=Individual patient use 3=Other studies	observestudytype
A.3	Information on Sender and Receiver of Case Safety Report	Header			
A.3.1	Sender	Header/entity			**sender**
A.3.1.1	Type		1N	1=Pharmaceutical Company 2=Regulatory Authority 3=Health professional 4=Regional Pharmacovigilance Center 5=WHO Collaborating Center for International Drug Monitoring 6=Other	sendertype
A.3.1.2	Sender Identifier	Sender organization	60AN		senderorganization

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
A.3.1.3a	Sender Identifier	Sender department	60AN		senderdepartment
A.3.1.3b	Sender Identifier	Title	10AN		sendertitle
A.3.1.3c	Sender Identifier	Given name	35AN		sendergivename
A.3.1.3d	Sender Identifier	Middle name	15AN		sendermiddlename
A.3.1.3e	Sender Identifier	Family name	35AN		senderfamilyname
A.3.1.4a	Sender's Address	Street address	100AN		senderstreetaddress
A.3.1.4b	Sender's Address	City	35AN		sendercity
A.3.1.4c	Sender's Address	State or Province	40AN		senderstate
A.3.1.4d	Sender's Address	Postcode	15AN		senderpostcode
A.3.1.4e	Sender's Address	Country Code	2A	ISO3166	sendercountrycode
A.3.1.4f	Sender's Telephone Number	Telephone	10AN		sendertel
A.3.1.4g	Sender's Telephone Number	Telephone extension	5AN		sendertelextension
A.3.1.4h	Sender's Telephone Number	Telephone country code	3AN		sendertelcountrycode
A.3.1.4i	Sender's Fax Number	Fax	10AN		senderfax
A.3.1.4j	Sender's Fax Number	Fax extension	5AN		senderfaxextension
A.3.1.4k	Sender's Fax Number	Fax country code	3AN		senderfaxcountrycode
A.3.1.4l	Sender's E-mail Address	E-mail address	100AN		senderemailaddress
A.3.2	Receiver	Header/entity			**receiver**
A.3.2.1	Type		1N	1=Pharmaceutical Company 2=Regulatory Authority 4=Regional Pharmacovigilance Center 5=WHO Collaborating Center for International	receivertype

For Japan, field length must be two times the current length when AN or A.

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
				Drug Monitoring 6=Other	
A.3.2.2a	Receiver identifier	Receiver organization	60AN		receiverorganization
A.3.2.2b	Receiver identifier	Receiver department	60AN		receiverdepartment
A.3.2.2c	Receiver identifier	Title	10AN		receivertitle
A.3.2.2d	Receiver identifier	Given name	35AN		receivergivename
A.3.2.2e	Receiver identifier	Middle name	15AN		receivermiddlename
A.3.2.2f	Receiver identifier	Family name	35AN		receiverfamilyname
A.3.2.3a	Receiver's Address	Street address	100AN		receiverstreetaddress
A.3.2.3b	Receiver's Address	City	35AN		receivercity
A.3.2.3c	Receiver's Address	State or Province	40AN		receiverstate
A.3.2.3d	Receiver's Address	Postcode	15AN		receiverpostcode
A.3.2.3e	Receiver's Address	Country Code	2A	ISO3166	receivercountrycode
A.3.2.3f	Receiver's Telephone Number	Telephone	10AN		receivertel
A.3.2.3g	Receiver's Telephone Number	Telephone extension	5AN		receivertelextension
A.3.2.3h	Receiver's Telephone Number	Telephone country code	3AN		receivertelcountrycode
A.3.2.3i	Receiver's Fax Number	Fax	10AN		receiverfax

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
A.3.2.3j	Receiver's Fax Number	Fax extension	5AN		receiverfaxextension
A.3.2.3k	Receiver's Fax Number	Fax country code	3AN		receiverfaxcountrycode
A.3.2.3l	Receiver's E-mail Address	E-mail address	100AN		receiveremailaddress
B	Information on the Case	Header			
B.1	Patient characteristics	Header/entity			**patient**
B.1.1	Patient		10AN		patientinitial
B.1.1.1a	Patient medical record number(s) and source(s) of the record number	GP medical record number	20AN		patientgpmedicalrecordnumb
B.1.1.1b	Patient medical record number(s) and source(s) of the record number	Specialist record number	20AN		patientspecialistrecordnumb
B.1.1.1c	Patient medical record number(s) and source(s) of the record number	Hospital record number	20AN		patienthospitalrecordnumb
B.1.1.1d	Patient medical record number(s) and source(s) of the record number	Investigation number	20AN		patientinvestigationnumb
B.1.2	Age information	Header			
B.1.2.1a	Date of birth	Date format	3N	102 - Format CCYYMMDD	patientbirthdateformat
B.1.2.1b	Date of birth		8N	CCYYMMDD	patientbirthdate
B.1.2.2a	Age at time of onset of reaction/event	Age value	5N		patientonsetage
B.1.2.2b	Age at time of onset of reaction/event	Age unit	3N	800 = Decade 801=Year 802=Month 803=Week 804=Day 805=Hour	patientonsetageunit

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.1.2.2.1a	Gestation period when reaction/event was observed in the fetus	Gestation period when reaction/event was observed in the fetus	3N		gestationperiod
B.1.2.2.1b	Gestation period when reaction/event was observed in the fetus unit	Unit	3N	802=Month 803=Week 804=Day 810=Trimester	gestationperiodunit
B.1.2.3	Patient age group		1N	1=Neonate 2=Infant 3=Child 4=Adolescent 5=Adult 6=Elderly	patientagegroup
B.1.3	Weight (kg)		6N		patientweight
B.1.4	Height (cm)		3N		patientheight
B.1.5	Sex		1N	ISO 5218 1=Male 2=Female	patientsex
B.1.6a	Last menstrual period date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	lastmenstrualdateformat
B.1.6b	Last menstrual period date		8N		patientlastmenstrualdate
B.1.7	Relevant medical history and concurrent conditions	Header		Area below should be a repeatable block	**medicalhistoryepisode**
B.1.7.1a.1	MedDRA version for Medical History		8AN		patientepisodenamemeddraversion
B.1.7.1a.2	Structured information	Disease / surgical procedure / etc.	250AN		patientepisodename
B.1.7.1b	Start Date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	patientmedicalstartdateformat
B.1.7.1c	Start Date		8N		patientmedicalstartdate

For Japan, field length must be two times the current length when AN or A.

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.1.7.1d	Continuing		1N	1=Yes 2=No 3=Unknown	patientmedicalcontinue
B.1.7.1e	End Date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	patientmedicalenddateformat
B.1.7.1f	End Date		8N		patientmedicalenddate
B.1.7.1g	Comments		100AN		patientmedicalcomment
		entity			**(patient)**
B.1.7.2	Text for relevant medical history and concurrent conditions		10000AN		patientmedicalhistorytext
B.1.8	Relevant past drug history (repeat as necessary)	Header/entity		Area below should be a repeatable block	**patientpastdrugtherapy**
B.1.8a	Name of Drug as Reported		100AN		patientdrugname
B.1.8b	Start Date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	patientdrugstartdateformat
B.1.8c	Start Date		8N		patientdrugstartdate
B.1.8d	End Date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	patientdrugenddateformat
B.1.8e	End Date		8N		patientdrugenddate
B.1.8f.1	MedDRA version for indication		8AN		patientindicationmeddraversion
B.1.8f.2	Indication		250AN		patientdrugindication
B.1.8g.1	MedDRA version for reaction		8AN		patientdrgreactionmeddraversion
B.1.8g.2	Reaction		250AN		patientdrugreaction
B.1.9	In case of death:	Header/entity			**patientdeath**
B.1.9.1a	Date of death	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	patientdeathdateformat
B.1.9.1b	Date of death		8N		patientdeathdate

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
		entity			**patientdeathcause**
B.1.9.2.a	MedDRA version for reported cause(s) of death		8AN		patientdeathreportmeddraversion
B.1.9.2.b	Reported cause(s) of death (repeat as necessary)		250AN	Should be a repeatable field	patientdeathreport
		entity			**(patientdeath)**
B.1.9.3	Was autopsy done?		1N	1=Yes 2=No 3=Unknown	patientautopsyyesno
		entity			**patientautopsy**
B.1.9.4a	MedDRA version for autopsy-determined cause(s) of death		8AN		patientdetermautopsmeddraversion
B.1.9.4b	Autopsy-determined cause(s) of death (repeat as necessary)		250AN	Should be a repeatable field	patientdetermineautopsy
B.1.10	For a parent-child/fetus report, information concerning the parent	Header/entity			**parent**
B.1.10.1	Parent identification	Parent initials	10AN		parentidentification
B.1.10.2	Parent age information	Header			
B.1.10.2.1a	Date of birth of parent	Date format	3N	102 – Format CCYYMMDD	parentbirthdateformat
B.1.10.2.1b	Date of birth of parent		8N	CCYYMMDD	parentbirthdate
B.1.10.2.2a	Age of parent	Age Value	2N		parentage
B.1.10.2.2b	Age of parent	Age unit	3N	801=Year	parentageunit
B.1.10.3a	Last menstrual period date	Date format	3N	102 – Format CCYYMMDD	parentlastmenstrualdateformat
B.1.10.3b	Last menstrual period date		8N	CCYYMMDD	parentlastmenstrualdate
B.1.10.4	Weight (kg) of parent		6N		parentweight
B.1.10.5	Height (cm) of parent		3N		parentheight
B.1.10.6	Sex of parent		1N	ISO 5218 1=Male 2=Female	parentsex
B.1.10.7	Relevant medical history and concurrent conditions of parent	Header/entity		Area below should be a repeatable block	**parentmedicalhistoryepisode**

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.1.10.7.1a.1	MedDRA version for parent medical history		8AN		parentmdepisodemeddraversion
B.1.10.7.1a.2	Structured information	Disease / surgical procedure/ etc.	250AN		parentmedicalepisodename
B.1.10.7.1b	Start Date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	parentmedicalstartdateformat
B.1.10.7.1c	Start Date		8N		parentmedicalstartdate
B.1.10.7.1d	Continuing		1N	1=Yes 2=No 3=Unknown	parentmedicalcontinue
B.1.10.7.1e	End Date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	parentmedicalenddateformat
B.1.10.7.1f	End Date		8N		parentmedicalenddate
B.1.10.7.1g	Comments		100AN		parentmedicalcomment
		entity			**(parent)**
B.1.10.7.2	Text for relevant medical history and concurrent conditions of parent (not including reaction/event)		10000AN		parentmedicalrelevanttext
B.1.10.8	Relevant past drug history	Header/entity		Area below should be a repeatable block	**parentpastdrugtherapy**
B.1.10.8a	Name of drug as reported		100AN		parentdrugname
B.1.10.8b	Start date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	parentdrugstartdateformat
B.1.10.8c	Start date		8N		parentdrugstartdate
B.1.10.8d	End date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	parentdrugenddateformat
B.1.10.8e	End date		8N		parentdrugenddate
B.1.10.8f.1	MedDRA version for		8AN		parentdrgindicationmeddraver

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
	indication				sion
B.1.10.8f.2	Indication		250AN		parentdrugindication
B.1.10.8g.1	MedDRA version for reaction		8AN		parentdrgreactionmeddraversion
B.1.10.8g.2	Reactions (if any and known)		250AN		parentdrugreaction
B.2	Reaction(s)/Event(s)	Header/entity		Area below should be a repeatable block	**reaction**
B.2.i.0	Reaction/event as reported by primary source		200AN		primarysourcereaction
B.2.i.1.a	MedDRA version for reaction/event term LLT		8AN		reactionmeddraversionllt
B.2.i.1.b	Reaction/event in MedDRA terminology (LLT)		250AN		reactionmeddrallt
B.2.i.2.a	MedDRA version for reaction/event term PT		8AN		reactionmeddraversionpt
B.2.i.2.b	Reaction/event MedDRA term (PT)		250AN		reactionmeddrapt
B.2.i.3	Term highlighted by the reporter		1N	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	termhighlighted
B.2.i.4a	Date of start of reaction/event	Date format	3N	102 - Format CCYYMMDD, 203 - Format CCYYMMDDHHMM, 610 - Format CCYYMM, 602 - Format CCYY	reactionstartdateformat
B.2.i.4b	Date of start of reaction/event		12N		reactionstartdate

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.2.i.5a	Date of end of reaction/event	Date format	3N	102 - Format CCYYMMDD, 203 - Format CCYYMMDDHHMM, 610 - Format CCYYMM, 602 - Format CCYY	reactionenddateformat
B.2.i.5b	Date of end of reaction/event		12N		reactionenddate
B.2.i.6a	Duration of reaction/event		5N		reactionduration
B.2.i.6b	Duration of reaction/event	Duration unit	3N	801=Year 802=Month 803=Week 804=Day 805=Hour 806=Minute 807=Second	reactiondurationunit
B.2.i.7.1a	Time interval between beginning of suspect drug administration and start of reaction/event		5N		reactionfirsttime
B.2.i.7.1b	Time interval unit between suspect drug administration and start of reaction/event	Time interval unit	3N	801=Year 802=Month 803=Week 804=Day 805=Hour 806=Minute 807=Second	reactionfirsttimeunit
B.2.i.7.2a	Time interval between last dose and start of reaction/event		5N		reactionlasttime
B.2.i.7.2b	Time interval unit between last dose and start of reaction/event	Time interval unit	3N	801=Year 802=Month 803=Week 804=Day 805=Hour 806=Minute 807=Second	reactionlasttimeunit

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.2.i.8	Outcome of reaction/event at the time of last observation		1N	1=recovered/resolved 2=recovering/resolving 3=not recovered/not resolved 4=recovered/resolved with sequelae 5=fatal 6=unknown	reactionoutcome
B.3	Results of tests and procedures relevant to the investigation of the patient:	Header/entity		Area below should be a repeatable block	**test**
B.3.1a	Structured information (repeat as necessary)	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	testdateformat
B.3.1b	Date		8N		testdate
B.3.1c	Test		100AN		testname
B.3.1d	Result		50AN		testresult
B.3.1e	Unit		35AN		testunit
B.3.1.1	Normal low range		50AN		lowtestrange
B.3.1.2	Normal high range		50AN		hightestrange
B.3.1.3	More information available (Y/N)		1N	1=Yes 2= No	moreinformation
		entity			**(patient)**
B.3.2	Results of tests and procedures relevant to the investigation of the patient:		2000AN		resultstestsprocedures
B.4	Drug(s) Information	Header/entity		Area below should be a repeatable block	**drug**
B.4.k.1	Characterization of drug role		1N	1=Suspect 2=Concomitant 3=Interacting	drugcharacterization
B.4.k.2	Drug identification	Header			
B.4.k.2.1	Proprietary medicinal product name		70AN		medicinalproduct
		entity			**activesubstance**
B.4.k.2.2	Active Drug substance names		100AN		activesubstancename
		entity			**(drug)**

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.4.k.2.3	Identification of the country where the drug was obtained		2A	ISO3166	obtaindrugcountry
B.4.k.3	Batch/lot number		35AN		drugbatchnumb
B.4.k.4	Holder and authorization/application number of drug	Header			
B.4.k.4.1	Authorization/Application Number		35AN		drugauthorizationnumb
B.4.k.4.2	Country of authorization/application		2A	ISO3166	drugauthorizationcountry
B.4.k.4.3	Name of holder/applicant		60AN		drugauthorizationholder
B.4.k.5	Structured Dosage Information:	Header			
B.4.k.5.1	dose (number)		8N		drugstructuredosagenumb
B.4.k.5.2	dose (unit)		3N	001=kg kilogram(s) 002=G gram(s) 003=Mg milligram(s) 004=µg microgram(s) 005=ng nanogram(s) 006=pg picogram(s) 007=mg/kg milligram(s)/kilogram 008=µg/kg microgram(s)/kilogram 009=mg/m 2 milligram(s)/sq. meter 010=µg/ m 2 microgram(s)/ sq. Meter 011=l litre(s) 012=ml millilitre(s) 013=µl microlitre(s) 014=Bq becquerel(s) 015=GBq gigabecquerel(s) 016=MBq megabecquerel(s) 017=Kbq kilobecquerel(s) 018=Ci curie(s) 019=MCi millicurie(s) 020=µCi microcurie(s) 021=NCi nanocurie(s)	drugstructuredosageunit

For Japan, field length must be two times the current length when AN or A.

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
				022=Mol mole(s) 023=Mmol millimole(s) 024=µmol micromole(s) 025=Iu international unit(s) 026=Kiu iu(1000s) 027=Miu iu(1,000,000s) 028=iu/kg iu/kilogram 029=Meq milliequivalent(s) 030=% percent 031=Gtt drop(s) 032=DF dosage form	
B.4.k.5.3	number of separate dosages		3N		drugseparatedosagenumb
B.4.k.5.4	number of units in the interval		3N		drugintervaldosageunitnumb
B.4.k.5.5	definition of the interval		3AN	801=Year 802=Month 803=Week 804=Day 805=Hour 806=Minute	drugintervaldosagedefinition
B.4.k.5.6	cumulative dose to first reaction (number)		10N		drugcumulativedosagenumb
B.4.k.5.7	cumulative dose to first reaction (unit)		3AN		drugcumulativedosageunit
B.4.k.6	Dosage text		100AN		drugdosagetext
B.4.k.7	Pharmaceutical form (Dosage form)		50AN		drugdosageform
B.4.k.8	Route of administration		3N	001 = Auricular (otic) 002 = Buccal 003 = Cutaneous 004 = Dental 005 = Endocervical 006 = Endosinusial 007 = Endotracheal 008 = Epidural 009 = Extra-amniotic 010 = Hemodialysis 011 = Intra corpus cavernosum 012 = Intra-amniotic 013 = Intra-arterial 014 = Intra-articular	drugadministrationroute

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
				015 = Intra-uterine 016 = Intracardiac 017 = Intracavernous 018 = Intracerebral 019 = Intracervical 020 = Intracisternal 021 = Intracorneal 022 = Intracoronary 023 = Intradermal 024 = Intradiscal (intraspinal) 025 = Intrahepatic 026 = Intralesional 027 = Intralymphatic 028 = Intramedullar (bone marrow) 029 = Intrameningeal 030 = Intramuscular 031 = Intraocular 032 = Intrapericardial 033 = Intraperitoneal 034 = Intrapleural 035 = Intrasynovial 036 = Intratumor 037 = Intrathecal 038 = Intrathoracic 039 = Intratracheal 040 = Intravenous bolus 041 = Intravenous drip 042 = Intravenous (not otherwise specified) 043 = Intravesical 044 = Iontophoresis 045 = Nasal 046 = Occlusive dressing technique 047 = Ophthalmic 048 = Oral 049 = Oropharingeal 050 = Other 051 = Parenteral 052 = Periarticular 053 = Perineural 054 = Rectal 055 = Respiratory (inhalation) 056 = Retrobulbar	

For Japan, field length must be two times the current length when AN or A.

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
				057 = Sunconjunctival 058 = Subcutaneous 059 = Subdermal 060 = Sublingual 061 = Topical 062 = Transdermal 063 = Transmammary 064 = Transplacental 065 = Unknown 066 = Urethral 067 = Vaginal	
B.4.k.9	Parent route of administration (in case of a parent child/fetus report)		3N	001 = Auricular (otic) 002 = Buccal 003 = Cutaneous 004 = Dental 005 = Endocervical 006 = Endosinusial 007 = Endotracheal 008 = Epidural 009 = Extra-amniotic 010 = Hemodialysis 011 = Intra corpus cavernosum 012 = Intra-amniotic 013 = Intra-arterial 014 = Intra-articular 015 = Intra-uterine 016 = Intracardiac 017 = Intracavernous 018 = Intracerebral 019 = Intracervical 020 = Intracisternal 021 = Intracorneal 022 = Intracoronary 023 = Intradermal 024 = Intradiscal (intraspinal) 025 = Intrahepatic 026 = Intralesional 027 = Intralymphatic 028 = Intramedullar (bone marrow) 029 = Intrameningeal 030 = Intramuscular 031 = Intraocular 032 = Intrapericardial 033 = Intraperitoneal	drugparadministration

For Japan, field length must be two times the current length when AN or A.

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
				034 = Intrapleural 035 = Intrasynovial 036 = Intratumor 037 = Intrathecal 038 = Intrathoracic 039 = Intratracheal 040 = Intravenous bolus 041 = Intravenous drip 042 = Intravenous (not otherwise specified) 043 = Intravesical 044 = Iontophoresis 045 = Nasal 046 = Occlusive dressing technique 047 = Ophthalmic 048 = Oral 049 = Oropharingeal 050 = Other 051 = Parenteral 052 = Periarticular 053 = Perineural 054 = Rectal 055 = Respiratory (inhalation) 056 = Retrobulbar 057 = Sunconjunctival 058 = Subcutaneous 059 = Subdermal 060 = Sublingual 061 = Topical 062 = Transdermal 063 = Transmammary 064 = Transplacental 065 = Unknown 066 = Urethral 067 = Vaginal	
B.4.k.10a	Gestation period at time of exposure		3N		reactiongestationperiod
B.4.k.10b	Gestation period at time of exposure	Gestation period unit	3N	802=Month 803=Week 804=Day 810=Trimester	reactiongestationperiodunit
B.4.k.11a	MedDRA version for indication		8AN		drugindicationmeddraversion

For Japan, field length must be two times the current length when AN or A.

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.4.k.11b	Indication for use in the case		250AN		drugindication
B.4.k.12a	Date of start of drug	Date format	3N	102 – Format CCYYMMDD, 610 – Format CCYYMM, 602 - Format CCYY	drugstartdateformat
B.4.k.12b	Date of start of drug		8N		drugstartdate
B.4.k.13	Time interval between drug administration and start of reaction/event	Header			
B.4.k.13.1a	Time interval between beginning of drug administration and start of reaction/event		5N		drugstartperiod
B.4.k.13.1b	Time interval between beginning of drug administration and start of reaction/event	Time unit	3N	801=Year 802=Month 803=Week 804=Day 805=Hour 806=Minute 807=Second	drugstartperiodunit
B.4.k.13.2a	Time interval between last dose of drug and start of reaction/event		5N		druglastperiod
B.4.k.13.2b	Time interval between last dose of drug and start of reaction/event	Time unit	3N	801=Year 802=Month 803=Week 804=Day 805=Hour 806=Minute 807=Second	druglastperiodunit
B.4.k.14a	Date of last administration	Date format	3N	102 – Format CCYYMMDD, 610 – Format CCYYMM, 602 - Format CCYY	drugenddateformat
B.4.k.14b	Date of last administration		8N		drugenddate
B.4.k.15a	Duration of drug administration		5N		drugtreatmentduration

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.4.k.15b	Duration of drug administration unit	Time unit	3N	801=Year 802=Month 803=Week 804=Day 805=Hour 806=Minute	drugtreatmentdurationunit
B.4.k.16	Action(s) taken with drug		1N	1=Drug withdrawn 2=Dose reduced 3=Dose increased 4=Dose not changed 5=Unknown 6=Not applicable	actiondrug
B.4.k.17	Effect of rechallenge (or re-exposure), for suspect drug(s) only	Header			
B.4.k.17.1	Did reaction recur on readministration?		1N	1=Yes 2= No 3 = Unknown	drugrecurreadministration
		entity			**drugrecurrence**
B.4.k.17.2a	MedDRA version for reaction(s)/event(s) recurred		8AN		drugrecuractionmeddraversion
B.4.k.17.2b	If yes, which reaction(s)/event(s) recurred?		250AN		drugrecuraction
B.4.k.18	Relatedness of drug to reaction(s)/event(s) (repeat as necessary)	Header/entity			**drugreactionrelatedness**
B.4.k.18.1a	MedDRA version for Reaction assessed		8AN		drugreactionassesmeddraversion
B.4.k.18.1b	Reaction assessed		250AN		drugreactionasses
B.4.k.18.2	Source of assessment		60AN		drugassessmentsource
B.4.k.18.3	Method of assessment		35AN		drugassessmentmethod
B.4.k.18.4	Result		35AN		drugresult
		entity			**(drug)**
B.4.k.19	Additional information on drug		100AN		drugadditional
B.5	Narrative case summary and further information:	Header/entity			**summary**

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.5.1	Case narrative including clinical course, therapeutic measures, outcome and additional relevant information.		20000 AN		narrativeincludeclinical
B.5.2	Reporter's comments		500AN		reportercomment
B.5.3a	MedDRA Version for Sender’s diagnosis		8AN		senderdiagnosismeddraversion
B.5.3b	Sender's diagnosis/syndrome and/or reclassification of reaction/event		250AN		senderdiagnosis
B.5.4	Sender's comments		2000AN		sendercomment

The following list describes the data types specified in the field length column of the attribute list:

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. "en". 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‘”^".

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".

A.2 ICH ICSR DTD (Document Type Definition)

```
<!DOCTYPE ichicsr
<!-- PUBLIC "-//ICHM2//DTD ICH ICSR Vers. 2.1//EN"  "ich-icsr-v2.1.dtd"  -->

<!--
  Individual Case Safety Report Document Type Definition

  This DTD is issued by the ICH M2 group and is public domain in
  nature.

        No one can claim copyright on this DTD.
        No commercial distribution is allowed.

The ICH is not responsible for any damage or financial loss resulting from use
of this DTD. This version is tentative in nature and changes are expected.
This DTD is subject to the ICH M2 change control procedures.
  Version 1.0, Release 1.0, October 17, 1997

1998-04-21 Modifications made by JPMA

1. Changed "resultstestsprocedures" to "resultstestsprocedures?".

2. Spelling correction "seriousnesslifethreatning" to
"seriousnesslifethreatening".

3. Spelling correction "seriousnessconginitalanomali" to
"seriousnesscongenitalanomali".

4. Changed ELEMENT "parentmedicalstructure" to "parentmedicalepisodename".

1998-09-27 Modifications made by FDA

5. Added lang attribute to ichicsr as #REQUIRED using a %lang.att entity.

6. Added lang attribute to all other elements as #IMPLIED.

7. Removed all unordered "&" connectors and replaced with the ordered
connector "," to be compatible with XML.

8. Changed the names of elements under "ichicsrmessageheader" to comply with
group decisions.

9. Removed all "old" elements.

10. Removed all sequence number entities.

11. Added Standard SGML character entities &lt;, &gt;, &amp; so that markup
can be escaped as necessary.

12. Removed the %act.rec; and %ope.rec; internal entities, thus removing all
support for the "(app | rep | del )" construct.

13. Root element of DTD is now "ichicsr" which allows one
"ichicsrmessageheader" followed by "safetyreport+".
```

14. The relationship between "drug" and "activesubstance" is now one to zero or many.

Version 2.0, Release 1.0, Date to be decided

Version 2.1, Release 1.0, agreed November 2000
Documentation of changes made in version 2.0 to version 2.1 should be completed for implementation.
Safety Report Version (ICH ICSR M2 Data Processing element) is not an E2BM data element, but rather
should be used for technical transmission purposes.
Date of final release of Version 2.1 February 1, 2001

After San Diego ICH 5, this DTD was fixed to be final version for Version 2.1.
Version 2.1, Release 2.0, agreed Feburary 2001.

-->

<!-- TECHNICAL NOTE

ICH ICSR SGML Declaration

To correctly parse an ICH ICSR SGML message requires the selection of the correct SGML declaration, along with this DTD, and the ICH ICSR SGML instance. This technical note provides guidance on which of several SGML declarations included with the ICH ICSR application to select based on the language and character set used within the ICH ICSR SGML instance. The method by which an SGML parser is told to use a specific declaration is parser specific.
The three most common methods are -

1. Tell the parser via the command line which declaration to use.

2. Tell the parser via a specific environment variable which declaration to use.

3. If the parser supports SGML Open catalogs, within the catalog file is a command that can tell the parser which declaration to use. SGML catalog files are an industry standard way to tell a parser how to find all of the pieces (declaration, DTD, SGML document instance) needed to successfully parse.

To cover all of the languages necessary to support the ICH ICSR application,ISO 10646 (UNICODE) would have to be used. If this were the case, then only one SGML declaration would be needed to support all ICH ICSR languages. Because UNICODE support is not available in all popular computer application programs, the ICH M2 EWG has recommended that a variety of character sets be used at this time, instead of a single UNICODE character encoding. For each of these different character encodings a different SGML declaration needs to be generated and used.

Five SGML declarations are included with the ICH ICSR distribution. They are described briefly below.

ich-icsr-latin1.dcl - This SGML declaration supports the ISO 8859-1 (Latin 1) character set. This character set supports English, and most Western European languages.

```
ich-icsr-latin7.dcl - This SGML declaration supports the ISO 8859-7 (Latin 7)
character set.  This character set supports Greek.

ich-icsr-sjis.dcl - This SGML declaration supports the Shift JIS character set
for encoding Japanese.

ich-icsr-utf8.dcl - This SGML declaration supports the ISO 10646 (UNICODE)
UTF-8 character set.  This character set supports almost all of the world's
currently written languages.

ich-icsr-mult.dcl - This SGML declaration will support all of the currently
defined ICHICSR languages, and it doesn't require the use of UNICODE.  It is
however a "hack" that relies on a fortuitous characteristic of the languages
currently being used within the ICH ICSR SGML application.

This hack works because the character set documented within an SGML
declaration is for the benefit of both the SGML parser and the programmer who
implements the SGML application.  The programmer needs detailed knowledge of
all the characters being used to correctly code an application.  The parser
only really needs to know about some of the characters.  In particular it
needs to know which characters signify an SGML event.  For instance that the
"<" character starts an SGML open tag, and the "</" character sequence starts
an SGML close tag.  All told, the parser needs to know very little.  Because
of the particular combination of character sets being used within the ICH ICSR
application, an SGML declaration can be defined that tells the parser just
what it needs to know and still work across all of the different  character
sets.  The catch is that this SGML declaration doesn't tell the programmer all
that she or he needs to know to correctly code the rest of the application.
If this declaration is used, the programmer will have to get this detailed
information from another source.

-->

<!-- ================================================================== -->
<!-- Entities                                                           -->
<!-- ================================================================== -->

<!-- Use the lang attribute to indicate the language of an elements     --
  -- content via an ISO 639 language Code.                              -->

<!ENTITY % lang.att "lang CDATA #IMPLIED">

<!-- Standard Character Entities to escape SGML special characters.     --
  -- When "<", ">", and "&" occur in text, they should be replaced      --
  -- by "&lt;", "&gt;", and "&amp;" respectively.                       -->

<!-- Less Than "<" -->
<!ENTITY lt     "&#38;#60;">

<!-- Greater Than ">" -->
<!ENTITY gt     "&#62;">

<!-- Ampersand "&" -->
<!ENTITY amp    "&#38;#38;">

<!-- ================================================================== -->
```

```
<!-- Elements and Attributes                                              -->
<!-- ================================================================== -->

<!ELEMENT ichicsr               - - (ichicsrmessageheader, safetyreport+)>
<!ATTLIST ichicsr
      lang  CDATA #REQUIRED
>

<!-- M.1 ICH ICSR Message Header Information -->

<!ELEMENT ichicsrmessageheader         - -
      (messagetype                  ,
      messageformatversion          ,
      messageformatrelease          ,
      messagenumb             ,
      messagesenderidentifier         ,
      messagereceiveridentifier     ,
        messagedateformat               ,
      messagedate)>
<!ATTLIST ichicsrmessageheader
      %lang.att;
>

<!-- M.1.1 Message Type -->
<!ELEMENT messagetype         - - (#PCDATA) >
<!ATTLIST messagetype
      %lang.att;
>

<!-- M.1.2 Message Format Version -->
<!ELEMENT messageformatversion      - - (#PCDATA) >
<!ATTLIST messageformatversion
      %lang.att;
>

<!-- M.1.3 Message Format Release -->
<!ELEMENT messageformatrelease      - - (#PCDATA) >
<!ATTLIST messageformatrelease
      %lang.att;
>

<!-- M.1.4 Message Number -->
<!ELEMENT messagenumb         - - (#PCDATA) >
<!ATTLIST messagenumb
      %lang.att;
>

<!-- M.1.5 Message Sender Identifier -->
<!ELEMENT messagesenderidentifier - - (#PCDATA) >
<!ATTLIST messagesenderidentifier
      %lang.att;
>

<!-- M.1.6 Message Receiver Identifier -->
<!ELEMENT messagereceiveridentifier - - (#PCDATA) >
<!ATTLIST messagereceiveridentifier
      %lang.att;
```

```
>

<!-- M.1.7a Message Date Format -->
<!ELEMENT messagedateformat     - -     (#PCDATA)>
<!ATTLIST messagedateformat
        %lang.att;
>

<!-- M.1.7b Message Date -->
<!ELEMENT messagedate   - -   (#PCDATA) >
<!ATTLIST messagedate
      %lang.att;
>

<!-- Individual Case Safety Report(s) Specifications -->
<!-- A.1 Identification of the case safety report   -->

<!ELEMENT safetyreport        - -
        (safetyreportversion?,
        safetyreportid              ,
      primarysourcecountry?         ,
      occurcountry?                   ,
        transmissiondateformat?         ,
      transmissiondate?               ,
      reporttype?                     ,
      serious?                        ,
      seriousnessdeath?               ,
      seriousnesslifethreatening?     ,
      seriousnesshospitalization?     ,
      seriousnessdisabling?           ,
      seriousnesscongenitalanomali?   ,
      seriousnessother?               ,
        receivedateformat?              ,
      receivedate?                    ,
        receiptdateformat               ,
      receiptdate                     ,
      additionaldocument?             ,
      documentlist?                   ,
      fulfillexpeditecriteria?        ,
      authoritynumb?                  ,
      companynumb?                    ,
      duplicate?                        ,
      casenullification?              ,
      nullificationreason?            ,
      medicallyconfirm?               ,
            (reportduplicate*               ,
            linkedreport*                   ,
            primarysource+                  ,
            sender                          ,
            receiver                        ,
            patient))>
<!ATTLIST safetyreport
        %lang.att;
>

<!ELEMENT reportduplicate     - -
        (duplicatesource?           ,
```

```
      duplicatenumb?)>
<!ATTLIST reportduplicate
      %lang.att;
>

<!ELEMENT linkedreport        - -     (linkreportnumb?)>
<!ATTLIST linkedreport
      %lang.att;
>

<!-- A.2 Primary source(s) of information -->
<!ELEMENT primarysource       - -
        (reportertitle?                 ,
      reportergivename?               ,
      reportermiddlename?             ,
      reporterfamilyname?             ,
      reporterorganization?           ,
      reporterdepartment?             ,
      reporterstreet?                 ,
      reportercity?                   ,
      reporterstate?                  ,
      reporterpostcode?               ,
      reportercountry?                ,
      qualification?                  ,
      literaturereference?            ,
      studyname?                      ,
      sponsorstudynumb?               ,
      observestudytype?)>
<!ATTLIST primarysource
      %lang.att;
>

<!-- A.3.1 Sender -->
<!ELEMENT sender                - -
      (sendertype?                    ,
      senderorganization              ,
      senderdepartment?               ,
      sendertitle?                    ,
      sendergivename?                 ,
      sendermiddlename?               ,
      senderfamilyname?               ,
      senderstreetaddress?            ,
      sendercity?                     ,
      senderstate?                    ,
      senderpostcode?                 ,
      sendercountrycode?              ,
      sendertel?                      ,
      sendertelextension?             ,
      sendertelcountrycode?           ,
      senderfax?                      ,
      senderfaxextension?             ,
      senderfaxcountrycode?           ,
      senderemailaddress?)>
<!ATTLIST sender
      %lang.att;
>
```

```
<!-- A.3.2 Receiver -->
<!ELEMENT receiver              - -
      (receivertype?                ,
      receiverorganization?         ,
      receiverdepartment?           ,
      receivertitle?                ,
      receivergivename?             ,
      receivermiddlename?           ,
      receiverfamilyname?           ,
      receiverstreetaddress?        ,
      receivercity?                 ,
      receiverstate?                ,
      receiverpostcode?             ,
      receivercountrycode?          ,
      receivertel?                  ,
      receivertelextension?         ,
      receivertelcountrycode?       ,
      receiverfax?                  ,
      receiverfaxextension?         ,
      receiverfaxcountrycode?       ,
      receiveremailaddress?)>
<!ATTLIST receiver
      %lang.att;
>

<!-- B.1 Patient characteristics -->
<!ELEMENT patient               - -
      (patientinitial?              ,
      patientgpmedicalrecordnumb?   ,
      patientspecialistrecordnumb?  ,
      patienthospitalrecordnumb?    ,
      patientinvestigationnumb?     ,
        patientbirthdateformat?       ,
      patientbirthdate?             ,
      patientonsetage?              ,
        patientonsetageunit?          ,
      gestationperiod?              ,
        gestationperiodunit?          ,
      patientagegroup?              ,
      patientweight?                ,
      patientheight?                ,
      patientsex?                   ,
        lastmenstrualdateformat?    ,
      patientlastmenstrualdate?     ,
      patientmedicalhistorytext?    ,
      resultstestsprocedures?       ,
            (medicalhistoryepisode*       ,
            patientpastdrugtherapy*       ,
            patientdeath?                 ,
            parent?                       ,
            reaction+                     ,
            test*                         ,
            drug+                         ,
            summary?))>
<!ATTLIST patient
      %lang.att;
>
```

```
<!-- B.1.7 Relevant medical history and concurrent -->
<!ELEMENT medicalhistoryepisode - -
        (patientepisodenamemeddraversion?,
        patientepisodename?          ,
        patientmedicalstartdateformat?   ,
      patientmedicalstartdate?         ,
      patientmedicalcontinue?          ,
        patientmedicalenddateformat?     ,
      patientmedicalenddate?           ,
      patientmedicalcomment?)>
<!ATTLIST medicalhistoryepisode
      %lang.att;
>

<!-- B.1.8 Relevant past drug history -->
<!ELEMENT patientpastdrugtherapy    - -
        (patientdrugname?               ,
        patientdrugstartdateformat?     ,
      patientdrugstartdate?           ,
        patientdrugenddateformat?       ,
      patientdrugenddate?             ,
      patientindicationmeddraversion?     ,
      patientdrugindication?          ,
      patientdrgreactionmeddraversion?,
      patientdrugreaction?)>

<!ATTLIST patientpastdrugtherapy
      %lang.att;
>

<!-- B.1.9 In case of death: -->
<!ELEMENT patientdeath        - -
        (patientdeathdateformat?        ,
      patientdeathdate?       ,
      patientautopsyyesno?          ,
            (patientdeathcause*     ,
            patientautopsy*)) >
<!ATTLIST patientdeath
      %lang.att;
>


<!ELEMENT patientdeathcause   - -
      (patientdeathreportmeddraversion?,
        patientdeathreport?)>
<!ATTLIST patientdeathcause
      %lang.att;
>

<!ELEMENT patientautopsy      - -
       (patientdetermautopsmeddraversion?,
         patientdetermineautopsy?)>
<!ATTLIST patientautopsy
      %lang.att;
>
```

```
<!-- B.1.10 For a parent-child / fetus report, information concerning the
parent: -->
<!ELEMENT parent                - -
      (parentidentification?          ,
        parentbirthdateformat?          ,
      parentbirthdate?                ,
      parentage?                      ,
        parentageunit?                  ,
        parentlastmenstrualdateformat?  ,
      parentlastmenstrualdate?      ,
      parentweight?                   ,
      parentheight?                   ,
      parentsex?                      ,
      parentmedicalrelevanttext?      ,
            (parentmedicalhistoryepisode*   ,
            parentpastdrugtherapy*))>
<!ATTLIST parent
      %lang.att;
>

<!-- B.1.10.7 Relevant medical history and concurrent conditions of parent -->
<!ELEMENT parentmedicalhistoryepisode - -
        (parentmdepisodemeddraversion?    ,
      parentmedicalepisodename?               ,
        parentmedicalstartdateformat?           ,
      parentmedicalstartdate?                 ,
      parentmedicalcontinue?                  ,
        parentmedicalenddateformat?             ,
      parentmedicalenddate?                   ,
      parentmedicalcomment?)>
<!ATTLIST parentmedicalhistoryepisode
      %lang.att;
>

<!-- B.1.10.8 Relevant past drug history -->
<!ELEMENT parentpastdrugtherapy - -
        (parentdrugname?                  ,
        parentdrugstartdateformat?        ,
      parentdrugstartdate?              ,
        parentdrugenddateformat?          ,
      parentdrugenddate?                ,
      parentdrgindicationmeddraversion? ,
      parentdrugindication?             ,
      parentdrgreactionmeddraversion?   ,
      parentdrugreaction?)>
<!ATTLIST parentpastdrugtherapy
      %lang.att;
>

<!-- B.2 Reaction(s) / Event(s) -->
<!ELEMENT reaction            - -
        (primarysourcereaction?         ,
      reactionmeddraversionllt?       ,
      reactionmeddrallt?            ,
      reactionmeddraversionpt?        ,
      reactionmeddrapt?             ,
      termhighlighted?                ,
```

```
        reactionstartdateformat?        ,
      reactionstartdate?              ,
        reactionenddateformat?          ,
      reactionenddate?                ,
      reactionduration?               ,
        reactiondurationunit?           ,
      reactionfirsttime?              ,
        reactionfirsttimeunit?          ,
      reactionlasttime?               ,
        reactionlasttimeunit?           ,
      reactionoutcome?)>
<!ATTLIST reaction
      %lang.att;
>

<!-- B.3 Results of tests and procedures relevant to the investigation of the
patient: -->
<!ELEMENT test                - -

        (testdateformat?                ,
        testdate?                       ,
      testname?                       ,
      testresult?                     ,
      testunit?                       ,
      lowtestrange?                   ,
      hightestrange?                  ,
      moreinformation?)>
<!ATTLIST test
      %lang.att;
>

<!ELEMENT drug                - -
      (drugcharacterization?          ,
      medicinalproduct?               ,
      obtaindrugcountry?              ,
      drugbatchnumb?                  ,
      drugauthorizationnumb?          ,
      drugauthorizationcountry?       ,
      drugauthorizationholder?        ,
      drugstructuredosagenumb?        ,
      drugstructuredosageunit?        ,
      drugseparatedosagenumb?         ,
      drugintervaldosageunitnumb?     ,
      drugintervaldosagedefinition?   ,
      drugcumulativedosagenumb?       ,
      drugcumulativedosageunit?       ,
      drugdosagetext?                 ,
      drugdosageform?                 ,
      drugadministrationroute?        ,
      drugparadministration?          ,
      reactiongestationperiod?        ,
        reactiongestationperiodunit?    ,
      drugindicationmeddraversion?  ,
      drugindication?                 ,
        drugstartdateformat?            ,
      drugstartdate?                  ,
      drugstartperiod?        ,
```

```
        drugstartperiodunit?            ,
      druglastperiod?               ,
        druglastperiodunit?             ,
        drugenddateformat?              ,
      drugenddate?                    ,
      drugtreatmentduration?          ,
        drugtreatmentdurationunit?      ,
      actiondrug?                     ,
      drugrecurreadministration?      ,
      drugadditional?                 ,
            (activesubstance*               ,
            drugrecurrence*                 ,
            drugreactionrelatedness*))>
<!ATTLIST drug
      %lang.att;
>

<!ELEMENT activesubstance     - -     (activesubstancename)>
<!ATTLIST activesubstance
      %lang.att;
>

<!ELEMENT drugrecurrence        - -
      (drugrecuractionmeddraversion?    ,
         drugrecuraction)>
<!ATTLIST drugrecurrence
      %lang.att;
>

<!-- B.4.k.18 Relatedness of drug to reaction / event -->
<!ELEMENT drugreactionrelatedness - -
        (drugreactionassesmeddraversion? ,
      drugreactionasses?              ,
      drugassessmentsource?           ,
      drugassessmentmethod?           ,
      drugresult?)>
<!ATTLIST drugreactionrelatedness
      %lang.att;
>

<!-- B.5 Narrative case summary and further information: -->
<!ELEMENT summary               - -
      (narrativeincludeclinical?      ,
      reportercomment?                ,
      senderdiagnosismeddraversion?               ,
      senderdiagnosis?                ,
      sendercomment?)>
<!ATTLIST summary
      %lang.att;
>

<!ELEMENT safetyreportversion - -   (#PCDATA)>
<!ATTLIST safetyreportversion
      %lang.att;
>

<!-- A.1.0.1 Sender's(case) Safety Report Unique Identifier -->
```

```
<!ELEMENT safetyreportid      - -   (#PCDATA)>
<!ATTLIST safetyreportid
      %lang.att;
>


<!-- A.1.1 Identification of the country of the primary -->
<!ELEMENT primarysourcecountry  - -     (#PCDATA)>
<!ATTLIST primarysourcecountry
      %lang.att;
>

<!-- A.1.2 Identification of the country where the reaction / event occurred -
->
<!ELEMENT occurcountry          - -     (#PCDATA)>
<!ATTLIST occurcountry
      %lang.att;
>


<!-- A.1.3a Date of this transmission format -->
<!ELEMENT transmissiondateformat - -    (#PCDATA)>
<!ATTLIST transmissiondateformat
       %lang.att;
>

<!-- A.1.3b Date of this transmission -->
<!ELEMENT transmissiondate      - -     (#PCDATA)>
<!ATTLIST transmissiondate
      %lang.att;
>

<!-- A.1.4 Type of report -->
<!ELEMENT reporttype            - -     (#PCDATA)>
<!ATTLIST reporttype
      %lang.att;
>

<!-- A.1.5.1 Serious -->
<!ELEMENT serious               - -     (#PCDATA)>
<!ATTLIST serious
      %lang.att;
>

<!-- A.1.5.2 Seriousness criteria -->
<!ELEMENT seriousnessdeath      - -     (#PCDATA)>
<!ATTLIST seriousnessdeath
      %lang.att;
>
<!ELEMENT seriousnesslifethreatening - -        (#PCDATA)>
<!ATTLIST seriousnesslifethreatening
      %lang.att;
>
<!ELEMENT seriousnesshospitalization - -        (#PCDATA)>
<!ATTLIST seriousnesshospitalization
      %lang.att;
>
```

```
<!ELEMENT seriousnessdisabling  - -     (#PCDATA)>
<!ATTLIST seriousnessdisabling
      %lang.att;
>
<!ELEMENT seriousnesscongenitalanomali - -      (#PCDATA)>
<!ATTLIST seriousnesscongenitalanomali
      %lang.att;
>
<!ELEMENT seriousnessother      - -     (#PCDATA)>
<!ATTLIST seriousnessother
      %lang.att;
>

<!-- A.1.6a Date report was first received from source format -->
<!ELEMENT receivedateformat     - -     (#PCDATA)>
<!ATTLIST receivedateformat
        %lang.att;
>

<!-- A.1.6b Date report was first received from source -->
<!ELEMENT receivedate           - -     (#PCDATA)>
<!ATTLIST receivedate
      %lang.att;
>

<!-- A.1.7a Date of receipt of the most recent information for this report -->
<!ELEMENT receiptdateformat     - -     (#PCDATA)>
<!ATTLIST receiptdateformat
        %lang.att;
>

<!-- A.1.7b Date of receipt of the most recent information for this report -->
<!ELEMENT receiptdate           - -     (#PCDATA)>
<!ATTLIST receiptdate
      %lang.att;
>

<!-- A.1.8.1 Are additional documents available -->
<!ELEMENT additionaldocument    - -     (#PCDATA)>
<!ATTLIST additionaldocument
      %lang.att;
>

<!-- A.1.8.2 List of documents held by sender -->
<!ELEMENT documentlist          - -     (#PCDATA)>
<!ATTLIST documentlist
      %lang.att;
>

<!-- A.1.9 Does this case fulfill the local criteria for an expedited report -
->
<!ELEMENT fulfillexpeditecriteria - -   (#PCDATA)>
<!ATTLIST fulfillexpeditecriteria
      %lang.att;
>

<!--
```

```
The A.1.10 - The worldwide unique case identification number must be populated
as per the following user guidance:

Only A.1.10.1 or A.1.10.2 should be used.  No case should ever have more than
one of these items completed.  The contents of whichever item is used should
remain unchanged for any transmissions subsequent to the original transmission.
When a regulator is the initial sender A.1.10.1 should be used. When an entity
other than a regulator is the initial sender, A.1.10.2 should be used. When a
sender has not previously received a valid E2B/M2 report electronically, the
identifiers (content and format) in A.1.0.1 and A.1.10.1 or A.1.10.2 should be
identical.  Retransmitters should use their own sender's (case) safety report
unique identifier (A.1.0.1), but not change A.1.10.1 or A.1.10.2. Examples are
available in attachment 3 of the E2BM document.
 The contents of the fields A.1.10.1 and/or A.1.10.2 should first list A.1.1 -
Identification of the country of primary source and secondly list A.3.1.2 -
Sender Identifier, Sender Organization, and lastly, the company international
case report number, delimited by hyphens.

For example, a report transmitted by a US company to a regulatory authority
would populate A.1.10.2 with "US-Company Name-12345", where "12345" is the
company's unique case report number.  In the event that the regulatory
authority transmitted this ICSR to another regulatory authority, A.1.10.2
would remain the same.  The regulatory authority would not populate A.1.10.1.

If the situation occurs where multiple reports are received about the same
case, such as a report from a physician and a report from another company, the
information may be merged.  One number will be maintained as the case number
in its original field and the second number will be listed as a suspected
duplicate.
-->
<!-- A.1.10.1 Regulatory authority's case report number -->
<!ELEMENT authoritynumb         - -     (#PCDATA)>
<!ATTLIST authoritynumb
      %lang.att;
>

<!-- A.1.10.2 Other sender's case report number -->
<!ELEMENT companynumb           - -     (#PCDATA)>
<!ATTLIST companynumb
      %lang.att;
>

<!-- A.1.11 Other case identifiers in previous transmissions -->
<!ELEMENT duplicate             - -     (#PCDATA)>
<!ATTLIST duplicate
      %lang.att;
>

<!-- A.1.11.1 Source(s) of the case identifier -->
<!ELEMENT duplicatesource       - -     (#PCDATA)>
<!ATTLIST duplicatesource
      %lang.att;
>

<!-- A.1.11.2 Case identifier(s) -->
<!ELEMENT duplicatenumb         - -     (#PCDATA)>
<!ATTLIST duplicatenumb
```

```
      %lang.att;
>

<!-- A.1.12 Identification number of the report which is linked to this report
-->
<!ELEMENT linkreportnumb        - -     (#PCDATA)>
<!ATTLIST linkreportnumb
      %lang.att;
>

<!-- A.1.13 Report nullification -->
<!ELEMENT casenullification     - -     (#PCDATA)>
<!ATTLIST casenullification
      %lang.att;
>

<!-- A.1.13.1 Reason for nullification -->
<!ELEMENT nullificationreason   - -     (#PCDATA)>
<!ATTLIST nullificationreason
      %lang.att;
>

<!-- A.1.14 Was the case medically confirmed, if not initially from health
professional? -->
<!ELEMENT medicallyconfirm      - -     (#PCDATA)>
<!ATTLIST medicallyconfirm
      %lang.att;
>

<!-- A.2.1.1a Reporter identifier -->
<!ELEMENT reportertitle         - -     (#PCDATA)>
<!ATTLIST reportertitle
      %lang.att;
>

<!-- A.2.1.1b Reporter identifier -->
<!ELEMENT reportergivename      - -     (#PCDATA)>
<!ATTLIST reportergivename
      %lang.att;
>

<!-- A.2.1.1c Reporter identifier -->
<!ELEMENT reportermiddlename    - -     (#PCDATA)>
<!ATTLIST reportermiddlename
      %lang.att;
>

<!-- A.2.1.1d Reporter identifier -->
<!ELEMENT reporterfamilyname    - -     (#PCDATA)>
<!ATTLIST reporterfamilyname
      %lang.att;
>

<!-- A.2.1.2a Reporter's address -->
<!ELEMENT reporterorganization  - -     (#PCDATA)>
<!ATTLIST reporterorganization
      %lang.att;
```

```
>

<!-- A.2.1.2b Reporter's address -->
<!ELEMENT reporterdepartment    - -     (#PCDATA)>
<!ATTLIST reporterdepartment
      %lang.att;
>

<!-- A.2.1.2c Reporter's address -->
<!ELEMENT reporterstreet        - -     (#PCDATA)>
<!ATTLIST reporterstreet
      %lang.att;
>

<!-- A.2.1.2d Reporter's address -->
<!ELEMENT reportercity          - -     (#PCDATA)>
<!ATTLIST reportercity
      %lang.att;
>

<!-- A.2.1.2e Reporter's address -->
<!ELEMENT reporterstate         - -     (#PCDATA)>
<!ATTLIST reporterstate
      %lang.att;
>

<!-- A.2.1.2f Reporter's address -->
<!ELEMENT reporterpostcode      - -     (#PCDATA)>
<!ATTLIST reporterpostcode
      %lang.att;
>

<!-- A.2.1.3 Country -->
<!ELEMENT reportercountry       - -     (#PCDATA)>
<!ATTLIST reportercountry
      %lang.att;
>

<!-- A.2.1.4 Qualification -->
<!ELEMENT qualification         - -     (#PCDATA)>
<!ATTLIST qualification
      %lang.att;
>

<!-- A.2.2 Literature reference(s) -->
<!ELEMENT literaturereference   - -     (#PCDATA)>
<!ATTLIST literaturereference
      %lang.att;
>

<!-- A.2.3.1 Study name -->
<!ELEMENT studyname             - -     (#PCDATA)>
<!ATTLIST studyname
      %lang.att;
>

<!-- A.2.3.2 Sponsor study number -->
```

```
<!ELEMENT sponsorstudynumb      - -     (#PCDATA)>
<!ATTLIST sponsorstudynumb
      %lang.att;
>

<!-- A.2.3.3 Study type in which the reactions / events were observed -->
<!ELEMENT observestudytype      - -     (#PCDATA)>
<!ATTLIST observestudytype
      %lang.att;
>

<!-- A.3.1.1 Sender type -->
<!ELEMENT sendertype            - -     (#PCDATA)>
<!ATTLIST sendertype
      %lang.att;
>

<!-- A.3.1.2 Sender organization -->
<!ELEMENT senderorganization    - -     (#PCDATA)>
<!ATTLIST senderorganization
      %lang.att;
>

<!-- A.3.1.3a Person responsible for sending the report -->
<!ELEMENT senderdepartment      - -     (#PCDATA)>
<!ATTLIST senderdepartment
      %lang.att;
>

<!-- A.3.1.3b Person responsible for sending the report -->
<!ELEMENT sendertitle           - -     (#PCDATA)>
<!ATTLIST sendertitle
      %lang.att;
>

<!-- A.3.1.3c Person responsible for sending the report -->
<!ELEMENT sendergivename        - -     (#PCDATA)>
<!ATTLIST sendergivename
      %lang.att;
>

<!-- A.3.1.3d Person responsible for sending the report -->
<!ELEMENT sendermiddlename      - -     (#PCDATA)>
<!ATTLIST sendermiddlename
      %lang.att;
>

<!-- A.3.1.3e Person responsible for sending the report -->
<!ELEMENT senderfamilyname      - -     (#PCDATA)>
<!ATTLIST senderfamilyname
      %lang.att;
>

<!-- A.3.1.4a Address, fax, telephone and E-mail address -->
<!ELEMENT senderstreetaddress   - -     (#PCDATA)>
<!ATTLIST senderstreetaddress
      %lang.att;
```

```
>

<!-- A.3.1.4b Address, fax, telephone and E-mail address -->
<!ELEMENT sendercity            - -     (#PCDATA)>
<!ATTLIST sendercity
      %lang.att;
>

<!-- A.3.1.4c Address, fax, telephone and E-mail address -->
<!ELEMENT senderstate           - -     (#PCDATA)>
<!ATTLIST senderstate
      %lang.att;
>

<!-- A.3.1.4d Address, fax, telephone and E-mail address -->
<!ELEMENT senderpostcode        - -     (#PCDATA)>
<!ATTLIST senderpostcode
      %lang.att;
>

<!-- A.3.1.4e Address, fax, telephone and E-mail address -->
<!ELEMENT sendercountrycode     - -     (#PCDATA)>
<!ATTLIST sendercountrycode
      %lang.att;
>

<!-- A.3.1.4f Address, fax, telephone and E-mail address -->
<!ELEMENT sendertel             - -     (#PCDATA)>
<!ATTLIST sendertel
      %lang.att;
>

<!-- A.3.1.4g Address, fax, telephone and E-mail address -->
<!ELEMENT sendertelextension    - -     (#PCDATA)>
<!ATTLIST sendertelextension
      %lang.att;
>

<!-- A.3.1.4h Address, fax, telephone and E-mail address -->
<!ELEMENT sendertelcountrycode  - -     (#PCDATA)>
<!ATTLIST sendertelcountrycode
      %lang.att;
>

<!-- A.3.1.4i Address, fax, telephone and E-mail address -->
<!ELEMENT senderfax             - -     (#PCDATA)>
<!ATTLIST senderfax
      %lang.att;
>

<!-- A.3.1.4j Address, fax, telephone and E-mail address -->
<!ELEMENT senderfaxextension    - -     (#PCDATA)>
<!ATTLIST senderfaxextension
      %lang.att;
>

<!-- A.3.1.4k Address, fax, telephone and E-mail address -->
```

```
<!ELEMENT senderfaxcountrycode  - -     (#PCDATA)>
<!ATTLIST senderfaxcountrycode
      %lang.att;
>

<!-- A.3.1.4l Address, fax, telephone and E-mail address -->
<!ELEMENT senderemailaddress    - -     (#PCDATA)>
<!ATTLIST senderemailaddress
      %lang.att;
>

<!-- A.3.2.1 Receiver type -->
<!ELEMENT receivertype          - -     (#PCDATA)>
<!ATTLIST receivertype
      %lang.att;
>

<!-- A.3.2.2a Receiver identifier -->
<!ELEMENT receiverorganization  - -     (#PCDATA)>
<!ATTLIST receiverorganization
      %lang.att;
>

<!-- A.3.2.2b Receiver identifier -->
<!ELEMENT receiverdepartment    - -     (#PCDATA)>
<!ATTLIST receiverdepartment
      %lang.att;
>

<!-- A.3.2.2c Receiver identifier -->
<!ELEMENT receivertitle         - -     (#PCDATA)>
<!ATTLIST receivertitle
      %lang.att;
>

<!-- A.3.2.2d Receiver identifier -->
<!ELEMENT receivergivename      - -     (#PCDATA)>
<!ATTLIST receivergivename
      %lang.att;
>

<!-- A.3.2.2e Receiver identifier -->
<!ELEMENT receivermiddlename    - -     (#PCDATA)>
<!ATTLIST receivermiddlename
      %lang.att;
>

<!-- A.3.2.2f Receiver identifier -->
<!ELEMENT receiverfamilyname    - -     (#PCDATA)>
<!ATTLIST receiverfamilyname
      %lang.att;
>

<!-- A.3.2.3a Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiverstreetaddress - -     (#PCDATA)>
<!ATTLIST receiverstreetaddress
      %lang.att;
```

```
>

<!-- A.3.2.3b Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receivercity          - -     (#PCDATA)>
<!ATTLIST receivercity
      %lang.att;
>

<!-- A.3.2.3c Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiverstate         - -     (#PCDATA)>
<!ATTLIST receiverstate
      %lang.att;
>

<!-- A.3.2.3d Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiverpostcode      - -     (#PCDATA)>
<!ATTLIST receiverpostcode
      %lang.att;
>

<!-- A.3.2.3e Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receivercountrycode   - -     (#PCDATA)>
<!ATTLIST receivercountrycode
      %lang.att;
>

<!-- A.3.2.3f Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receivertel           - -     (#PCDATA)>
<!ATTLIST receivertel
      %lang.att;
>

<!-- A.3.2.3g Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receivertelextension  - -     (#PCDATA)>
<!ATTLIST receivertelextension
      %lang.att;
>

<!-- A.3.2.3h Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receivertelcountrycode - -    (#PCDATA)>
<!ATTLIST receivertelcountrycode
      %lang.att;
>

<!-- A.3.2.3i Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiverfax           - -     (#PCDATA)>
<!ATTLIST receiverfax
      %lang.att;
>

<!-- A.3.2.3j Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiverfaxextension  - -     (#PCDATA)>
<!ATTLIST receiverfaxextension
      %lang.att;
>

<!-- A.3.2.3k Receiver's address, fax, telephone and E-mail address -->
```

```
<!ELEMENT receiverfaxcountrycode - -    (#PCDATA)>
<!ATTLIST receiverfaxcountrycode
      %lang.att;
>

<!-- A.3.2.3l Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiveremailaddress  - -     (#PCDATA)>
<!ATTLIST receiveremailaddress
      %lang.att;
>

<!-- B.1.1 Patient -->
<!ELEMENT patientinitial        - -     (#PCDATA)>
<!ATTLIST patientinitial
      %lang.att;
>

<!-- B.1.1.1a Patient medical record number(s) and source(s) -->
<!ELEMENT patientgpmedicalrecordnumb - -        (#PCDATA)>
<!ATTLIST patientgpmedicalrecordnumb
      %lang.att;
>

<!-- B.1.1.1b Patient medical record number(s) and source(s) -->
<!ELEMENT patientspecialistrecordnumb - -       (#PCDATA)>
<!ATTLIST patientspecialistrecordnumb
      %lang.att;
>

<!-- B.1.1.1c Patient medical record number(s) and source(s) -->
<!ELEMENT patienthospitalrecordnumb - - (#PCDATA)>
<!ATTLIST patienthospitalrecordnumb
      %lang.att;
>

<!-- B.1.1.1d Patient medical record number(s) and source(s) -->
<!ELEMENT patientinvestigationnumb - -  (#PCDATA)>
<!ATTLIST patientinvestigationnumb
      %lang.att;
>

<!-- B.1.2.1a Date of birth format -->
<!ELEMENT patientbirthdateformat - -    (#PCDATA)>
<!ATTLIST patientbirthdateformat
        %lang.att;
>

<!-- B.1.2.1b Date of birth -->
<!ELEMENT patientbirthdate      - -     (#PCDATA)>
<!ATTLIST patientbirthdate
      %lang.att;
>

<!-- B.1.2.2a Age at time of onset of reaction / event -->
<!ELEMENT patientonsetage       - -     (#PCDATA)>
<!ATTLIST patientonsetage
      %lang.att;
```

```
>

<!-- B.1.2.2b Age at time of onset of reaction / event unit -->
<!ELEMENT patientonsetageunit   - -     (#PCDATA)>
<!ATTLIST patientonsetageunit
        %lang.att;
>

<!-- B.1.2.2.1a Gestation period when reaction / event was observed in the
fetus -->
<!ELEMENT gestationperiod       - -     (#PCDATA)>
<!ATTLIST gestationperiod
      %lang.att;
>

<!-- B.1.2.2.1b Gestation period when reaction / event was observed in the
fetus unit -->
<!ELEMENT gestationperiodunit  - -     (#PCDATA)>
<!ATTLIST gestationperiodunit
        %lang.att;
>

<!-- B.1.2.3 Patient age group -->
<!ELEMENT patientagegroup       - -     (#PCDATA)>
<!ATTLIST patientagegroup
      %lang.att;
>

<!-- B.1.3 Weight (kg) -->
<!ELEMENT patientweight         - -     (#PCDATA)>
<!ATTLIST patientweight
      %lang.att;
>

<!-- B.1.4 Height (cm) -->
<!ELEMENT patientheight         - -     (#PCDATA)>
<!ATTLIST patientheight
      %lang.att;
>

<!-- B.1.5 Sex -->
<!ELEMENT patientsex            - -     (#PCDATA)>
<!ATTLIST patientsex
      %lang.att;
>

<!-- B.1.6a Last menstrual period date format -->
<!ELEMENT lastmenstrualdateformat - - (#PCDATA)>
<!ATTLIST lastmenstrualdateformat
        %lang.att;
>

<!-- B.1.6b Last menstrual period date -->
<!ELEMENT patientlastmenstrualdate - -  (#PCDATA)>
<!ATTLIST patientlastmenstrualdate
      %lang.att;
>
```

```
<!-- B.1.7.1a.2 Structured information -->
<!ELEMENT patientepisodename - - (#PCDATA)>
<!ATTLIST patientepisodename
      %lang.att;
>

<!-- B.1.7.1b Start date format -->
<!ELEMENT patientmedicalstartdateformat - - (#PCDATA)>
<!ATTLIST patientmedicalstartdateformat
       %lang.att;
>

<!-- B.1.7.1c Start date -->
<!ELEMENT patientmedicalstartdate - -   (#PCDATA)>
<!ATTLIST patientmedicalstartdate
      %lang.att;
>

<!-- B.1.7.1d Continuing -->
<!ELEMENT patientmedicalcontinue - -    (#PCDATA)>
<!ATTLIST patientmedicalcontinue
      %lang.att;
>

<!-- B.1.7.1e End date format -->
<!ELEMENT patientmedicalenddateformat - - (#PCDATA)>
<!ATTLIST patientmedicalenddateformat
       %lang.att;
>

<!-- B.1.7.1f End date -->
<!ELEMENT patientmedicalenddate - -     (#PCDATA)>
<!ATTLIST patientmedicalenddate
      %lang.att;
>

<!-- B.1.7.1g Comments -->
<!ELEMENT patientmedicalcomment - -     (#PCDATA)>
<!ATTLIST patientmedicalcomment
      %lang.att;
>

<!-- B.1.7.2 Text for relevant medical history and concurrent conditions -->
<!ELEMENT patientmedicalhistorytext - - (#PCDATA)>
<!ATTLIST patientmedicalhistorytext
      %lang.att;
>

<!-- B.1.8a Name of drug -->
<!ELEMENT patientdrugname       - -     (#PCDATA)>
<!ATTLIST patientdrugname
      %lang.att;
>

<!-- B.1.8b Start date format -->
<!ELEMENT patientdrugstartdateformat - - (#PCDATA)>
```

```
<!ATTLIST patientdrugstartdateformat
        %lang.att;
>

<!-- B.1.8c Start date -->
<!ELEMENT patientdrugstartdate  - -     (#PCDATA)>
<!ATTLIST patientdrugstartdate
      %lang.att;
>

<!-- B.1.8d End date format -->
<!ELEMENT patientdrugenddateformat - -  (#PCDATA)>
<!ATTLIST patientdrugenddateformat
        %lang.att;
>

<!-- B.1.8e End date -->
<!ELEMENT patientdrugenddate    - -     (#PCDATA)>
<!ATTLIST patientdrugenddate
      %lang.att;
>

<!-- B.1.8f.2 Indication -->
<!ELEMENT patientdrugindication - -     (#PCDATA)>
<!ATTLIST patientdrugindication
      %lang.att;
>

<!-- B.1.8g.2 Reaction     -->
<!-- Added in version V2.1 -->
<!ELEMENT patientdrugreaction   - -     (#PCDATA)>
<!ATTLIST patientdrugreaction
      %lang.att;
>
<!-- B.1.9.1a Date of death format -->
<!ELEMENT patientdeathdateformat - -    (#PCDATA)>
<!ATTLIST patientdeathdateformat
        %lang.att;
>

<!-- B.1.9.1b Date of death -->
<!ELEMENT patientdeathdate      - -     (#PCDATA)>
<!ATTLIST patientdeathdate
      %lang.att;
>

<!-- B.1.9.2b Reported cause of death -->
<!ELEMENT patientdeathreport    - -     (#PCDATA)>
<!ATTLIST patientdeathreport
      %lang.att;
>

<!-- B.1.9.3 Was autopsy done? -->
<!ELEMENT patientautopsyyesno   - -     (#PCDATA)>
<!ATTLIST patientautopsyyesno
      %lang.att;
>
```

```
<!-- B.1.9.4b Autopsy-determined causes(s) of death -->
<!ELEMENT patientdetermineautopsy - -   (#PCDATA)>
<!ATTLIST patientdetermineautopsy
      %lang.att;
>

<!-- B.1.10.1 Parent identification -->
<!ELEMENT parentidentification  - -     (#PCDATA)>
<!ATTLIST parentidentification
      %lang.att;
>

<!-- B.1.10.2.1a Date of birth of parent format -->
<!ELEMENT parentbirthdateformat - -     (#PCDATA)>
<!ATTLIST parentbirthdateformat
        %lang.att;
>

<!-- B.1.10.2.1b Date of birth of parent -->
<!ELEMENT parentbirthdate       - -     (#PCDATA)>
<!ATTLIST parentbirthdate
      %lang.att;
>

<!-- B.1.10.2.2a Age of parent -->
<!ELEMENT parentage             - -     (#PCDATA)>
<!ATTLIST parentage
      %lang.att;
>

<!-- B.1.10.2.2b Age of parent unit -->
<!ELEMENT parentageunit         - -     (#PCDATA)>
<!ATTLIST parentageunit
        %lang.att;
>

<!-- B.1.10.3a Last menstrual period format -->
<!ELEMENT parentlastmenstrualdateformat - -   (#PCDATA)>
<!ATTLIST parentlastmenstrualdateformat
        %lang.att;
>

<!-- B.1.10.3b Last menstrual period -->
<!ELEMENT parentlastmenstrualdate - -   (#PCDATA)>
<!ATTLIST parentlastmenstrualdate
      %lang.att;
>

<!-- B.1.10.4 Weight (kg) of parent -->
<!ELEMENT parentweight          - -     (#PCDATA)>
<!ATTLIST parentweight
      %lang.att;
>

<!-- B.1.10.5 Height (cm) of parent -->
<!ELEMENT parentheight          - -     (#PCDATA)>
```

```
<!ATTLIST parentheight
      %lang.att;
>

<!-- B.1.10.6 Sex of parent -->
<!ELEMENT parentsex             - -     (#PCDATA)>
<!ATTLIST parentsex
      %lang.att;
>

<!-- B.1.10.7.1a.2 Structured information -->
<!ELEMENT parentmedicalepisodename - -  (#PCDATA)>
<!ATTLIST parentmedicalepisodename
      %lang.att;
>
<!-- B.1.10.7.1b Start date format -->
<!ELEMENT parentmedicalstartdateformat - - (#PCDATA)>
<!ATTLIST parentmedicalstartdateformat
        %lang.att;
>

<!-- B.1.10.7.1c Start date -->
<!ELEMENT parentmedicalstartdate - -    (#PCDATA)>
<!ATTLIST parentmedicalstartdate
      %lang.att;
>

<!-- B.1.10.7.1d Continuing -->
<!ELEMENT parentmedicalcontinue - -     (#PCDATA)>
<!ATTLIST parentmedicalcontinue
      %lang.att;
>
<!-- B.1.10.7.1e End date format -->
<!ELEMENT parentmedicalenddateformat - - (#PCDATA)>
<!ATTLIST parentmedicalenddateformat
        %lang.att;
>

<!-- B.1.10.7.1f End date -->
<!ELEMENT parentmedicalenddate  - -     (#PCDATA)>
<!ATTLIST parentmedicalenddate
      %lang.att;
>

<!-- B.1.10.7.1g Comments -->
<!ELEMENT parentmedicalcomment  - -     (#PCDATA)>
<!ATTLIST parentmedicalcomment
      %lang.att;
>

<!-- B.1.10.7.2 Text for relevant medical history and concurrent conditions
(not including reaction / event) of parent -->
<!ELEMENT parentmedicalrelevanttext - - (#PCDATA)>
<!ATTLIST parentmedicalrelevanttext
      %lang.att;
>
```

```
<!-- B.1.10.8a Name of drug as -->
<!ELEMENT parentdrugname        - -     (#PCDATA)>
<!ATTLIST parentdrugname
      %lang.att;
>

<!-- B.1.10.8b Start date format -->
<!ELEMENT parentdrugstartdateformat - - (#PCDATA)>
<!ATTLIST parentdrugstartdateformat
       %lang.att;
>

<!-- B.1.10.8c Start date -->
<!ELEMENT parentdrugstartdate   - -     (#PCDATA)>
<!ATTLIST parentdrugstartdate
      %lang.att;
>
<!-- B.1.10.8d End date format -->
<!ELEMENT parentdrugenddateformat - -   (#PCDATA)>
<!ATTLIST parentdrugenddateformat
       %lang.att;
>

<!-- B.1.10.8e End date -->
<!ELEMENT parentdrugenddate     - -     (#PCDATA)>
<!ATTLIST parentdrugenddate
      %lang.att;
>

<!-- B.1.10.8f.2 Indication -->
<!ELEMENT parentdrugindication  - -     (#PCDATA)>
<!ATTLIST parentdrugindication
      %lang.att;
>

<!-- B.1.10.8g.2 Reactions (if any and known) -->
<!ELEMENT parentdrugreaction    - -     (#PCDATA)>
<!ATTLIST parentdrugreaction
      %lang.att;
>

<!-- B.2.i.0 Reaction / event as reported by primary -->
<!ELEMENT primarysourcereaction - -     (#PCDATA)>
<!ATTLIST primarysourcereaction
      %lang.att;
>

<!-- B.2.i.3 Term highlighted by the reporter -->
<!ELEMENT termhighlighted       - -     (#PCDATA)>
<!ATTLIST termhighlighted
      %lang.att;
>

<!-- B.2.i.4a Date of start of reaction / event format -->
<!ELEMENT reactionstartdateformat - -   (#PCDATA)>
<!ATTLIST reactionstartdateformat
       %lang.att;
```

```
>

<!-- B.2.i.4b Date of start of reaction / event -->
<!ELEMENT reactionstartdate     - -     (#PCDATA)>
<!ATTLIST reactionstartdate
      %lang.att;
>
<!-- B.2.i.5a Date of end of reaction / event format -->
<!ELEMENT reactionenddateformat - -     (#PCDATA)>
<!ATTLIST reactionenddateformat
       %lang.att;
>

<!-- B.2.i.5b Date of end of reaction / event -->
<!ELEMENT reactionenddate       - -     (#PCDATA)>
<!ATTLIST reactionenddate
      %lang.att;
>

<!-- B.2.i.6a Duration of reaction / event -->
<!ELEMENT reactionduration      - -     (#PCDATA)>
<!ATTLIST reactionduration
      %lang.att;
>

<!-- B.2.i.6b Duration of reaction / event unit -->
<!ELEMENT reactiondurationunit   - -     (#PCDATA)>
<!ATTLIST reactiondurationunit
       %lang.att;
>

<!-- B.2.i.7.1a Time interval between beginning of suspect drug administration
and start of reaction / event -->
<!ELEMENT reactionfirsttime     - -     (#PCDATA)>
<!ATTLIST reactionfirsttime
      %lang.att;
>

<!-- B.2.i.7.1b Time interval between beginning of suspect drug administration
and start of reaction / event unit -->
<!ELEMENT reactionfirsttimeunit - -     (#PCDATA)>
<!ATTLIST reactionfirsttimeunit
       %lang.att;
>

<!-- B.2.i.7.2a Time interval between last dose and start of reaction / event
-->
<!ELEMENT reactionlasttime      - -     (#PCDATA)>
<!ATTLIST reactionlasttime
      %lang.att;
>

<!-- B.2.i.7.2b Time interval between last dose and start of reaction / event
unit -->
<!ELEMENT reactionlasttimeunit  - -     (#PCDATA)>
<!ATTLIST reactionlasttimeunit
       %lang.att;
```

```
>

<!-- B.2.i.8 Outcome of reaction / event at the time of last observation -->
<!ELEMENT reactionoutcome       - -     (#PCDATA)>
<!ATTLIST reactionoutcome
      %lang.att;
>

<!-- B.3.1a Date format -->
<!ELEMENT testdateformat        - -     (#PCDATA)>
<!ATTLIST testdateformat
        %lang.att;
>

<!-- B.3.1b Date -->
<!ELEMENT testdate              - -     (#PCDATA)>
<!ATTLIST testdate
      %lang.att;
>

<!-- B.3.1c Test -->
<!ELEMENT testname              - -     (#PCDATA)>
<!ATTLIST testname
      %lang.att;
>

<!-- B.3.1d Result -->
<!ELEMENT testresult            - -     (#PCDATA)>
<!ATTLIST testresult
      %lang.att;
>

<!-- B.3.1e Unit -->
<!ELEMENT testunit              - -     (#PCDATA)>
<!ATTLIST testunit
      %lang.att;
>

<!-- B.3.1.1 Normal low range -->
<!ELEMENT lowtestrange          - -     (#PCDATA)>
<!ATTLIST lowtestrange
      %lang.att;
>

<!-- B.3.1.2 Normal high range -->
<!ELEMENT hightestrange         - -     (#PCDATA)>
<!ATTLIST hightestrange
      %lang.att;
>

<!-- B.3.1.3 More information available (Y/N) -->
<!ELEMENT moreinformation       - -     (#PCDATA)>
<!ATTLIST moreinformation
      %lang.att;
>
```

```
<!-- B.3.2 Results of tests and procedures relevant to the investigation of
the patient -->
<!ELEMENT resultstestsprocedures - -    (#PCDATA)>
<!ATTLIST resultstestsprocedures
      %lang.att;
>

<!-- B.4.k.1 Characterization of drug -->
<!ELEMENT drugcharacterization  - -     (#PCDATA)>
<!ATTLIST drugcharacterization
      %lang.att;
>

<!-- B.4.k.2.1 Proprietary medicinal product name -->
<!ELEMENT medicinalproduct      - -     (#PCDATA)>
<!ATTLIST medicinalproduct
      %lang.att;
>

<!-- B.4.k.2.2 Active drug substance names -->
<!ELEMENT activesubstancename   - -     (#PCDATA)>
<!ATTLIST activesubstancename
      %lang.att;
>

<!-- B.4.k.2.3 Identification of the country where the drug was obtained -->
<!ELEMENT obtaindrugcountry     - -     (#PCDATA)>
<!ATTLIST obtaindrugcountry
      %lang.att;
>

<!-- B.4.k.3 Batch / lot number -->
<!ELEMENT drugbatchnumb         - -     (#PCDATA)>
<!ATTLIST drugbatchnumb
      %lang.att;
>

<!-- B.4.k.4.1 Authorization / application number -->
<!ELEMENT drugauthorizationnumb - -     (#PCDATA)>
<!ATTLIST drugauthorizationnumb
      %lang.att;
>

<!-- B.4.k.4.2 Country of authorization / application -->
<!ELEMENT drugauthorizationcountry - -  (#PCDATA)>
<!ATTLIST drugauthorizationcountry
      %lang.att;
>

<!-- B.4.k.4.3 Name of holder/applicant -->
<!ELEMENT drugauthorizationholder - -   (#PCDATA)>
<!ATTLIST drugauthorizationholder
      %lang.att;
>

<!-- B.4.k.5.1 Dose (number) -->
<!ELEMENT drugstructuredosagenumb - -   (#PCDATA)>
```

```
<!ATTLIST drugstructuredosagenumb
      %lang.att;
>

<!-- B.4.k.5.2 Dose (unit) -->
<!ELEMENT drugstructuredosageunit - -   (#PCDATA)>
<!ATTLIST drugstructuredosageunit
      %lang.att;
>

<!-- B.4.k.5.3 Number of separate -->
<!ELEMENT drugseparatedosagenumb - -    (#PCDATA)>
<!ATTLIST drugseparatedosagenumb
      %lang.att;
>

<!-- B.4.k.5.4 Number of units in the interval -->
<!ELEMENT drugintervaldosageunitnumb - -        (#PCDATA)>
<!ATTLIST drugintervaldosageunitnumb
      %lang.att;
>

<!-- B.4.k.5.5 Definition of the interval -->
<!ELEMENT drugintervaldosagedefinition - -      (#PCDATA)>
<!ATTLIST drugintervaldosagedefinition
      %lang.att;
>

<!-- B.4.k.5.6 Cumulative dose to first reaction (number) -->
<!ELEMENT drugcumulativedosagenumb - -  (#PCDATA)>
<!ATTLIST drugcumulativedosagenumb
      %lang.att;
>

<!-- B.4.k.5.7 Cumulative dose to first reaction (unit) -->
<!ELEMENT drugcumulativedosageunit - -  (#PCDATA)>
<!ATTLIST drugcumulativedosageunit
      %lang.att;
>

<!-- B.4.k.6 Dosage text -->
<!ELEMENT drugdosagetext        - -     (#PCDATA)>
<!ATTLIST drugdosagetext
      %lang.att;
>

<!-- B.4.k.7 Pharmaceutical form (Dosage form) -->
<!ELEMENT drugdosageform        - -     (#PCDATA)>
<!ATTLIST drugdosageform
      %lang.att;
>

<!-- B.4.k.8 Route of administration -->
<!ELEMENT drugadministrationroute - -   (#PCDATA)>
<!ATTLIST drugadministrationroute

      %lang.att;
```

```
>

<!-- B.4.k.9 Parent route of administration (in case of a parent child / fetus
report) -->
<!ELEMENT drugparadministration - -     (#PCDATA)>
<!ATTLIST drugparadministration
      %lang.att;
>

<!-- B.4.k.10a Gestation period at time of exposure -->
<!ELEMENT reactiongestationperiod - -   (#PCDATA)>
<!ATTLIST reactiongestationperiod
      %lang.att;
>

<!-- B.4.k.10b Gestation period at time of exposure unit -->
<!ELEMENT reactiongestationperiodunit   - -     (#PCDATA)>
<!ATTLIST reactiongestationperiodunit
        %lang.att;
>

<!-- B.4.k.11b Indication for use in the case -->
<!ELEMENT drugindication        - -     (#PCDATA)>
<!ATTLIST drugindication
      %lang.att;
>

<!-- B.4.k.12a Date of start of drug format -->
<!ELEMENT drugstartdateformat   - -     (#PCDATA)>
<!ATTLIST drugstartdateformat
        %lang.att;
>

<!-- B.4.k.12b Date of start of drug -->
<!ELEMENT drugstartdate         - -     (#PCDATA)>
<!ATTLIST drugstartdate
      %lang.att;
>

<!-- B.4.k.13.1a Time interval between beginning of drug administration and
start of reaction / event -->
<!ELEMENT drugstartperiod     - -     (#PCDATA)>
<!ATTLIST drugstartperiod
      %lang.att;
>

<!-- B.4.k.13.1b Time interval between beginning of drug administration and
start of reaction / event unit -->
<!ELEMENT drugstartperiodunit   - -     (#PCDATA)>
<!ATTLIST drugstartperiodunit
        %lang.att;
>

<!-- B.4.k.13.2a Time interval between last dose of drug and start of reaction
/ event -->
<!ELEMENT druglastperiod      - -     (#PCDATA)>
<!ATTLIST druglastperiod
```

```
      %lang.att;
>

<!-- B.4.k.13.2b Time interval between last dose of drug and start of reaction
/ event unit -->
<!ELEMENT druglastperiodunit    - -     (#PCDATA)>
<!ATTLIST druglastperiodunit
        %lang.att;
>

<!-- B.4.k.14a Date of last administration format -->
<!ELEMENT drugenddateformat     - -     (#PCDATA)>
<!ATTLIST drugenddateformat
        %lang.att;
>

<!-- B.4.k.14b Date of last administration -->
<!ELEMENT drugenddate           - -     (#PCDATA)>
<!ATTLIST drugenddate
      %lang.att;
>

<!-- B.4.k.15a Duration of drug administration unit -->
<!ELEMENT drugtreatmentduration - -     (#PCDATA)>
<!ATTLIST drugtreatmentduration
      %lang.att;
>

<!-- B.4.k.15b Duration of drug administration unit -->
<!ELEMENT drugtreatmentdurationunit - - (#PCDATA)>
<!ATTLIST drugtreatmentdurationunit
        %lang.att;
>

<!-- B.4.k.16 Action(s) taken with drug -->
<!ELEMENT actiondrug            - -     (#PCDATA)>
<!ATTLIST actiondrug
      %lang.att;
>

<!-- B.4.k.17.1 Did reaction recur on readministration? -->
<!ELEMENT drugrecurreadministration - - (#PCDATA)>
<!ATTLIST drugrecurreadministration
      %lang.att;
>

<!-- B.4.k.17.2b If yes, which reaction / event recurred? -->
<!ELEMENT drugrecuraction       - -     (#PCDATA)>
<!ATTLIST drugrecuraction
      %lang.att;
>

<!-- B.4.k.18.1b Reaction assessed -->
<!ELEMENT drugreactionasses     - -     (#PCDATA)>
<!ATTLIST drugreactionasses
      %lang.att;
>
```

```
<!-- B.4.k.18.2 Source of assessment -->
<!ELEMENT drugassessmentsource  - -     (#PCDATA)>
<!ATTLIST drugassessmentsource
      %lang.att;
>

<!-- B.4.k.18.3 Method of assessment -->
<!ELEMENT drugassessmentmethod  - -     (#PCDATA)>
<!ATTLIST drugassessmentmethod
      %lang.att;
>

<!-- B.4.k.18.4 Result -->
<!ELEMENT drugresult            - -     (#PCDATA)>
<!ATTLIST drugresult
      %lang.att;
>

<!-- B.4.k.19 Additional information on drug -->
<!ELEMENT drugadditional        - -     (#PCDATA)>
<!ATTLIST drugadditional
      %lang.att;
>

<!-- B.5.1 Case narrative including clinical course, therapeutic measures,
outcome and additional relevant information -->
<!ELEMENT narrativeincludeclinical - -  (#PCDATA)>
<!ATTLIST narrativeincludeclinical
      %lang.att;
>

<!-- B.5.2 Reporter's comments -->
<!ELEMENT reportercomment       - -     (#PCDATA)>
<!ATTLIST reportercomment
      %lang.att;
>

<!-- B.5.3b Sender's diagnosis / syndrome and / or reclassification of
reaction / event -->
<!ELEMENT senderdiagnosis       - -     (#PCDATA)>
<!ATTLIST senderdiagnosis
      %lang.att;
>

<!-- B.5.4 Sender's comments -->
<!ELEMENT sendercomment         - -     (#PCDATA)>
<!ATTLIST sendercomment
      %lang.att;
>

<!-- B.1.7.1a.1 MedDRA version for medical history -->
<!-- Added in version V2.1                          -->

<!ELEMENT patientepisodenamemeddraversion         - -     (#PCDATA)>
<!ATTLIST patientepisodenamemeddraversion
    %lang.att;
```

```
>

<!-- B.1.9.2a MedDRA version for reported cause(s) of death -->
<!-- Added in version V2.1                                  -->
<!ELEMENT patientdeathreportmeddraversion        - -     (#PCDATA)>
<!ATTLIST patientdeathreportmeddraversion
    %lang.att;
>

<!-- B.1.9.4a MedDRA version for autopsy-determined cause(s) of death -->
<!-- Added in version V2.1                                            -->
<!ELEMENT patientdetermautopsmeddraversion        - -     (#PCDATA)>
<!ATTLIST patientdetermautopsmeddraversion
    %lang.att;
>

<!-- B.1.10.7.1a.1 MedDRA version for parent medical history -->
<!-- Added in version V2.1                                   -->
<!ELEMENT parentmdepisodemeddraversion         - -     (#PCDATA)>
<!ATTLIST parentmdepisodemeddraversion
    %lang.att;
>

<!-- B.1.8f.1 MedDRA version for indication -->
<!-- Added in version V2.1                  -->
<!ELEMENT patientindicationmeddraversion         - -     (#PCDATA)>
<!ATTLIST patientindicationmeddraversion
    %lang.att;
>
<!-- B.1.10.8g.1 MedDRA version for indication -->
<!-- Added in version V2.1                     -->
<!ELEMENT parentdrgreactionmeddraversion         - -     (#PCDATA)>
<!ATTLIST parentdrgreactionmeddraversion
    %lang.att;
>
<!-- B.1.10.8f.1 MedDRA version for indication -->
<!-- Added in version V2.1                     -->
<!ELEMENT parentdrgindicationmeddraversion         - -     (#PCDATA)>
<!ATTLIST parentdrgindicationmeddraversion
    %lang.att;
>

<!-- B.4.k.11a MedDRA version for indication -->
<!-- Added in version V2.1                   -->
<!ELEMENT drugindicationmeddraversion         - -     (#PCDATA)>
<!ATTLIST drugindicationmeddraversion
    %lang.att;
>

<!-- B.1.8g.1 MedDRA version for reaction -->
<!-- Added in version V2.1                -->
<!ELEMENT patientdrgreactionmeddraversion         - -     (#PCDATA)>
<!ATTLIST patientdrgreactionmeddraversion
    %lang.att;
>

<!-- B.4.k.18.1a MedDRA version for reaction assessed -->
```

```
<!-- Added in version V2.1                                -->
<!ELEMENT drugreactionassesmeddraversion         - -     (#PCDATA)>
<!ATTLIST drugreactionassesmeddraversion
    %lang.att;
>


<!-- B.2.i.2a MedDRA version for reaction/event term PT -->
<!-- Added in version V2.1                               -->
<!ELEMENT reactionmeddraversionpt         - -     (#PCDATA)>
<!ATTLIST reactionmeddraversionpt
    %lang.att;
>

<!-- B.2.i.2b MedDRA PT for reaction/event term -->
<!-- Added in version V2.1                      -->
<!ELEMENT reactionmeddrapt         - -     (#PCDATA)>
<!ATTLIST reactionmeddrapt
    %lang.att;
>

<!-- B.2.i.1a MedDRA version for reaction/event term LLT -->
<!-- Added in version V2.1                               -->
<!ELEMENT reactionmeddraversionllt         - -     (#PCDATA)>
<!ATTLIST reactionmeddraversionllt
    %lang.att;
>

<!-- B.2.i.1b MedDRA LLT for reaction/event term -->
<!-- Added in version V2.1                      -->
<!ELEMENT reactionmeddrallt         - -     (#PCDATA)>
<!ATTLIST reactionmeddrallt
    %lang.att;
>

<!-- B.4.k.17.2a MedDRA version for reaction/event recurred -->
<!-- Added in version V2.1                                  -->
<!ELEMENT drugrecuractionmeddraversion        - -     (#PCDATA)>
<!ATTLIST drugrecuractionmeddraversion
    %lang.att;
>


<!-- B.5.3a MedDRA version for senders diagnosis or syndrome -->
<!-- Added in version V2.1                                   -->
<!ELEMENT senderdiagnosismeddraversion         - -     (#PCDATA)>
<!ATTLIST senderdiagnosismeddraversion
    %lang.att;
>


]>
```

A.3 Declaration (DCL) Files for Multi-Language Character Sets

Five SGML declarations are included with the ICH ICSR distribution.

ichicsr-latin1.dcl - This SGML declaration supports the ISO 8859-1 (Latin 1) character set. This character set supports English, and most Western European languages.

```
<!SGML  "ISO 8879:1986"
   --
        SGML Declaration for ICHICSR SGML Applications using ISO Latin 1.
        This Declaration is a virtual copy of the SGML Declaration
      for HyperText Markup Language version 3.2.

      With support for ISO Latin-1 and increased limits
        for tag and literal lengths etc.
   --

   CHARSET
         BASESET  "ISO 646:1983//CHARSET
                   International Reference Version
                   (IRV)//ESC 2/5 4/0"
         DESCSET  0   9   UNUSED
                  9   2   9
                  11  2   UNUSED
                  13  1   13
                  14  18  UNUSED
                  32  95  32
                  127 1   UNUSED
         BASESET  "ISO Registration Number 100//CHARSET
                   ECMA-94 Right Part of
                   Latin Alphabet Nr. 1//ESC 2/13 4/1"
         DESCSET  128  32   UNUSED
                  160  96    32

   CAPACITY   SGMLREF
              TOTALCAP        200000
              GRPCAP          150000
              ENTCAP          150000

   SCOPE    DOCUMENT
   SYNTAX
      SHUNCHAR CONTROLS 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
               17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 127
      BASESET  "ISO 646:1983//CHARSET
                International Reference Version
                (IRV)//ESC 2/5 4/0"
      DESCSET  0 128 0

      FUNCTION
              RE            13
              RS            10
              SPACE         32
              TAB SEPCHAR    9

      NAMING   LCNMSTRT ""
```

```
              UCNMSTRT ""
              LCNMCHAR ".-"
              UCNMCHAR ".-"
              NAMECASE GENERAL YES
                       ENTITY  NO
      DELIM   GENERAL  SGMLREF
              SHORTREF SGMLREF
      NAMES   SGMLREF
      QUANTITY SGMLREF
              ATTSPLEN 65536
              LITLEN   65536
              NAMELEN  32
              PILEN    65536
              TAGLVL   100
              TAGLEN   65536
              GRPGTCNT 150
              GRPCNT   64

   FEATURES
     MINIMIZE
       DATATAG  NO
       OMITTAG  NO
       RANK     NO
       SHORTTAG YES
     LINK
       SIMPLE   NO
       IMPLICIT NO
       EXPLICIT NO
     OTHER
       CONCUR   NO
       SUBDOC   NO
       FORMAL   YES
   APPINFO      NONE
>
```

ichicsr-latin7.dcl - This SGML declaration supports the ISO 8859-7 (Latin 7) character set. This character set supports Greek.

```
<!SGML  "ISO 8879:1986"
   --
        SGML Declaration for ICHICSR SGML Applications using ISO Latin 7.
        This Declaration is a virtual copy of the SGML Declaration
      for HyperText Markup Language version 3.2.

      With support for ISO Latin-7 and increased limits
        for tag and literal lengths etc.
   --

   CHARSET
         BASESET  "ISO 646:1983//CHARSET
                   International Reference Version
                   (IRV)//ESC 2/5 4/0"
         DESCSET  0   9   UNUSED
                  9   2   9
                  11  2   UNUSED
                  13  1   13
                  14  18  UNUSED
                  32  95  32
                  127 1   UNUSED
         BASESET  "ISO Registration Number 100//CHARSET
                   ECMA-94 Right Part of
                   Latin Alphabet Nr. 1//ESC 2/13 4/7"
         DESCSET  128  32   UNUSED
                  160  96    32

   CAPACITY   SGMLREF
              TOTALCAP        200000
              GRPCAP          150000
              ENTCAP          150000

   SCOPE    DOCUMENT
   SYNTAX
      SHUNCHAR CONTROLS 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
               17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 127
      BASESET  "ISO 646:1983//CHARSET
                International Reference Version
                (IRV)//ESC 2/5 4/0"
      DESCSET  0 128 0

      FUNCTION
               RE            13
               RS            10
               SPACE         32
               TAB SEPCHAR    9

      NAMING   LCNMSTRT ""
               UCNMSTRT ""
               LCNMCHAR ".-"
               UCNMCHAR ".-"
               NAMECASE GENERAL YES
                        ENTITY  NO
```

```
      DELIM    GENERAL  SGMLREF
               SHORTREF SGMLREF
      NAMES    SGMLREF
      QUANTITY SGMLREF
               ATTSPLEN 65536
               LITLEN   65536
               NAMELEN  32
               PILEN    65536
               TAGLVL   100
               TAGLEN   65536
               GRPGTCNT 150
               GRPCNT   64

   FEATURES
     MINIMIZE
       DATATAG  NO
       OMITTAG  NO
       RANK     NO
       SHORTTAG YES
     LINK
       SIMPLE   NO
       IMPLICIT NO
       EXPLICIT NO
     OTHER
       CONCUR   NO
       SUBDOC   NO
       FORMAL   YES
   APPINFO      NONE
>
```

ichicsr-sjis.dcl – This SGML declaration supports the Shift JIS character set for encoding Japanese.

```
<!SGML  "ISO 8879:1986"

CHARSET

BASESET
"ISO 646-1983//CHARSET International Reference Version (IRV) //ESC 2/5 4/0"
DESCSET
0   9   UNUSED
9   2   9
11  2   UNUSED
13  1   13
14  18  UNUSED
32  95  32
127 1   UNUSED
BASESET
"ISO Registration Number 87 and 168//CHARSET
JIS X 0208-1990 Japanese Character Set//ESC 2/6 4/0 ESC 2/4 4/2"
DESCSET
128 127 128
255 1   UNUSED

CAPACITY SGMLREF

TOTALCAP  99000000
ATTCAP    1000000
ATTCHCAP   1000000
AVGRPCAP   1000000
ELEMCAP    1000000
ENTCAP    1000000
ENTCHCAP   1000000
GRPCAP    1000000
EXGRPCAP          1000000
EXNMCAP           1000000
NOTCAP            1000000
NOTCHCAP          1000000
MAPCAP            1000000
LKSETCAP          1000000
LKNMCAP           1000000
IDCAP   32000000
IDREFCAP  32000000

SCOPE    DOCUMENT
SYNTAX
SHUNCHAR CONTROLS 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
           18 19 20 21 22 23 24 25 26 27 28 29 30 31 127 255

BASESET
"ISO 646-1983//CHARSET International Reference Version (IRV) //ESC 2/5 4/0"
DESCSET
0   9   UNUSED
9   2   9
11  2   UNUSED
13  1   13
14  18  UNUSED
```

```
32  95  32
127 1   UNUSED
BASESET
"ISO Registration Number 87 and 168//CHARSET
JIS X 0208-1990 Japanese Character Set//ESC 2/6 4/0 ESC 2/4 4/2"
DESCSET
128 127 128
255 1   UNUSED

FUNCTION RE 13
     RS 10
     SPACE  32
     TAB    SEPCHAR 9

NAMING   LCNMSTRT
"&#128;&#129;&#130;&#131;&#132;&#133;&#134;&#135;&#136;&#137;&#138;&#139;&#140
;&#141;&#142;&#143;&#144;&#145;&#146;&#147;&#148;&#149;&#150;&#151;&#152;&#153
;&#154;&#155;&#156;&#157;&#158;&#159; &#161;&#162;&#163;&#164;&#165;&#166
;&#167;&#168;&#169;&#170;&#171;&#172;&#173;&#174;&#175;&#176;&#177;&#178;&#179
;&#180;&#181;&#182;&#183;&#184;&#185;&#186;&#187;&#188;&#189;&#190;&#191;&#192
;&#193;&#194;&#195;&#196;&#197;&#198;&#199;&#200;&#201;&#202;&#203;&#204;&#205
;&#206;&#207;&#208;&#209;&#210;&#211;&#212;&#213;&#214;&#215;&#216;&#217;&#218
;&#219;&#220;&#221;&#222;&#223;&#224;&#225;&#226;&#227;&#228;&#229;&#230;&#231
;&#232;&#233;&#234;&#235;&#236;&#237;&#238;&#239;&#240;&#241;&#242;&#243;&#244
;&#245;&#246;&#247;&#248;&#249;&#250;&#251;&#252;&#253;&#254;"
            UCNMSTRT
"&#128;&#129;&#130;&#131;&#132;&#133;&#134;&#135;&#136;&#137;&#138;&#139;&#140
;&#141;&#142;&#143;&#144;&#145;&#146;&#147;&#148;&#149;&#150;&#151;&#152;&#153
;&#154;&#155;&#156;&#157;&#158;&#159; &#161;&#162;&#163;&#164;&#165;&#166
;&#167;&#168;&#169;&#170;&#171;&#172;&#173;&#174;&#175;&#176;&#177;&#178;&#179
;&#180;&#181;&#182;&#183;&#184;&#185;&#186;&#187;&#188;&#189;&#190;&#191;&#192
;&#193;&#194;&#195;&#196;&#197;&#198;&#199;&#200;&#201;&#202;&#203;&#204;&#205
;&#206;&#207;&#208;&#209;&#210;&#211;&#212;&#213;&#214;&#215;&#216;&#217;&#218
;&#219;&#220;&#221;&#222;&#223;&#224;&#225;&#226;&#227;&#228;&#229;&#230;&#231
;&#232;&#233;&#234;&#235;&#236;&#237;&#238;&#239;&#240;&#241;&#242;&#243;&#244
;&#245;&#246;&#247;&#248;&#249;&#250;&#251;&#252;&#253;&#254;"
--
NAMING   LCNMSTRT ""
     UCNMSTRT ""
--
          LCNMCHAR "-."
          UCNMCHAR "-."
          NAMECASE GENERAL YES
               ENTITY   NO

    DELIM    GENERAL  SGMLREF
             SHORTREF SGMLREF
    NAMES    SGMLREF
    QUANTITY   SGMLREF    LITLEN     4096
               GRPCNT       200
               NAMELEN      32
               ATTCNT       160

FEATURES
    MINIMIZE DATATAG NO OMITTAG  NO RANK     NO SHORTTAG YES
    LINK     SIMPLE  NO IMPLICIT NO EXPLICIT NO
    OTHER    CONCUR  NO SUBDOC   NO FORMAL   YES
```

```
APPINFO NONE
>
```

ichicsr-utf8.dcl – This SGML declaration supports the ISO 10646 (UNICODE) UTF-8 character set. This character set supports almost all of the worlds currently written languages.

```
<!SGML  "ISO 8879:1986 (WWW)"
    --
        SGML Declaration for ICH SGML Applications using Unicode.
        This Declaration is a virtual copy of the SGML Declaration
      for HyperText Markup Language version 4.0 as modified by
      James Clark to work with SP.

        With support for the first 17 planes of ISO 10646 and
        increased limits for tag and literal lengths etc.

        Modified by jjc to work around SP's 16-bit character limit.
        Modified by jjc to support hex character references.
    --

    CHARSET
          BASESET  "ISO Registration Number 177//CHARSET
                    ISO/IEC 10646-1:1993 UCS-4 with
                    implementation level 3//ESC 2/5 2/15 4/6"
         DESCSET 0       9       UNUSED
                 9       2       9
                 11      2       UNUSED
                 13      1       13
                 14      18      UNUSED
                 32      95      32
                 127     1       UNUSED
                 128     32      UNUSED
              -- jjc: changed the rest of the DESCSET.
                 Note that surrogates are not declared UNUSED;
                 this allows non-BMP characters to be parsed. --
                 160     65376   160
              -- 160     55136   160
                 55296   2048    UNUSED
                 57344   1056768 57344 --

CAPACITY        SGMLREF
                TOTALCAP        150000
                GRPCAP          150000
                ENTCAP          150000

SCOPE    DOCUMENT
SYNTAX
         SHUNCHAR CONTROLS 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
           17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 127
         BASESET  "ISO 646IRV:1991//CHARSET
                   International Reference Version
                   (IRV)//ESC 2/8 4/2"
         DESCSET  0 128 0

         FUNCTION
                  RE            13
                  RS            10
                  SPACE         32
                  TAB SEPCHAR    9
```

```
          NAMING   LCNMSTRT ""
                   UCNMSTRT ""
                   LCNMCHAR ".-_:"
                   UCNMCHAR ".-_:"
                   NAMECASE GENERAL YES
                            ENTITY  NO
          DELIM    GENERAL  SGMLREF
                            HCRO "&#38;#X" -- added by jjc --
                   SHORTREF SGMLREF
          NAMES    SGMLREF
          QUANTITY SGMLREF
                   ATTCNT   60      -- increased --
                   ATTSPLEN 65536   -- These are the largest values --
                   LITLEN   65536   -- permitted in the declaration --
                   NAMELEN  32      -- Avoid fixed limits in actual --
                   PILEN    65536   -- implementations of HTML UA's --
                   TAGLVL   100
                   TAGLEN   65536
                   GRPGTCNT 150
                   GRPCNT   64

FEATURES
  MINIMIZE
    DATATAG  NO
    OMITTAG  NO
    RANK     NO
    SHORTTAG YES
  LINK
    SIMPLE   NO
    IMPLICIT NO
    EXPLICIT NO
  OTHER
    CONCUR   NO
    SUBDOC   NO
    FORMAL   YES
  APPINFO NONE
>
```

ichicsr-mult.dcl – Running in direct contradiction to what has been said up to this point, this SGML declaration will support all of the currently defined ICHICSR languages, and it doesn't require the use of UNICODE. It is however a "hack" that relies on a fortuitous characteristic of the languages currently being used within the ICHICSR SGML application**.**

This hack works because the character set documented within an SGML declaration is for the benefit of both the SGML parser, and the programmer who implements the SGML application. The programmer needs detailed knowledge of **all** the characters being used to correctly code an application. The parser only really needs to about **some** of the characters. In particular it needs to know which characters signify an SGML event. For instance that the "<" character starts an SGML open tag , and the "</" character sequence starts an SGML close tag. All told, the parser needs to know very little. Because of the particular combination of character sets being used within the ICHICSR application, an SGML declaration can be defined that tells the parser just what it needs to know and still work across all of the different character sets. The catch is that this SGML declaration doesn't tell the programmer all that she or he needs to know to correctly code the rest of the application. If this declaration is used, the programmer will have to get this detailed information from another source.

```
<!SGML  "ISO 8879:1986"
   --
        SGML Declaration for ICHICSR SGML Applications that will
      allow an SGML parser to parse SJIS, and ISO Latin 1-9 without an error.

      Note: This is not strictly speaking a correct SGML declaration, as
      it does not correctly document the character set being used.
      Instead, it simply ignores all characters except for the ones that are
      imporant to the SGML parser.  These characters are expected to be found
      at the standard ASCII code points.

      With support for increased limits for tag and literal lengths etc.
   --

   CHARSET
         BASESET  "ISO 646:1983//CHARSET
                   International Reference Version
                   (IRV)//ESC 2/5 4/0"
         DESCSET  0   9   UNUSED
                  9   2   9
                  11  2   UNUSED
                  13  1   13
                  14  18  UNUSED
                  32  95  32
                  127 1   UNUSED
         BASESET  "ISO Registration Number 100//CHARSET
                   ECMA-94 Right Part of
                   Latin Alphabet Nr. 1//ESC 2/13 4/1"
         DESCSET  128  127  128
                  255  1    UNUSED

   CAPACITY   SGMLREF
              TOTALCAP        200000
              GRPCAP          150000
              ENTCAP          150000

   SCOPE    DOCUMENT
   SYNTAX
      SHUNCHAR CONTROLS 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
```

```
            17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 127
    BASESET  "ISO 646:1983//CHARSET
              International Reference Version
              (IRV)//ESC 2/5 4/0"
    DESCSET  0 128 0

    FUNCTION
            RE            13
            RS            10
            SPACE         32
            TAB SEPCHAR    9

    NAMING   LCNMSTRT ""
             UCNMSTRT ""
             LCNMCHAR ".-"
             UCNMCHAR ".-"
             NAMECASE GENERAL YES
                      ENTITY  NO
    DELIM    GENERAL  SGMLREF
             SHORTREF SGMLREF
    NAMES    SGMLREF
    QUANTITY SGMLREF
             ATTSPLEN 65536
             LITLEN   65536
             NAMELEN  32
             PILEN    65536
             TAGLVL   100
             TAGLEN   65536
             GRPGTCNT 150
             GRPCNT   64

  FEATURES
    MINIMIZE
      DATATAG  NO
      OMITTAG  NO
      RANK     NO
      SHORTTAG YES
    LINK
      SIMPLE   NO
      IMPLICIT NO
      EXPLICIT NO
    OTHER
      CONCUR   NO
      SUBDOC   NO
      FORMAL   YES
  APPINFO      NONE
>
```

A.4 ICH M2 Numeric Codes for Unit List (E2BM Attachment 1)

Please use the ICH M2 numeric codes to populate fields that require the E2BM unit list (Attachment 1).

Unit List		**ICH-M2 Numeric Codes**
Mass		
kg	kilogram(s)	001
G	gram(s)	002
Mg	milligram(s)	003
µg	microgram(s)	004
ng	nanogram(s)	005
pg	picogram(s)	006
mg/kg	milligram(s)/kilogram	007
µg/kg	microgram(s)/kilogram	008
mg/m^2	milligram(s)/sq. meter	009
$\mu g/ m^2$	microgram(s)/ sq. meter	010
Volume		
l	litre(s)	011
ml	millilitre(s)	012
µl	microlitre(s)	013
Radioactivity		
Bq	becquerel(s)	014
GBq	gigabecquerel(s)	015
MBq	megabecquerel(s)	016
Kbq	kilobecquerel(s)	017
Ci	curie(s)	018
MCi	millicurie(s)	019
µCi	microcurie(s)	020
NCi	nanocurie(s)	021
Other		
Mol	mole(s)	022
Mmol	millimole(s)	023
µmol	micromole(s)	024
Iu	international unit(s)	025
Kiu	iu(1000s)	026
Miu	iu(1,000,000s)	027
iu/kg	iu/kilogram	028
Meq	milliequivalent(s)	029
%	percent	030

Gtt drop(s)	031
DF dosage form	032
Definition of Interval List	**Proposed ICH-M2 Codes**
Seconds	807
Minutes	806
Hours	805
Days	804
Weeks	803
Months	802
Years	801
Trimester	810
Cyclical	811
As Necessary	812
Total	813

A.5 Routes of Administration (E2BM Attachment 2)

Please use the ICH M2 numeric codes to populate fields that require the E2BM routes of administration (Attachment 2).

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

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

A.6 ICH ICSR Acknowledgment Message

The ICSR Acknowledgment Message is being provided to help Industry and Regulators verify the usability and compliance of the transmitted data as per ICH recommendations. The ICSR Acknowledgment Message is comprised of two sections, each occurring once; the ICSR message header section and the acknowledgment section. The acknowledgment section is comprised of two portions, a message acknowledgment portion which occurs once, and a report acknowledgment portion which can occur one time, many times, or not at all. The acknowledgment sections can be used to communicate to the sender the results of the validation of the transmitted data set. Listed below are the details of the specification:

Data Element	Title	Description	DTD Descriptor	Field Length	Field Value	Required
M.1	ICSR Message Header	Header/Entity	ichicsrmessageheader			
M.1.1	Message Type	Type of Information Being Transmitted	messagetype	16 AN	ichicsrack	Yes
M.1.2	Message Format Version	Version Number of Message Format	messageformatversion	3AN		Yes
M.1.3	Message Format Release	Release number of the Message Format	messageformatrelease	3AN		Yes
M.1.4	Message Number	Message Number	messagenumb	100AN		Yes
M.1.5	Message Sender Identifier	Message Sender Identifier	messagesenderidentifier	60AN		Yes
M.1.6	Message Receiver Identifier	Message Receiver Identifier	messagereceiveridentifier	60AN		Yes
M.1.7a	Message Date	Message Date Format	messagedateformat	3N	204 – Format CCYYMMDDHHMMSS	Yes
M.1.7b	Message Date		messagedate	14N	CCYYMMDDHHMMSS	Yes
A.1	Message Acknowledgment	Header/Entity	messageacknowledgment			
A.1.1	ICSR Message Number	Message Number	icsrmessagenumb	100AN		Yes
A.1.2	Local Message Number	Local Message Number	localmessagenumb	100AN	Locally Assigned	
A.1.3	ICSR Message Sender ID	Message Sender Identifier	icsrmessagesenderidentifier	60AN		Yes
A.1.4	ICSR Message Receiver ID	Message Receiver Identifier	icsrmessagereceiveridentifier	60AN		Yes
A.1.5a	ICSR Message Date	Message Date Format	icsrmessagedateformat	3N	204 – Format CCYYMMDDHHMMSS	Yes
A.1.5b	ICSR Message Date		icsrmessagedate	14N	CCYYMMDDHHMMSS	Yes

A.1.6	Transmission Acknowledgment Code	Response from Agency on Transmission	transmissionacknowledgmentcode	2N	01= All Reports loaded into database 02 = ICSR Error, not all reports loaded into the database, check section B 03= SGML parsing error, no data extracted	Yes
A.1.7	Parsing Error Message	Description of the SGML Parsing Error Encountered	parsingerrormessage	250 AN		
B.1.	Report Acknowledgment	Header/Entity	reportacknowledgment			
B.1.1	Safety Report ID (E2BM- A.1.0.1)	Safety Report Identifier	safetyreportid	100AN		
B.1.2	Safety Report Version Number		safetyreportversion	2AN		
B.1.3	Local Report Number		localreportnumber	100AN		
B.1.4	Regulatory authority's case report number (E2BM- A.1.10.1)		authoritynumber	100AN		
B.1.5	Other Sender's case report number (E2BM- A.1.10.2)		companynumber	100AN		
B.1.7a	Date of receipt of the most recent information (E2BM- A.1.7)	Receipt Date Format	receiptdateformat	3N	102 – Format CCYYMMDD	
B.1.7b	Date of receipt of the most recent information (E2BM- A.1.7)		receiptdate	8N	CCYYMMDD	
B.1.8	Acknowledgment Code for a Report	Report Level Acknowledgment (If there is an error code, re-send only the specified report.)	reportacknowledgmentcode	2N	01=Report Loaded Successfully 02=Report Not Loaded	Yes
B.1.9	Error Message or Comment	Description of the Specific Error or Errors Encountered	errormessagecomment	250AN		

Note: The double line border depicts a repeatable block

Element Descriptions for Acknowledgment of ICSRs

M.1 ICSR Message Header
This is the standard ICH M2 message header, similar to the message header in the ICH ICSR DTD. This section specifies the message type, such as ICSR Acknowledgments, version, and release number of the DTD. This message header section assumes the establishment of an EDI trading partnership agreement that will help drive the designation of the message identification number, sender ID, receiver ID, message date, and the acknowledgment for the submission of the SGML file containing multiple ICSRs.

M.1.1 Message type
The message type contains information on the type of information being transmitted. It is specified in ESTRI recommendation 5.3. When creating an ICSR Acknowledgment SGML message, the value of this field should be "ichicsrack".

M.1.2 Message Format Version
The message format version contains the version number of the DTD and it is specified in ESTRI recommendation 5.3. The value of the version number can be obtained from the documentation section of the ICSR Acknowledgment Message DTD.

M.1.3 Message Format Release
The message format release contains the release number of the message format version number of the DTD and it is specified in ESTRI recommendation 5.3. The value of the release number can be obtained from the documentation section of the ICSR Acknowledgment Message DTD.

M.1.4 Message Number, sender defined message number (unique to the sender)
The message number is a unique tracking number assigned to a specific acknowledgment message file by the sender of the acknowledgment. This message number is unique to the sender.

M.1.5 Message Sender Identifier
This field identifies the sender of the acknowledgment, e.g. receiver of the ICH ICSR message, ICSR Attribute List A.3.2.2a.

M.1.6 Message Receiver Identifier
This field identifies the receiver of the acknowledgment, e.g. sender of the ICH ICSR message, ICSR Attribute List A.3.1.2.

M.1.7a and b Message Date and Format
The message date is the date on which the acknowledgment message was initiated.

A.1 Message Acknowledgment
This is a section header that specifies the ICH ICSR message that is being acknowledged. This section also assumes the establishment of an EDI trading partnership agreement that will help drive the designation of the message identification number, local message number, sender ID, receiver ID, message date, and the acknowledgment for the submission of the SGML file containing multiple ICSRs.

A.1.1 ICSR Message Number, Sender defined message number (unique to the sender)
The ICSR message number is a unique tracking number assigned to a specific ICH ICSR message file by the sender. This ICSR message number is unique to the sender of the ICH ICSR message.

A.1.2 Local Message Number
The local message number is a value assigned to the ICH ICSR message by the receiving organization. The length, data type, and value are determined by the receiving organization.

A.1.3 ICSR Message Sender Identifier
This field identifies the sender of the ICSR reports, e.g. ICSR Attribute List A.3.1.2, sender of case safety report forms.

A.1.4 ICSR Message Receiver Identifier
This field identifies the receiver of the ICSR reports, e.g. ICSR Attribute List A.3.2.2a, receiver of case safety report forms.

A.1.5a and b ICSR Message Date and Format
The ICSR message date is the date on which the ICH ICSR message was initiated.

A.1.6 Transmission Acknowledgment Code
The transmission acknowledgment field is a 2AN field that will inform the sender of the ICH ICSR message to either re-send the complete transmission or await acknowledgment on individual reports.

Values:
01 = All Reports loaded into database
02 = ICSR Error, not all reports loaded into the database, check section B
03 = SGML parsing error, no data extracted

A.1.7 Parsing Error Message
The Parsing Error Message field is a 250 character field that can be used to briefly describe the types of SGML errors detected while parsing the file. This field is used when the value of A.1.6 is 03.

B.1. Report Acknowledgment
This is a section header for acknowledging each report included in the ICH ICSR message file. This section specifies the required elements to acknowledge the data format, data length, and data type, to ensure the information is loadable into the receiver's database. This section will be a repeatable section for each report that will be acknowledged. This section will be included in the acknowledgment message if the value for A.1.6 above is "02". In other words, there can be 0 to many occurrences of this section.

B.1.1 Safety Report ID
The safety report identifier is the number assigned by the sender to identify each ICSR.

B.1.2 Safety Report Version Number
The safety report version is a number assigned by the sender of the ICSR to differentiate the different versions of an ICSR.

B.1.3 Local Report Number
The local report number is a value assigned to each ICSR by the receiving organization of the ICH ICSR message.

B.1.4 Regulatory Authority's Case Report Number (E2BM: A.1.10.1).
B.1.4 is a unique identifier that is equivalent to the national regulatory authority's case report number. It will be the same value assigned to the E2BM field A.1.10.1.

B.1.5 Other Sender's case report number (E2BM: A.1.10.2)

B.1.5 is a company unique identifier assigned by a company and is the same as the value assigned to E2BM field A.1.10.2. As the E2BM Step 4 document version 4.4 specifies, companies should ensure a single international number to facilitate the unique identification of a report that may have been sent to many places and subject to multiple re-transmissions.

B.1.7 a and b Date of Receipt of the Most Recent Information (E2BM: A.1.7)
This field must be used to record the date of the most recent information of the case. It is the same as the value assigned to the E2BM field A.1.7.

B.1.8 Acknowledgment Code for a Report
This field will be used to indicate if a report was successfully loaded into the application data base or if it failed the loading process. If there is an error, the application may indicate the nature of the error in the text field B.1.9. The field B.1.8 is 2AN and will contain one of following values:

01 = Report Loaded Successfully
02 = Report Not Loaded

B.1.9 Error Message or Comment
This field is a 250 character field that can be used to briefly describe the error message and the relevant field to help the sender of the ICSR correct the problem. This field is not intended to contain a complete list of errors found with a report. The extent of the error reporting is application dependent. As a minimum the application should describe the first error encountered when trying to load a report into the database.

A.7 ICH ICSR Acknowledgment DTD

```
<!DOCTYPE ichicsrack [
<!-- PUBLIC "-//ICHM2//DTD ICH ICSR Acknowledgment Vers. 1.1//EN"  "ich-icsrack-v1.1.dtd"  -->

<!--
 Individual Case Safety Report Acknowledgment Document Type Definition

 The DTD issued by the ICH M2 group and is public domain in nature.

        No one can claim copyright on this DTD.
        No commercial distribution is allowed.

 The ICH is not responsible for any damage or financial loss resulting from
 use of this DTD. This version is tentative in nature and changes are expected.
 This DTD is subject to the ICH M2 change control procedures.

 Version 1.0, Release 1.0
  Version 1.1, Release 1.0, Date to be decided
-->

<!-- TECHNICAL NOTE

                    ICH ICSR SGML Declaration

To correctly parse an ICH ICSR SGML message requires the selection of the
correct SGML declaration, along with this DTD, and the ICH ICSR SGML instance.
This technical note provides guidance on which of several SGML declarations
included with the ICH ICSR application to select based on the language and
character set used within the ICH ICSR SGML instance.  The method by which
an SGML parser is told to use a specific declaration is parser specific.
The three most common methods are:

1. Tell the parser via the command line which declaration to use.

2. Tell the parser via a specific environment variable which declaration
to use.

3. If the parser supports SGML Open catalogs, within the catalog file
is a command that can tell the parser which declaration to use.  SGML
catalog files are an industry standard way to tell a parser how to find
all of the pieces (declaration, DTD, SGML document instance) needed to
successfully parse.

To cover all of the languages necessary to support the ICH ICSR application,
ISO 10646 (UNICODE) would have to be used.  If this were the case, then only
one SGML declaration would be needed to support all ICH ICSR languages.
Because UNICODE support is not available in all popular computer application
programs, the ICH M2 EWG has recommended that a variety of character sets be
used at this time, instead of a single UNICODE character encoding.  For each
of these different character encodings a different SGML declaration needs to
be generated and used.

Five SGML declarations are included with the ICH ICSR distribution.  They
are described briefly below.
```

ich-icsr-latin1.dcl - This SGML declaration supports the ISO 8859-1 (Latin 1) character set. This character set supports English, and most Western European languages.

ich-icsr-latin7.dcl - This SGML declaration supports the ISO 8859-7 (Latin 7) character set. This character set supports Greek.

ich-icsr-sjis.dcl - This SGML declaration supports the Shift JIS character set for encoding Japanese.

ich-icsr-utf8.dcl - This SGML declaration supports the ISO 10646 (UNICODE) UTF-8 character set. This character set supports almost all of the worlds currently written languages.

ich-icsr-mult.dcl - This SGML declaration will support all of the currently defined ICHICSR languages, and it doesn't require the use of UNICODE. It is however a "hack" that relies on a fortuitous characteristic of the languages currently being used within the ICH ICSR SGML application.

This hack works because the character set documented within an SGML declaration is for the benefit of both the SGML parser, and the programmer who implements the SGML application. The programmer needs detailed knowledge of all the characters being used to correctly code an application. The parser only really needs to about some of the characters. In particular it needs to know which characters signify an SGML event. For instance that the "<" character starts an SGML open tag, and the "</" character sequence starts an SGML close tag. All told, the parser needs to know very little. Because of the particular combination of character sets being used within the ICH ICSR application, an SGML declaration can be defined that tells the parser just what it needs to know and still work across all of the different character sets. The catch is that this SGML declaration doesn't tell the programmer all that she or he needs to know to correctly code the rest of the application. If this declaration is used, the programmer will have to get this detailed information from another source.

-->

```
<!-- ================================================================== -->
<!-- Entities                                                           -->
<!-- ================================================================== -->

<!-- Use the lang attribute to indicate the language of an              --
  -- elements content via an ISO 639 language Code.                     -->

<!ENTITY % lang.att "lang CDATA #IMPLIED">

<!-- Standard Character Entities to escape SGML special characters.     --
  -- When "<", ">", and "&" occur in text, they should be replaced      --
  -- by "&lt;", "&gt;", and "&amp;" respectfully.                       -->

<!-- Less Than "<" -->
<!ENTITY lt     "&#38;#60;">

<!-- Greater Than ">" -->
<!ENTITY gt     "&#62;">
```

```
<!-- Ampersand "&" -->
<!ENTITY amp    "&#38;#38;">

<!-- ================================================================== -->
<!-- Elements and Attributes                                            -->
<!-- ================================================================== -->

<!ELEMENT ichicsrack              - -
                  (ichicsrmessageheader      ,
                  acknowledgment)>
<!ATTLIST ichicsrack
        lang      CDATA #REQUIRED
>

<!-- M.1 ICH ICSR Message Header Information -->

<!ELEMENT ichicsrmessageheader        - -
        (messagetype                      ,
        messageformatversion              ,
        messageformatrelease              ,
        messagenumb                       ,
        messagesenderidentifier       ,
        messagereceiveridentifier  ,
     messagedateformat            ,
        messagedate)>
<!ATTLIST ichicsrmessageheader
        %lang.att;
>

<!-- M.1.1 Message Type -->
<!ELEMENT messagetype                 - - (#PCDATA) >
<!ATTLIST messagetype
        %lang.att;
>

<!-- M.1.2 Message Format Version -->
<!ELEMENT messageformatversion        - - (#PCDATA) >
<!ATTLIST messageformatversion
        %lang.att;
>

<!-- M.1.3 Message Format Release -->
<!ELEMENT messageformatrelease        - - (#PCDATA) >
<!ATTLIST messageformatrelease
        %lang.att;
>

<!-- M.1.4 Message Number -->
<!ELEMENT messagenumb                 - - (#PCDATA) >
<!ATTLIST messagenumb
        %lang.att;
>

<!-- M.1.5 Message Sender Identifier -->
<!ELEMENT messagesenderidentifier - - (#PCDATA) >
<!ATTLIST messagesenderidentifier
```

```
        %lang.att;
>

<!-- M.1.6 Message Receiver Identifier -->
<!ELEMENT messagereceiveridentifier - - (#PCDATA) >
<!ATTLIST messagereceiveridentifier
        %lang.att;
>

<!-- M.1.7a Message Date Format -->
<!ELEMENT messagedateformat  - -  (#PCDATA)>
<!ATTLIST messagedateformat
    %lang.att;
>

<!-- M.1.7b Message Date -->
<!ELEMENT messagedate        - -  (#PCDATA) >
<!ATTLIST messagedate
        %lang.att;
>

<!-- A.1 ICSR Acknowledgment Message-->
<!ELEMENT acknowledgment              - -
        (messageacknowledgment        ,
        reportacknowledgment*)>
<!ATTLIST acknowledgment
        %lang.att;
>

<!-- A.1 Message Acknowledgment -->
<!ELEMENT messageacknowledgment       - -
        (icsrmessagenumb              ,
    localmessagenumb?         ,
        icsrmessagesenderidentifier   ,
        icsrmessagereceiveridentifier ,
    icsrmessagedateformat     ,
        icsrmessagedate               ,
        transmissionacknowledgmentcode ,
        parsingerrormessage?)>
<!ATTLIST messageacknowledgment
        %lang.att;
>

<!-- A.1.1 ICSR Message Number -->
<!ELEMENT icsrmessagenumb     - -  (#PCDATA)>
<!ATTLIST icsrmessagenumb
        %lang.att;
>

<!-- A.1.2 Local Message Number -->
<!ELEMENT localmessagenumb    - -  (#PCDATA)>
<!ATTLIST localmessagenumb
    %lang.att;
>

<!-- A.1.3 ICSR Message Sender Identifier -->
```

```
<!ELEMENT icsrmessagesenderidentifier - -          (#PCDATA)>
<!ATTLIST icsrmessagesenderidentifier
        %lang.att;
>

<!-- A.1.4 ICSR Message Receiver Identifier -->
<!ELEMENT icsrmessagereceiveridentifier - -        (#PCDATA)>
<!ATTLIST icsrmessagereceiveridentifier
        %lang.att;
>

<!-- A.1.5a ICSR Message Date Format -->
<!ELEMENT icsrmessagedateformat    - -    (#PCDATA)>
<!ATTLIST icsrmessagedateformat
      %lang.att;
>

<!-- A.1.5b ICSR Message Date -->
<!ELEMENT icsrmessagedate      - -        (#PCDATA)>
<!ATTLIST icsrmessagedate
        %lang.att;
>

<!-- A.1.6 Transmission Acknowledgment -->
<!ELEMENT transmissionacknowledgmentcode - -  (#PCDATA)>
<!ATTLIST transmissionacknowledgmentcode
        %lang.att;
>

<!-- A.1.7 Parsing Error Message -->
<!ELEMENT parsingerrormessage - -        (#PCDATA)>
<!ATTLIST parsingerrormessage
        %lang.att;
>

<!-- B.1 Report Acknowledgment -->
<!ELEMENT reportacknowledgment          - -
        (safetyreportid             ,
      safetyreportversion?          ,
      localreportnumb?              ,
        authoritynumb?              ,
        companynumb?                ,
            receiptdateformat?      ,
        receiptdate?                ,
        reportacknowledgmentcode    ,
        errormessagecomment?)>
<!ATTLIST reportacknowledgment
        %lang.att;
>

<!-- B.1.1 Safety Report Identification -->
<!ELEMENT safetyreportid        - -        (#PCDATA)>
<!ATTLIST safetyreportid
        %lang.att;
>
```

```
<!-- B.1.2 Safety Report Version -->
<!ELEMENT safetyreportversion  - -  (#PCDATA)>
<!ATTLIST safetyreportversion
      %lang.att;
>

<!-- B.1.3 Local Report Number -->
<!ELEMENT localreportnumb  - -  (#PCDATA)>
<!ATTLIST localreportnumb
      %lang.att;
>

<!-- B.1.4  Regulatory authority's case report number (E2BM - A.1.10.1)-->
<!ELEMENT authoritynumb  - -  (#PCDATA)>
<!ATTLIST authoritynumb
      %lang.att;
>

<!-- B.1.5 Other Sender's case report number (E2BM - A.1.10.2) -->
<!ELEMENT companynumb  - -  (#PCDATA)>
<!ATTLIST companynumb
      %lang.att;
>


<!-- B.1.7a Receipt Date Format -->
<!ELEMENT receiptdateformat  - -  (#PCDATA)>
<!ATTLIST receiptdateformat
      %lang.att;
>

<!-- B.1.7b Date of receipt of the most recent information (E2BM - A.1.7) -->
<!ELEMENT receiptdate  - -  (#PCDATA)>
<!ATTLIST receiptdate
      %lang.att;
>

<!-- B.1.8 Acknowledgment Code for a report -->
<!ELEMENT reportacknowledgmentcode  - -  (#PCDATA)>
<!ATTLIST reportacknowledgmentcode
      %lang.att;
>

<!-- B.1.9 Error Message or Comment -->
<!ELEMENT errormessagecomment  - -  (#PCDATA)>
<!ATTLIST errormessagecomment
      %lang.att;
>
]>
```

A.8 Sample SGML Data File for the ICH ICSR Acknowledgment DTD

```
<ichicsrack lang="en">
 <ichicsrmessageheader>
  <messagetype>ichicsrack</messagetype>
  <messageformatversion>1.0</messageformatversion>
  <messageformatrelease>1.0</messageformatrelease>
  <messagenumb>00000010016328</messagenumb>
  <messagesenderidentifier>FDA</messagesenderidentifier>
  <messagereceiveridentifier>pharmaceutical
company</messagereceiveridentifier>
  <messagedateformat>204</messagedateformat>
  <messagedate>19980716</messagedate>
 </ichicsrmessageheader>
 <acknowledgment>
  <messageacknowledgment>
   <icsrmessagenumb>100052365478900</icsrmessagenumb>
   <localmessagenumb></localmessagenumb>
   <icsrmessagesenderidentifier>pharmaceutical
company</icsrmessagesenderidentifier>
   <icsrmessagereceiveridentifier>FDA</icsrmessagereceiveridentifier>
   <icsrmessagedateformat>102</icsrmessagedateformat>
   <icsrmessagedate>19980715</icsrmessagedate>
   <transmissionacknowledgmentcode>02</transmissionacknowledgmentcode>
   <parsingerrormessage></parsingerrormessage>
  </messageacknowledgment>
  <reportacknowledgment>
   <safetyreportid></safetyreportid>
   <safetyreportversion></safetyreportversion>
   <localreportnumb>US-FDA-authority report number 10052410</localreportnumb>
   <authoritynumb></authoritynumb>
   <companynumb>US-pharmaceutical company-Report1</companynumb>

   <receiptdateformat>102</receiptdateformat>
   <receiptdate>19980701</receiptdate>
   <reportacknowledgmentcode>02</reportacknowledgmentcode>
   <errormessagecomment>there are several errors that must be corrected before
re-submitting:  check field lengths and ISO codes for REACTION section of
report.</errormessagecomment>
  </reportacknowledgment>
 </acknowledgment>
</ichicsrack>
```

B.0 GLOSSARY

DCL SGML Declaration File

DTD Document Type Definition

EWG Expert Working Group

ICH International Conference on Harmonisation

ICH_ICSR.DTD Individual Case Safety Report Document Type Definition

ICSR Individual Case Safety Report

Rec. 5.2 ICH M2 Recommendation 5.2: SGML DTD Electronic Format for the Exchange of Individual Case Safety reports (E2B Message)

Rec. 5.3 ICH M2 Recommendation 5.3: EDI Header Specification for the E2B Message

SGML Standard Generalized Mark-up Language