ICH M2 EWG

Electronic Transmission of Individual Case Safety Reports Message Specification
(ICH ICSR DTD Version 2.1)
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# Electronic Transmission of Individual Case Safety Reports Message Specification

*Document Version 2.3  November 9, 2000*

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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
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- 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](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.

M2 Entities and Relationships

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 intended 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

**ATTRIBUTES**
- messagetype = ichicsr
- messageformatversion
- messagenumber
- messagesenderidentifier
- messagereceiveridentifier
- messagedateformat
- messagedate
- primarysource
- reportduplicates
- patient
- sender
- receiver
- linkedreport
- safetyreportid
- safetyreportversion
- receiptdateformat
- receiptdate
- authoritynumber
- companynumber
- casenullification

**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>.
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<td>&lt;reportduplicate&gt;&lt;reportduplicatesq&gt;001&lt; duplicatesource&gt; smith, coopers, barnies, and young pharmaceuticals &lt;/duplicatesource&gt;&lt;dupl catenumb&gt;nmbr1234567891011121314151617181920&lt;/ dupl catenumb&gt;&lt;reportduplicatesq&gt;002&lt; duplicatesource&gt; smith, coopers, barnies, and young pharmaceuticals &lt;/duplicatesource&gt;&lt;dupl catenumb&gt; number12345678910111213141516171819&lt;/ dupl catenumb&gt;&lt;reportduplicatesq&gt;&lt;reportduplicate&gt;</td>
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- 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 "&lt;", "&gt;", and "&amp;" 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 differentiate 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.
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</primarysourcecountry>. 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>
• 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:
```xml
<!ELEMENT safetyreport - -
  (safetyreportversion?,
   safetyreportid?,
   primariesourcecountry?,
   occurcountry?,
   transmissiondateformat?,
   transmissiondate?,
   reporttype?,
   serious?,
   seriousnessdeath?,
   seriousnesslifethreatening?,
   seriousnesshospitalization?,
   seriousnessdisabling?,
   seriousnesscongenitalanomaly?,
   seriousnessother?,
   receivedateformat?,
   receivedate?,
   receiptdateformat?,
   receiptdate?,
   additionaldocument?,
   ...)
```

Sample SGML data file:
```xml
<safetyreport>
  <safetyreportversion>1</safetyreportversion>
  <safetyreportid>US-XYZ-12345</safetyreportid>

  <primarysourcecountry>US</primarysourcecountry>

</safetyreport>
```
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:

```
```

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 usable 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 decrpts 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

ICH ICSR Specifications
ICH ICSR DTD Version 2.1
November 2000
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.
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**

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

**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)

<table>
<thead>
<tr>
<th>Data Element</th>
<th>Title</th>
<th>Description</th>
<th>Field Length</th>
<th>Field Value</th>
<th>DTD Descriptor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>M.1 ICH ICSR Message Header</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M.1</td>
<td>ICH ICSR Message Header</td>
<td>Header/Entity</td>
<td></td>
<td></td>
<td>ichicsrmessageheader</td>
</tr>
<tr>
<td>M.1.1</td>
<td>Message Type</td>
<td>Type of information being transmitted</td>
<td>16AN</td>
<td>ichicsr</td>
<td>messagetype</td>
</tr>
<tr>
<td>M.1.2</td>
<td>Message Format Version</td>
<td>Version number of Message Format</td>
<td>3AN</td>
<td></td>
<td>messageformatversion</td>
</tr>
<tr>
<td>M.1.3</td>
<td>Message Format Release</td>
<td>Release number of the Message Format</td>
<td>3AN</td>
<td></td>
<td>messageformatrelease</td>
</tr>
<tr>
<td>M.1.4</td>
<td>Message Number</td>
<td>Message Number</td>
<td>100AN</td>
<td></td>
<td>messagenumb</td>
</tr>
<tr>
<td>M.1.5</td>
<td>Message Sender Identifier</td>
<td>Message Sender Identifier</td>
<td>60AN</td>
<td></td>
<td>messagesenderidentifier</td>
</tr>
<tr>
<td>M.1.6</td>
<td>Message Receiver Identifier</td>
<td>Message Receiver Identifier</td>
<td>60AN</td>
<td></td>
<td>messagereceiveridentifier</td>
</tr>
<tr>
<td>M.1.7a</td>
<td>Message Date</td>
<td>Message Date Format (include as an attribute)</td>
<td>3N</td>
<td>204 – Format CCYYMMDDHHMMSS</td>
<td>messagedateformat</td>
</tr>
<tr>
<td>M.1.7b</td>
<td>Message Date</td>
<td>Message Date</td>
<td>14N</td>
<td>CCYYMMDDHHMMSS</td>
<td>messagedate</td>
</tr>
</tbody>
</table>

### 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 |

ICH ICSR Specifications  ICH ICSR DTD Version 2.1  November 2000

For Japan, field length must be two times the current length when AN or A.
<table>
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<tr>
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### Electronic Transmission of Individual Case Safety Reports Message Specification

**Document Version 2.3  November 9, 2000**

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For Japan, field length must be two times the current length when AN or A.
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### Electronic Transmission of Individual Case Safety Reports Message Specification

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ICH ICSR DTD Version 2.1
November 2000
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For Japan, field length must be two times the current length when AN or A.
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2=No, not highlighted by the reporter, NOT serious  
3=Yes, highlighted by the reporter, SERIOUS  
4=No, not highlighted by the reporter, SERIOUS |
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203 - Format CCYYMMDDHHMM,  
610 - Format CCYYMM,  
602 - Format CCYY |
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### Data Element | Title | Description | Field Length | Field Value | DTD Descriptor
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B.2.1.8 | 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 CCYMMDD, 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 | 
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 | 
B.4.k.2.2 | Active Drug substance names | 100AN | | activesubstancename | 

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For Japan, field length must be two times the current length when AN or A.
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035 = Intrasynovial  
036 = Intratumor  
037 = Intrathecal  
038 = Intrathecal  
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 = Oropharyngeal  
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 | reactiongestationperiod |
| B.4.k.10b    | Gestation period at time of exposure | 3N | 802=Month  
803=Week  
804=Day  
810=Trimester | reactiongestationperiodunit |
<p>| B.4.k.11a    | MedDRA version for indication | 8AN | AN drugindicationmeddraversion |</p>
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<td>Header</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B.4.k.17.1</td>
<td>Did reaction recur on readministration?</td>
<td></td>
<td>1N</td>
<td>1=Yes 2= No 3 = Unknown</td>
<td>drugrecurreadadministration</td>
</tr>
<tr>
<td>B.4.k.17.2a</td>
<td>MedDRA version for reaction(s)/event(s) recurred</td>
<td></td>
<td>8AN</td>
<td></td>
<td>drugrecurationmeddraversion</td>
</tr>
<tr>
<td>B.4.k.17.2b</td>
<td>If yes, which reaction(s)/event(s) recurred?</td>
<td></td>
<td>250AN</td>
<td></td>
<td>drugrecuration</td>
</tr>
<tr>
<td>B.4.k.18</td>
<td>Relatedness of drug to reaction(s)/event(s) (repeat as necessary)</td>
<td>Header/entity</td>
<td></td>
<td></td>
<td>drugreactionrelatedness</td>
</tr>
<tr>
<td>B.4.k.18.1a</td>
<td>MedDRA version for Reaction assessed</td>
<td></td>
<td>8AN</td>
<td></td>
<td>drugreactionassesmeddraversi on</td>
</tr>
<tr>
<td>B.4.k.18.1b</td>
<td>Reaction assessed</td>
<td></td>
<td>250AN</td>
<td></td>
<td>drugreactionasses</td>
</tr>
<tr>
<td>B.4.k.18.2</td>
<td>Source of assessment</td>
<td></td>
<td>60AN</td>
<td></td>
<td>drugassessmentsource</td>
</tr>
<tr>
<td>B.4.k.18.3</td>
<td>Method of assessment</td>
<td></td>
<td>35AN</td>
<td></td>
<td>drugassessmentmethod</td>
</tr>
<tr>
<td>B.4.k.18.4</td>
<td>Result</td>
<td></td>
<td>35AN</td>
<td></td>
<td>drugresult</td>
</tr>
<tr>
<td>B.4.k.19</td>
<td>Additional information on drug</td>
<td></td>
<td>100AN</td>
<td></td>
<td>drugadditional</td>
</tr>
<tr>
<td>B.5</td>
<td>Narrative case summary and further information:</td>
<td>Header/entity</td>
<td></td>
<td></td>
<td>summary</td>
</tr>
</tbody>
</table>
### 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

--> 

<!-- 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 ICHICSZR 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 -->
<!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;">  

<!ELEMENT ichicsr -->
<!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)>

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<!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? ,
occurrencecountry? ,
transmissiondateformat? ,
transmissiondate? ,
reporttype? ,
serious? ,
seriousnessdeath? ,
seriousnesslifethreatening? ,
seriousnesshospitalization? ,
seriousnessdisabling? ,
seriousnesscongenitalanomaly? ,
seriousnessother? ,
receivedateformat? ,
receivedate? ,
receiptdateformat ,
receiptdate ,
additionaldocument? ,
documentlist? ,
fulfillexpeditecriteria? ,
authoritynumb? ,
companynumb? ,
duplicate? ,
casenullification? ,
nullificationreason? ,
medicallyconfirm? ,
(reportduplicates* ,
linkedreport* ,
primarysource+ ,
sender ,
receiver ,
patient))>
<!ATTLIST safetyreport
%lang.att;
>
<!ELEMENT reportduplicates - -
(duplicatesource? ,
duplicatenumb?)>
<!ATTLIST reportduplicates
%lang.att;
>
<!ELEMENT linkedreport - - (linkreportnumb?)>
<!ATTLIST linkedreport %lang.att;>

<!-- A.2 Primary source(s) of information -->
<!ELEMENT primarysource - -
    (reporter_title?,
     reporter_givenname?,
     reporter_middlename?,
     reporter_familyname?,
     reporter_organization?,
     reporter_department?,
     reporter_street?,
     reporter_city?,
     reporter_state?,
     reporter_postcode?,
     reporter_country?,
     qualification?,
     literature_reference?,
     study_name?,
     sponsor_study_number?,
     observe_study_type?)>
<!ATTLIST primarysource %lang.att;>

<!-- A.3.1 Sender -->
<!ELEMENT sender - -
    (sender_type?,
     sender_organization,
     sender_department?,
     sender_title?,
     sender_givenname?,
     sender_middlename?,
     sender_familyname?,
     sender_countryname?,
     sender_street_address?,
     sender_city?,
     sender_state?,
     sender_postcode?,
     sender_country_code?,
     sender_tel?,
     sender_telextension?,
     sender_tel_country_code?,
     sender_fax?,
     sender_faxextension?,
     sender_fax_country_code?,
     sender_emailaddress?)>
<!ATTLIST sender %lang.att;>

<!-- A.3.2 Receiver -->
<!ELEMENT receiver - -
    (receiver_type?,
     receiver_organization?,
     receiver_emailaddress?)>
<!DOCTYPE html PUBLIC "-//W3C//DTD HTML 4.01 Transitional//EN"
"http://www.w3.org/TR/html4/loose.dtd">
<html xmlns="http://www.w3.org/1999/xhtml">
<body>

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receiverdepartment?,
receivertitle?,
receivergivenname?,
receivermiddlename?,
receiverfamilyname?,
receiverstreetaddress?,
receivercity?,
receiverstate?,
receiverpostcode?,
receivercountrycode?,
receiver?,
receiverextension?,
receivercountrycode?,
receiverfax?,
receiverfaxextension?,
receiverfaxcountrycode?,
receiveremailaddress?)>

<!ATTLIST receiver
%lang.att;
>

<!-- B.1 Patient characteristics -->
<!ELEMENT patient - -
(patientinitial?,
patientgmpmedicalrecordnumb?,
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?,

)>

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<!-- B.1.8 Relevant past drug history -->
<!ELEMENT patientpastdrugtherapy (patientdrugname?,
  patientdrugstartdateformat?,
  patientdrugstartdate?,
  patientdrugenddateformat?,
  patientdrugenddate?,
  patientindicationmeddraversion?,
  patientdrugindication?,
  patientdrgreactionmeddraversion?,
  patientdrgreaction?)>
<!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?)>
<!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? ,
  parentdrgindication? ,
  parentdrgreactionmeddraversion? ,
  parentdrgreaction?)>
<!ATTLIST parentpastdrugtherapy
%lang.att;> 

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

parentbirthdateformat? ,
parentbirthdate? ,
parentage? ,
parentageunit? ,
parentlastmenstrualdateformat? ,
parentlastmenstrualdate? ,
parentweight? ,
parentheight? ,
parensex? ,
parentmedicalrelevanttext? ,
 (parentmedicalhistoryepisode* ,
  parentpastdrugtherapy*))>
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? ,

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

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

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

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

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

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

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

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

<!-- 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.

```xml
<!-- 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 reportergivenname - - (#PCDATA)>
<!ATTLIST reportergivenname
%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 reportercountry - - (#PCDATA)>
<!ATTLIST reportercountry %lang.att;>

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

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

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

<!-- A.2.3.1 Study name -->
<!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 sendergivenname - - (PCDATA)>
<!ATTLIST sendergivenname
%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;  
> 
<!ELEMENT senderstate - - (#PCDATA)>  
<!ATTLIST senderstate  
%lang.att;  
> 
<!ELEMENT senderpostcode - - (#PCDATA)>  
<!ATTLIST senderpostcode  
%lang.att;  
> 
<!ELEMENT sendercountrycode - - (#PCDATA)>  
<!ATTLIST sendercountrycode  
%lang.att;  
> 
<!ELEMENT sendertel - - (#PCDATA)>  
<!ATTLIST sendertel  
%lang.att;  
> 
<!ELEMENT sendertelextension - - (#PCDATA)>  
<!ATTLIST sendertelextension  
%lang.att;  
> 
<!ELEMENT sendertelcountrycode - - (#PCDATA)>  
<!ATTLIST sendertelcountrycode  
%lang.att;  
> 
<!ELEMENT senderfax - - (#PCDATA)>  
<!ATTLIST senderfax  
%lang.att;  
> 
<!ELEMENT senderfaxextension - - (#PCDATA)>  
<!ATTLIST senderfaxextension  
%lang.att;  
> 
<!ELEMENT senderfaxcountrycode - - (#PCDATA)>  
<!ATTLIST senderfaxcountrycode  
%lang.att;  
>
<!-- A.3.1.4.1 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 receivergivenname - - (#PCDATA)>
<!ATTLIST receivergivenname
%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;
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<!-- 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)>
<!-- 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 -->
<!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

<!-- 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;>
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<!-- 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;
<!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.5.3 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 -->
<!ELEMENT patientepisodenamemeddraversion - - (#PCDATA)>
<!ATTLIST patientepisodenamemeddraversion
%lang.att;>

<!-- B.1.9.2a MedDRA version for reported cause(s) of death -->
<!ELEMENT patientdeathreportmeddraversion - - (#PCDATA)>
<!ATTLIST patientdeathreportmeddraversion
%lang.att;>
<!-- B.1.9.4a MedDRA version for autopsy-determined cause(s) of death -->
<!ELEMENT patientdetermautopsmeddraversion - - (#PCDATA)>
<!ATTLIST patientdetermautopsmeddraversion %lang.att; >

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

<!-- B.1.8f.1 MedDRA version for indication -->
<!ELEMENT patientindicationmeddraversion - - (#PCDATA)>
<!ATTLIST patientindicationmeddraversion %lang.att; >

<!-- B.1.10.8g.1 MedDRA version for indication -->
<!ELEMENT parentdrgreactionmeddraversion - - (#PCDATA)>
<!ATTLIST parentdrgreactionmeddraversion %lang.att; >

<!-- B.1.10.8f.1 MedDRA version for indication -->
<!ELEMENT parentdrgindicationmeddraversion - - (#PCDATA)>
<!ATTLIST parentdrgindicationmeddraversion %lang.att; >

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

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

<!-- B.4.k.18.1a MedDRA version for reaction assessed -->
<!ELEMENT drugreactionassesmeddraversion - - (#PCDATA)>
<!ATTLIST drugreactionassesmeddraversion %lang.att; >

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

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

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

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

<!-- B.5.3a MedDRA version for senders diagnosis or syndrome-->
<!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.

```xml
<!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 32 127
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 SEPCCHAR 9

NAMING    LCNMSTRT ""
```

ICH ICSR Specifications ICH ICSR DTD Version 2.10 November 2000
UCNMSTRT " "
LCNMCHAR ".-"
UCNMCHAR ".-"
NAMECASE GENERAL YES
ENTITY NO
DELM GENERAL SGMLREF
SHORTREF SGMLREF
NAMES SGMLREF
QUANTITY SGMLREF
ATTSPLEN 65536
LITLEN 65536
NAMELEN 32
PILEN 65536
TAGLVL 100
TAGLEN 65536
GRPGTCNT 150
GRFPCNT 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
>

ICH ICSR Specifications  ICH ICSR DTD Version 2.10  November 2000
ichiesr-latin7.dcl - This SGML declaration supports the ISO 8859-7 (Latin 7) character set. This character set supports Greek.

```xml
<!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
```

ICH ICSR Specifications  ICH ICSR DTD Version 2.10  November 2000
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
IMPLIED NO
EXPLICIT NO
OTHER
CONCUR NO
SUBDOC NO
FORMAL YES
APPINFO NONE

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

<!SGML "ISO 8879:1986"

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
ATTCCAP 1000000
ATTCHCAP 1000000
AVGRPCAP 1000000
ELEMCCAP 1000000
ENTCCAP 1000000
ENTCHCAP 1000000
GRPCAP 1000000
EXGRPCAP 1000000
EXNMCAP 1000000
NOTCCAP 1000000
NOTCHCAP 1000000
MAPCAP 1000000
LKNMCCAP 1000000
LKNMCCAP 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

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ICH ICSR Specifications ICH ICSR DTD Version 2.10 November 2000

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 SEPCCHAR 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;&\#160;&\#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;&\#160;&\#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

ICH ICSR Specifications ICH ICSR DTD Version 2.10 November 2000
ichiesr-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.

```xml
<!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  18   UNUSED
   13  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
   SHUNCCHAR 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
```

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

DELMET GENERAL SGMLREF
HCRO "&amp;#38;#X" -- added by jje --
SHORTREF SGMLREF

NAMES SGMLREF
QUANTITY SGMLREF
ATTCTN 60  -- increased --
ATTSPLEN 65536  -- These are the largest values --
LITALN 65536  -- permitted in the declaration --
NAMELEN 32  -- Avoid fixed limits in actual --
PILEN 65536  -- implementations of HTML UA's --
TAGLVL 100
TAGLEN 65536
GRPCTCN 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

>
ichiesr-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 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 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 important 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
GRP CAP 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
Electronic Transmission of Individual Case Safety Reports Message Specification

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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
   ATTSPLLEN 65536
   LITLEN 65536
   NAMELEN 32
   PILEN 65536
   TAGLVL 100
   TAGLEN 65536
   GRPCTCNT 150
   GRPCNT 64

FEATURES
   MINIMIZE
   DATATAG NO
   OMITTAG NO
   RANK NO
   SHORTTAG YES

   LINK
   SIMPLE NO
   IMPPLICIT 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).

<table>
<thead>
<tr>
<th>Unit List</th>
<th>ICH-M2 Numeric Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mass</strong></td>
<td></td>
</tr>
<tr>
<td>kg kilogram(s)</td>
<td>001</td>
</tr>
<tr>
<td>G gram(s)</td>
<td>002</td>
</tr>
<tr>
<td>Mg milligram(s)</td>
<td>003</td>
</tr>
<tr>
<td>µg microgram(s)</td>
<td>004</td>
</tr>
<tr>
<td>ng nanogram(s)</td>
<td>005</td>
</tr>
<tr>
<td>pg picogram(s)</td>
<td>006</td>
</tr>
<tr>
<td>mg/kg milligram(s)/kilogram</td>
<td>007</td>
</tr>
<tr>
<td>µg/kg microgram(s)/kilogram</td>
<td>008</td>
</tr>
<tr>
<td>mg/m² milligram(s)/sq. meter</td>
<td>009</td>
</tr>
<tr>
<td>µg/ m² microgram(s)/sq. meter</td>
<td>010</td>
</tr>
<tr>
<td><strong>Volume</strong></td>
<td></td>
</tr>
<tr>
<td>l litre(s)</td>
<td>011</td>
</tr>
<tr>
<td>ml millilitre(s)</td>
<td>012</td>
</tr>
<tr>
<td>µl microlitre(s)</td>
<td>013</td>
</tr>
<tr>
<td><strong>Radioactivity</strong></td>
<td></td>
</tr>
<tr>
<td>Bq becquerel(s)</td>
<td>014</td>
</tr>
<tr>
<td>GBq gigabecquerel(s)</td>
<td>015</td>
</tr>
<tr>
<td>MBq megabecquerel(s)</td>
<td>016</td>
</tr>
<tr>
<td>Kbq kilobecquerel(s)</td>
<td>017</td>
</tr>
<tr>
<td>Ci curie(s)</td>
<td>018</td>
</tr>
<tr>
<td>MCI millicurie(s)</td>
<td>019</td>
</tr>
<tr>
<td>µCi microcurie(s)</td>
<td>020</td>
</tr>
<tr>
<td>NCi nanocurie(s)</td>
<td>021</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
</tr>
<tr>
<td>mol mole(s)</td>
<td>022</td>
</tr>
<tr>
<td>Mmol millimole(s)</td>
<td>023</td>
</tr>
<tr>
<td>µmol micromole(s)</td>
<td>024</td>
</tr>
<tr>
<td>Iu international unit(s)</td>
<td>025</td>
</tr>
<tr>
<td>Kiu iu(1000s)</td>
<td>026</td>
</tr>
<tr>
<td>Miu iu(1,000,000s)</td>
<td>027</td>
</tr>
<tr>
<td>iu/kg iu/kilogram</td>
<td>028</td>
</tr>
<tr>
<td>Meq milliequivalent(s)</td>
<td>029</td>
</tr>
<tr>
<td>% percent</td>
<td>030</td>
</tr>
<tr>
<td>Definition of Interval List</td>
<td>Proposed ICH-M2 Codes</td>
</tr>
<tr>
<td>----------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Gtt drop(s)</td>
<td>031</td>
</tr>
<tr>
<td>DF dosage form</td>
<td>032</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Seconds</td>
<td>807</td>
</tr>
<tr>
<td>Minutes</td>
<td>806</td>
</tr>
<tr>
<td>Hours</td>
<td>805</td>
</tr>
<tr>
<td>Days</td>
<td>804</td>
</tr>
<tr>
<td>Weeks</td>
<td>803</td>
</tr>
<tr>
<td>Months</td>
<td>802</td>
</tr>
<tr>
<td>Years</td>
<td>801</td>
</tr>
<tr>
<td>Trimester</td>
<td>810</td>
</tr>
<tr>
<td>Cyclical</td>
<td>811</td>
</tr>
<tr>
<td>As Necessary</td>
<td>812</td>
</tr>
<tr>
<td>Total</td>
<td>813</td>
</tr>
</tbody>
</table>
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).

<table>
<thead>
<tr>
<th>Description</th>
<th>ICH M2 Numeric Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auricular (otic)</td>
<td>001</td>
</tr>
<tr>
<td>Buccal</td>
<td>002</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>003</td>
</tr>
<tr>
<td>Dental</td>
<td>004</td>
</tr>
<tr>
<td>Endocervical</td>
<td>005</td>
</tr>
<tr>
<td>Endosinusial</td>
<td>006</td>
</tr>
<tr>
<td>Endotracheal</td>
<td>007</td>
</tr>
<tr>
<td>Epidural</td>
<td>008</td>
</tr>
<tr>
<td>Extra-amniotic</td>
<td>009</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>010</td>
</tr>
<tr>
<td>Intra corpus cavernosum</td>
<td>011</td>
</tr>
<tr>
<td>Intra-amniotic</td>
<td>012</td>
</tr>
<tr>
<td>Intra-arterial</td>
<td>013</td>
</tr>
<tr>
<td>Intra-artericular</td>
<td>014</td>
</tr>
<tr>
<td>Intra-uterine</td>
<td>015</td>
</tr>
<tr>
<td>Intracardiac</td>
<td>016</td>
</tr>
<tr>
<td>Intracavernous</td>
<td>017</td>
</tr>
<tr>
<td>Intracerebral</td>
<td>018</td>
</tr>
<tr>
<td>Intracervical</td>
<td>019</td>
</tr>
<tr>
<td>Intracisternal</td>
<td>020</td>
</tr>
<tr>
<td>Intracorneal</td>
<td>021</td>
</tr>
<tr>
<td>Intracoronary</td>
<td>022</td>
</tr>
<tr>
<td>Intradermal</td>
<td>023</td>
</tr>
<tr>
<td>Intradiscal (intraspinal)</td>
<td>024</td>
</tr>
<tr>
<td>Intrahepatic</td>
<td>025</td>
</tr>
<tr>
<td>Intralesional</td>
<td>026</td>
</tr>
<tr>
<td>Intralymphatic</td>
<td>027</td>
</tr>
<tr>
<td>Intramedullar (bone marrow)</td>
<td>028</td>
</tr>
<tr>
<td>Intrameningeal</td>
<td>029</td>
</tr>
<tr>
<td>Intramuscular</td>
<td>030</td>
</tr>
<tr>
<td>Intraocular</td>
<td>031</td>
</tr>
<tr>
<td>Intrapericardial</td>
<td>032</td>
</tr>
<tr>
<td>Intraperitoneal</td>
<td>033</td>
</tr>
<tr>
<td>Intrapleural</td>
<td>034</td>
</tr>
<tr>
<td>Intrasynovial</td>
<td>035</td>
</tr>
<tr>
<td>Intratumor</td>
<td>036</td>
</tr>
<tr>
<td>Intrathecal</td>
<td>037</td>
</tr>
<tr>
<td>Intrathoracic</td>
<td>038</td>
</tr>
<tr>
<td>Intratracheal</td>
<td>039</td>
</tr>
<tr>
<td>Intravenous bolus</td>
<td>040</td>
</tr>
<tr>
<td>Intravenous drip</td>
<td>041</td>
</tr>
<tr>
<td>Route</td>
<td>Code</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Intravenous (not otherwise specified)</td>
<td>042</td>
</tr>
<tr>
<td>Intravesical</td>
<td>043</td>
</tr>
<tr>
<td>Iontophoresis</td>
<td>044</td>
</tr>
<tr>
<td>Nasal</td>
<td>045</td>
</tr>
<tr>
<td>Occlusive dressing technique</td>
<td>046</td>
</tr>
<tr>
<td>Ophthalmic</td>
<td>047</td>
</tr>
<tr>
<td>Oral</td>
<td>048</td>
</tr>
<tr>
<td>Oropharyngeal</td>
<td>049</td>
</tr>
<tr>
<td>Other</td>
<td>050</td>
</tr>
<tr>
<td>Parenteral</td>
<td>051</td>
</tr>
<tr>
<td>Periarticular</td>
<td>052</td>
</tr>
<tr>
<td>Perineural</td>
<td>053</td>
</tr>
<tr>
<td>Rectal</td>
<td>054</td>
</tr>
<tr>
<td>Respiratory (inhalation)</td>
<td>055</td>
</tr>
<tr>
<td>Retrobulbar</td>
<td>056</td>
</tr>
<tr>
<td>Sunconjunctival</td>
<td>057</td>
</tr>
<tr>
<td>Subcutaneous</td>
<td>058</td>
</tr>
<tr>
<td>Subdermal</td>
<td>059</td>
</tr>
<tr>
<td>Sublingual</td>
<td>060</td>
</tr>
<tr>
<td>Topical</td>
<td>061</td>
</tr>
<tr>
<td>Transdermal</td>
<td>062</td>
</tr>
<tr>
<td>Transmammary</td>
<td>063</td>
</tr>
<tr>
<td>Transplacental</td>
<td>064</td>
</tr>
<tr>
<td>Unknown</td>
<td>065</td>
</tr>
<tr>
<td>Urethral</td>
<td>066</td>
</tr>
<tr>
<td>Vaginal</td>
<td>067</td>
</tr>
</tbody>
</table>
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:

<table>
<thead>
<tr>
<th>Data Element</th>
<th>Title</th>
<th>Description</th>
<th>DTD Descriptor</th>
<th>Field Length</th>
<th>Field Value</th>
<th>Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.1</td>
<td>ICSR Message Header</td>
<td>Header/Entity</td>
<td>ichicsrmessageheader</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M.1.1</td>
<td>Message Type</td>
<td>Type of Information Being Transmitted</td>
<td>messagetype</td>
<td>16 AN</td>
<td>ichicsrack</td>
<td>Yes</td>
</tr>
<tr>
<td>M.1.2</td>
<td>Message Format Version</td>
<td>Version Number of Message Format</td>
<td>messageformatversion</td>
<td>3AN</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>M.1.3</td>
<td>Message Format Release</td>
<td>Release number of the Message Format</td>
<td>messageformatrelease</td>
<td>3AN</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>M.1.4</td>
<td>Message Number</td>
<td>Message Number</td>
<td>messagenumb</td>
<td>100AN</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>M.1.5</td>
<td>Message Sender Identifier</td>
<td>Message Sender Identifier</td>
<td>messagesenderidentifier</td>
<td>60AN</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>M.1.6</td>
<td>Message Receiver Identifier</td>
<td>Message Receiver Identifier</td>
<td>messagereceiveridentifier</td>
<td>60AN</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>M.1.7a</td>
<td>Message Date</td>
<td>Message Date Format</td>
<td>messagedateformat</td>
<td>3N</td>
<td>204 – Format CCYYMMDDHHMMSS</td>
<td>Yes</td>
</tr>
<tr>
<td>M.1.7b</td>
<td>Message Date</td>
<td>messagedate</td>
<td>14N</td>
<td>CCYYMMDDHHMMSS</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>A.1</td>
<td>Message Acknowledgment</td>
<td>Header/Entity</td>
<td>messageacknowledgment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.1.1</td>
<td>ICSR Message Number</td>
<td>Message Number</td>
<td>icrsmessagenumb</td>
<td>100AN</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>A.1.2</td>
<td>Local Message Number</td>
<td>Local Message Number</td>
<td>localmessagenumb</td>
<td>100AN</td>
<td>Locally Assigned</td>
<td></td>
</tr>
<tr>
<td>A.1.3</td>
<td>ICSR Message Sender ID</td>
<td>Message Sender Identifier</td>
<td>icrsmessagesenderidentifier</td>
<td>60AN</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>A.1.4</td>
<td>ICSR Message Receiver ID</td>
<td>Message Receiver Identifier</td>
<td>icrsmessagereceiveridentifier</td>
<td>60AN</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>A.1.5a</td>
<td>ICSR Message Date</td>
<td>Message Date Format</td>
<td>icrsmessagedateformat</td>
<td>3N</td>
<td>204 – Format CCYYMMDDHHMMSS</td>
<td>Yes</td>
</tr>
<tr>
<td>A.1.5b</td>
<td>ICSR Message Date</td>
<td>icrsmessagedate</td>
<td>14N</td>
<td>CCYYMMDDHHMMSS</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>
### A.1.6 Transmission Acknowledgment Code

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
<th>Value</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response from Agency on Transmission</td>
<td>transmissionacknowledgmentcode</td>
<td>2N</td>
<td></td>
</tr>
<tr>
<td></td>
<td>01= All Reports loaded into database</td>
<td>02 = ICSR Error, not all reports loaded into the database, check section B</td>
<td></td>
</tr>
<tr>
<td></td>
<td>03= SGML parsing error, no data extracted</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### A.1.7 Parsing Error Message

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
<th>Value</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description of the SGML Parsing Error Encountered</td>
<td>parsingerrormessage</td>
<td>250 AN</td>
<td></td>
</tr>
</tbody>
</table>

### B.1. Report Confirmation

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
<th>Value</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Header/Entity</td>
<td>reportacknowledgment</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### B.1.1 Safety Report ID

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
<th>Value</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety Report Identifier</td>
<td>safetyreportid</td>
<td>100AN</td>
<td></td>
</tr>
</tbody>
</table>

#### B.1.2 Safety Report Version Number

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
<th>Value</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety Report Version</td>
<td>safetyreportversion</td>
<td>2AN</td>
<td></td>
</tr>
</tbody>
</table>

#### B.1.3 Local Report Number

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
<th>Value</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local Report Number</td>
<td>localreportnumber</td>
<td>100AN</td>
<td></td>
</tr>
</tbody>
</table>

#### B.1.4 Regulatory authority's case report number

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
<th>Value</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory authority's case report number</td>
<td>authoritynumber</td>
<td>100AN</td>
<td></td>
</tr>
</tbody>
</table>

#### B.1.5 Other Sender’s case report number

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
<th>Value</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other Sender’s case report number</td>
<td>companynumber</td>
<td>100AN</td>
<td></td>
</tr>
</tbody>
</table>

#### B.1.7a Date of receipt of the most recent information

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
<th>Value</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receipt Date Format</td>
<td>receiptdateformat</td>
<td>3N</td>
<td></td>
</tr>
<tr>
<td>Date of receipt of the most recent information</td>
<td>receiptdate</td>
<td>8N</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CCYYMM DD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### B.1.8 Acknowledgment Code for a Report

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
<th>Value</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Report Level Acknowledgment (If there is an error code, re-send only the specified report.)</td>
<td>reportacknowledgmentcode</td>
<td>2N</td>
<td></td>
</tr>
<tr>
<td>Acknowledgment Code for a Report</td>
<td></td>
<td>01=Report Loaded Successfully</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>02=Report Not Loaded</td>
<td></td>
</tr>
</tbody>
</table>

#### B.1.9 Error Message or Comment

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
<th>Value</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description of the Specific Error or Errors Encountered</td>
<td>errormessagecomment</td>
<td>250AN</td>
<td></td>
</tr>
</tbody>
</table>
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)
ICH ICSR Specifications  ICH ICSR DTD Version 2.10  November 2000
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        -->
<!-- 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 "&amp;";>

<!-- 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
>

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<!-- 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.1.1 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;>

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

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

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

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

<!ELEMENT parsingerrormessage - - (#PCDATA)>
<!ATTLIST parsingerrormessage
%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

```xml
<ichicsrack lang="en">
  <ichicsrmessageheader>
    <messagetype>ichicsrack</messagetype>
    <messageformatversion>1.0</messageformatversion>
    <messageformatrelease>1.0</messageformatrelease>
    <messagenumb>0000010016328</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

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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</thead>
<tbody>
<tr>
<td>DCL</td>
<td>SGML Declaration File</td>
</tr>
<tr>
<td>DTD</td>
<td>Document Type Definition</td>
</tr>
<tr>
<td>EWG</td>
<td>Expert Working Group</td>
</tr>
<tr>
<td>ICH</td>
<td>International Conference on Harmonisation</td>
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<tr>
<td>ICH_ICSR.DTD</td>
<td>Individual Case Safety Report Document Type Definition</td>
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<tr>
<td>ICSR</td>
<td>Individual Case Safety Report</td>
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<tr>
<td>Rec. 5.2</td>
<td>ICH M2 Recommendation 5.2: SGML DTD Electronic Format for the Exchange of Individual Case Safety reports (E2B Message)</td>
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<tr>
<td>Rec. 5.3</td>
<td>ICH M2 Recommendation 5.3: EDI Header Specification for the E2B Message</td>
</tr>
<tr>
<td>SGML</td>
<td>Standard Generalized Mark-up Language</td>
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</table>