E2B(R) CLINICAL SAFETY DATA MANAGEMENT:

DATA ELEMENTS FOR TRANSMISSION OF INDIVIDUAL CASE SAFETY REPORTS

Revision 2

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

ICH HARMONISED TRIPARTITE GUIDELINE

REVISION OF THE ICH GUIDELINE ON CLINICAL SAFETY DATA MANAGEMENT:

DATA ELEMENTS FOR TRANSMISSION OF INDIVIDUAL CASE SAFETY REPORTS

E2B(R)

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PREAMBLE

This guideline provides additional information and clarification as well as some modifications to the ICH E2B guideline signed off on July 17, 1997 and modified as E2B(M) guideline in November 2000. It incorporates adjustments based on the experience gained after the implementation of the guideline in the three regions. It is recommended that the reader reviews this document as well as the companion document M2 ICSR Message Specification.

1. INTRODUCTION

1.1 Scope of this guideline

The objectives of the working group are to standardize the data elements for transmission of individual case safety reports by identifying and where necessary or advisable within a particular region, by defining the data elements for the transmission of all types of individual case safety reports, regardless of source and destination. This guideline includes data elements of case safety reports for both pre and post approval periods and covers both adverse drug reaction and adverse event reports. It is not intended that this format should be used for cases in the integrated safety summary of a marketing license application dossier. For adverse reactions encountered in clinical trials, this format should be used only for those subject to expedited reporting. The scope of this topic does not encompass the definition of database structures, the design of a paper report form, quality control/quality assurance aspects, or technical security issues.

1.2 Background

Because of national and international agreements, rules, and regulations, individual case safety reports of adverse drug reactions and adverse events should be transmitted

− from identified reporting sources to regulatory authorities and pharmaceutical companies;
− between regulatory authorities;
− between pharmaceutical companies and regulatory authorities;
− within authorities or pharmaceutical companies;
− from clinical investigators, via the sponsor, to ethics committees;
− from authorities to the World Health Organization (WHO) Collaborating Center for International Drug Monitoring.

The transmission of such individual case safety reports relies on paper-based formats (e.g., yellow cards, CIOMS I forms, MedWatch) or electronic media usually by on-line access, tape or file transfer. Considering the large number of potential participants in a world-wide exchange of information, there should be an electronic format capable of accommodating direct database to database transmission using message transfers. Successful electronic transmission of information relies on the definition of common data elements, provided in this document, and standard transmission procedures to be determined by the ICH Electronic Standards for the Transfer of Regulatory Information (ESTRI) Expert Working Group (M2).

1.3 Notes on format of this document

Section 2 and its subsections designated A and B contain notes that are directed toward clarifying the nature of the data that should be provided. In addition, there are notes to assist in defining the format that should be used to transmit the data. In order to distinguish between these notes, the format is presented in

standard type of a slightly smaller font.

If a data element has a limited set of choices, the options are presented in ***bold Italic type***.
The standard allows for this information to be transmitted in encoded format.

1.4 Definition of data elements

The format for individual case safety reports includes provisions for transmitting all the relevant data elements useful to assess an individual adverse drug reaction or adverse event report. The data elements are sufficiently comprehensive to cover complex reports from most sources, different data sets, and transmission situations or requirements; therefore, information for each and every data element will not be available for every transmission. In many, if not most instances, a substantial number of the data elements will not be known and therefore not included in the transmission. Where it was deemed important, provisions for unknown/not applicable were included (e.g., outcome, route of administration). However, since the transmission is intended to be electronic, it was thought to be unnecessary to include provisions to assign values of unknown for all data elements. Different ways of including the same data have been provided to cope with differing information contents: e.g., age information can be sent as date of birth and date of reaction/event, age at the time of reaction/event, or patient age group according to the available information (see section B.1.2 and the respective user guidance). In this example, age should be provided by the most precise available data element rather than including multiple elements of redundant data.
Structured data are strongly recommended in electronic transmission and provisions for including information in this way have been made. However, structuring of the data also implies the use of controlled vocabularies, which are not yet available for some data elements. Electronic transmission of individual case safety reports should be implemented with MedDRA and the ICH M5 data elements and standards where applicable. The version number of MedDRA for the ICSR should be provided in the new field A.1.0.2 and as indicated in the companion document. MedDRA terms and ICH M5 related standards should be provided as codes.

In certain instances, there are provisions for the transmission of some free text items, including a full text case summary narrative. The transmission of other unstructured data, such as full clinical records or images is outside the scope of this guideline. However technical recommendations are made in the companion document.

1.5 Minimum information

The minimum information for the transmission of a report should include at least one identifiable patient (section B.1), one identifiable reporter (section A.2), one reaction/event (section B.2), and one suspect drug with exceptions as described in user guidance of the section B.4. Because it is often difficult to obtain all the information, any one of several data elements is considered sufficient to define an identifiable patient (e.g., initials, age, sex) or an identifiable reporter (e.g., initials, address, qualification). It is also recognized that the patient and the reporter can be the same individual and still fulfill the minimum reporting criteria. Due to data privacy legislation in some countries the patient's initials cannot be exchanged between countries. However, field B.1.1 may still be populated and user guidance for this field is provided.

In addition, to properly process the report, the following administrative information should be provided: the sender's (case) safety report unique identifier (A.1.0.1), the date of the most recent information (A.1.7), the worldwide unique case identification number (A.1.10), the sender identifier (A.3.1.2), whether this case fulfills the local criteria for an expedited report (A.1.9), the type of report (A.1.4) and in the case of a "Report from study" the study type in which the reaction(s)/event(s) were observed (A.2.3.3).

1.6 General Principles

The complete information available for a case should be provided in each ICSR. This applies to all types of ICSRs, i.e., reports with initial information on the case, follow-up information, and cases highlighted for nullification. The information available should be reported in a fully structured format using the relevant E2B(R) data elements and the applicable standard terminology. Text fields are intended only for additional information, which could not be provided in structured format using a reference standard terminology. However, a case narrative, i.e., a description of the case, should be provided (section B.5). For international transmissions, English is the generally accepted language.

2. GUIDELINE: CONTENT OF THE DATA ELEMENTS

The message content contains header information followed by E2B Data Elements. See the M2 ICSR Message Specification for information about the header.

The data elements are divided into sections pertaining to:

A: Administrative and Identification Information
- A.1 - Identification of the case safety report
- A.2 - Primary source(s) of information
- A.3 - Information on sender and receiver of case safety report

B: Information on the Case:
- B.1 - Patient characteristics
- B.2 - Reaction(s)/event(s)
- B.3 - Results of tests and procedures relevant to the investigation of the patient
- B.4 - Drug(s) information
- B.5 - Narrative case summary and further information

A. ADMINISTRATIVE AND IDENTIFICATION INFORMATION

A.1 Identification of the case safety report

A.1.0.1 Sender's (case) safety report unique identifier

User Guidance:

This identifier should remain constant in subsequent transmissions of the case by the same sender. Retransmitters should replace this value with their own unique identifier. The value should be a concatenation of "country code-company or regulator name-report number". Country code is the country of the primary source of the report (A.1.1). The company or regulator name is an internationally unique abbreviation or code for the sender's organisation. The report number is the organisation's international case number. Each component is separated from the other by a hyphen. For example, a report transmitted by a company to a regulatory authority concerning a case from France would populate A.1.0.1 with "FR-companyname-12345" where 12345 is a company's unique case report number.

In the case of an organisational change, (e.g., a merger between companies or a name change), follow up reports should be identified in A.1.0.1 by the identifier of the newly named organisation. However, the worldwide unique case identifier number (A.1.10) used in previous transmissions of the case should remain the same (see below).

A.1.0.2 MedDRA version used in this case safety report

User Guidance:

See the companion document for appropriate format of the version. Only one version of MedDRA should be used to code all the relevant data elements. The version that should be used is always the last one released by the maintenance organisation.

A.1.1 Identification of the country of the primary source

User Guidance:

Generally, this item would be the only country provided. This country should be that of the reporter (see Glossary). Provisions have been made to include other countries for unusual cases concerning foreign travel and sources of manufactured material

(A.1.2 and B.4.k.2.3). For example a patient living in country A experienced headache while traveling in country B; this headache was suspected to be an adverse drug reaction and was reported by a healthcare professional in country C. This field should be populated with the code of country C. See the companion document for appropriate country codes.

A.1.2 Identification of the country where the reaction/event occurred

User Guidance:

This should be the country where the reaction occurred (i.e., the reaction occurred while the patient was traveling, but the report was made by a health professional on the patient's return). In the example provided in the paragraph above, this field should be populated with the code of country B, the country in which the traveler experienced the reaction.

A.1.3 Date of this transmission

User Guidance:

A full precision date should be used (i.e., day, month, year)

A.1.4 Type of report

- Spontaneous report
- Report from study
- Other
- Not available to sender (unknown)

User Guidance:

A separate category for the designation of a literature source is covered in item A.2.2 and is not duplicated in this section which is intended to capture the type of report. If the case in the literature arises from spontaneous observations, "type of report" should be ***Spontaneous report***. If the case arises from a study, "type of report" should be ***Report from study*** and the field A.2.3.3 should be populated with the appropriate value (see the User Guidance for that field). If it is unclear from the literature report whether or not the case(s) cited are spontaneous observations or whether they arise from a study, then this item should be ***Other***.

Differentiation between types of studies (e.g. clinical trials or others should be given in section A.2.3.3).

The ***Not available to sender*** option allows for the transmission of information by a secondary sender (e.g., regulatory authority) where the initial sender did not specify the type of report; it differs from ***Other,*** which indicates that the sender knows the type of report but cannot fit it into the categories provided.

A.1.5 Seriousness

User Guidance:

It is assumed that case seriousness is assessed by the reporter, otherwise it should be assessed by the sender.

A.1.5.1 Serious

-Yes/no

A.1.5.2 Seriousness criteria (more than one can be chosen)

- Results in death
- Is life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity (as per reporter's opinion)
- Is a congenital anomaly/birth defect
- Other medically important condition

User Guidance:

The terms ***life-threatening*** and ***other medically important condition*** are defined in the ICH E2A and E2D guidelines. All the criteria apply to the case as a whole and should not be confused with the outcome(s) of individual reactions(s)/event(s) that are provided in section B.2.i.6. In addition section B.2.i.2.2 can be used to identify the seriousness criteria of each reaction/event in accordance with the user guidance for that section.

A.1.6 Date report was first received from source

User Guidance:

For senders dealing with initial information, this should be the date the information was received from the primary source. When retransmitting information received from another regulatory agency or another company or any other secondary source, A.1.6 should be the date the retransmitter first received the information.

A full precision date should be used (i.e., day, month, year).

A.1.7 Date of the most recent information for this case

User Guidance:

This date should be changed each time follow up information is received by the sender. However if the case is amended for any other reason (e.g., internal review by the sender or expert opinion) this date should not be changed but the field A.1.13 should be populated with the value "amendment" indicating that the case was amended by the sender. (See the User Guidance for the field A.1.13)

Because reports are sent at different times to multiple receivers, the initial/follow up status is dependent upon the receiver. For this reason an item to capture follow-up status is not included. However, the date of receipt of the most recent information taken together with the "sender identifier" (A.3.2) and "sender's (case) report unique identifier" (A.1.0.1) provide a mechanism for each receiver to identify whether the report being transmitted is an initial or follow-up report. For this reason these items are considered critical for each transmission.
A full precision date should be used (i.e., day, month, year).

A.1.8 Additional available documents held by sender

A.1.8.1 Are additional documents available?

-yes/no

A.1.8.2 List of documents held by sender

User Guidance:

The documents received from the primary source (e.g., clinical records, hospital records, autopsy reports) should be listed. It is recognized that these documents might not be obtainable in many instances.

A.1.9 Does this case fulfill the local criteria for an expedited report?

- yes/no

User Guidance:

The definition of expedited is dependent upon the local regulatory requirements. This item should be used by the sender to indicate whether the case fulfills the local expedited requirements. When the countries of origin and destination of the transmission differ, the receiver should be aware that the information might not be applicable to the receiver's country's regulatory requirements.

A.1.10 Worldwide unique case identification number.

User Guidance:

Only A.1.10.1 or A.1.10.2 should be used. No case should 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. See examples in attachment 2.

A.1.10.1 Regulatory authority's case report number

A.1.10.2 Other sender's case report number

A.1.11 Other case identifiers in previous transmissions

-yes

User Guidance:

This item should be completed only if the answer is yes.

A.1.11.1 Source(s) of the case identifier (e.g., name of the company, name of regulatory agency) (repeat as necessary)

User Guidance:

This repeatable item should be used in conjunction with A.1.11.2 to provide all other case identifiers electronically transmitted, perhaps by multiple other senders. If the case has been received from another sender all other case identifiers included in A.1.11.1 and A.1.11.2 should be present. In addition the identifier of the previous sender (A.1.0.1) should be included here by the retransmitter. See examples in attachment 2

A.1.11.2 Case identifier(s)

A.1.12 Identification number of the report which is linked to this report (repeat as necessary)

User Guidance:

This section should be used to identify reports or cases that warrant being evaluated together. This includes, but is not limited to, a mother-child pair where both had reactions/events, siblings with common exposure, several reports involving the same patient (e.g., a report sent via paper without a valid E2B/M2 electronic report identifier), several similar reports from same reporter (cluster). The reason for the linkage between ICSRs should be provided in B.5.4. See examples in attachment 2.

A.1.13 Report nullification / amendment

- nullification

- amendment

User Guidance:

This item should be used to indicate that a previously transmitted report is either considered completely void (nullified), (for example when the whole case was found to be erroneous), or amended, (for example when after an internal review or according to an expert opinion some items have been modified such as adverse event terms, seriousness, seriousness criteria or causality assessment). It is important to use the same case report number previously submitted. The date originally reported in A.1.7 should not be changed in an amended report.

A.1.13.1 Reason for nullification / amendment (free text)

A.1.14 Was the case medically confirmed, if not initially from a health professional?

- yes/no

User Guidance:

This section should be completed if the primary source of information was a lawyer, consumer, or other non-health professional. It is important because of regional differences in regulations concerning lay reports.

A.2 Primary source(s) of information

The primary source(s) of the information is the person who reports the facts. This should be distinguished from senders (secondary sources) who are transmitting the information, (e.g., industry to regulatory authority).

Any or all of the three subsections (A.2.1, A.2.2, A.2.3) can be used. In the case of a published study or published individual case, the reporter would be the investigator or first author, and details on publication and trial type should also be provided.

A.2.1 Primary source(s) (repeat as necessary)

A.2.1.1 Reporter identifier (name or initials)

User Guidance:

The identification of the reporter could be prohibited by certain national confidentiality laws or directives. The information should be provided when it is in conformance with the regional confidentiality requirements. In any case, at least one subsection should be completed to ensure there is an identifiable reporter. If only the name of the reporter is known and providing this name is prohibited because of confidentiality requirements, initials can be used.

A.2.1.2 Reporter's address

User Guidance:

See the companion document for format specifications.

A.2.1.3 Country

User Guidance:

See the companion document for format specifications.

A.2.1.4 Qualification

- ***Physician***
- ***Pharmacist***
- ***Other health professional***
- ***Lawyer***
- ***Consumer or other non health professional***

User Guidance:

In some regions, consumer and lawyer reports should be transmitted only when there is medical confirmation.

A.2.2 Literature reference(s)

User Guidance:

References should be provided in the Vancouver Convention (known as "Vancouver style") as developed by the International Committee of Medical Journal Editors. The standard format, as well as formats for special situations can be found in the following reference which is in the Vancouver style. International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med 1997; 336:309-15.

A.2.3 Study identification

A.2.3.0 Study registration number

User Guidance

This field should be populated with the study registration number if applicable.

A.2.3.1 Study name

User Guidance:

This field should be populated by the study name as approved by the regulator in each region.

A.2.3.2 Sponsor study number

User Guidance:

This section should be completed only if the sender is the study sponsor or has been informed of the study number by the sponsor.

A.2.3.3 Study type in which the reaction(s)/event(s) were observed

- ***Clinical trials***
- ***Individual patient use*** *(e.g.,"compassionate use" or named patient basis)*
- ***Other studies*** *(e.g., pharmacoepidemiology, pharmacoeconomics, intensive monitoring)*

User Guidance:

This information should be provided if the field A.1.4 Type of report has been populated with "Report from study".

A.3 Information on sender of case safety report

A.3.1 Type

- ***Pharmaceutical company***
- ***Regulatory authority***
- ***Health professional***
- ***Regional pharmacovigilance center***
- ***WHO collaborating center for international drug monitoring***
- ***Other (e.g. distributor, study sponsor, or contract research organization)***

User Guidance:

In this context, a pharmaceutical company includes biotechnology companies and other manufacturers required to submit individual case safety reports.

A.3.2 Sender identifier

User Guidance:

Identifies the sender, (e.g., company name or regulatory authority name). It is important that this item should be completed.

A.3.3 Person responsible for sending the report

User Guidance:

The name of person in the company or agency who is responsible for the authorization of report dissemination. This would usually be the same person who signs the covering memo for paper submissions. The inclusion of the name of this person in the transmission could be subject to national or international regulations.

A.3.4 Sender's address, fax, telephone and E-mail address

B. INFORMATION ON THE CASE

B.1 Patient characteristics

User Guidance:

This section applies to the subject who experienced one or several adverse reactions/events.
In cases where a fetus or nursing infant is exposed to one or several drugs through the parent and experience one or several adverse reactions/events, information on both the parent and the child/fetus should be provided. Reports of these cases are referred to as parent-child/fetus reports. The following general principles should be used for filing these reports.

If there has been no reaction/event affecting the child/fetus, the parent-child/fetus report does not apply; i.e., the B.1 fields below apply only to the parent (mother or father) who experienced the adverse reaction/event.
For those cases describing miscarriage or fetal demise or early spontaneous abortion, only a parent report is applicable, i.e., the B.1. fields below apply to the mother. However, if suspect drug(s) were taken by the father this information should be indicated in the field B.4.k.13.
If both the parent and the child/fetus sustain adverse events, two separate reports, i.e., one for the parent (mother or father) and one for the child/fetus, should be provided but they should be linked by using sections A.1.12 in each report.

If only the child/fetus has an adverse reaction/event (other than early spontaneous abortion/fetal demise) the information provided in this section applies only to the child/fetus, and characteristics concerning the parent (mother or father) who was the source of exposure to the suspect drug should be provided in section B.1.10.

If both parents are the source of the suspect drug(s) then the case should reflect the mother's information in section B.1.10 and the case narrative (section B.5.1) should describe the entire case, including the father's information.

B.1.1 **Patient** (name or initials)

User Guidance:

It is important that this field is populated. The identification of the patient may be prohibited by certain national confidentiality

laws or directives. The information should be provided when it is in conformance with the confidentiality requirements. This also applies to medical record number(s) (B.1.1.1).
If the initials of the patient are unknown to the sender, this field should be populated with "UNKNOWN".
If the initials are known to the sender but cannot be transmitted due to data privacy requirements, this field should be populated with "PRIVACY".

B.1.1.1 Patient medical record number(s) and the source(s) of the record number (if allowable)

User Guidance:

Record numbers can include the health professional record(s) number(s), hospital record(s) number(s), or patient/subject identification number in a study. The source of the number should be specified to ensure the possibility of retrieval when possible and desirable.

B.1.2 Age information

User Guidance:

Only one of the elements describing age should be used. The choice should be based upon the most precise information available.

B.1.2.1 Date of birth

User Guidance:

If the full date of birth is not known, an incomplete date can be used. If only an approximate age is available this information can be captured in section B.1.2.2.

B.1.2.2 Age at time of onset of reaction/event

User Guidance:

If several reactions/events are in the report, the age at the time of the first reaction/event should be used. For fetal reaction(s)/event(s) the next item B.1.2.2.1 "Gestation period when reaction/event was observed in the fetus" should be used.
When providing the age in decades, please note that, for example, the 7th decade refers to a person in his/her 60's.
See the companion document for format specifications.

B.1.2.2.1 Gestation period when reaction/event was observed in the fetus

User Guidance:

The gestation period at the time of exposure is captured in section B.4.k.9. See the companion document for format specifications.

B.1.2.3 Patient age group (as per reporter)

- ***Neonate***
- ***Infant***
- ***Child***
- ***Adolescent***
- ***Adult***
- ***Elderly***

User Guidance:

These terms are not defined in this document and are intended to be used as they were reported by the primary source. This section should be completed only when the age is not provided more specifically in sections B.1.2.1 or B.1.2.2.

B.1.3 Body weight (kg)

User Guidance:

Body weight at the time of the event/reaction.

B.1.4 Height (cm)

B.1.5 Sex

User guidance:

See the companion document for format specifications.

B.1.6 Last menstrual period date

User guidance:

Imprecise dates can be included, (i.e., month, and year or year only). See the companion document for format specifications.

B.1.7 Relevant medical history and concurrent conditions (not including reaction/event)

B.1.7.1 Structured information on relevant medical history including onset and resolution date as well as relevant comments. (repeat as necessary)

Disease / surgical procedure / etc.	Start date	Continuing Y/N/U	End date	Comments	Family history Y

User Guidance:

Medical judgment should be exercised in completing this section. Information pertinent to understanding the case is desired (such as diseases, conditions such as pregnancy, surgical procedures, psychological trauma, risk factors, etc.). In case of prematurity, the birth weight should be recorded in the comments. Each of the items in the table can be repeated as appropriate. If precise dates are not known and a text description aids in understanding the medical history, or if concise additional information is helpful in showing the relevance of the past medical history, this information can be included in the Comments column. In order to identify relevant medical information of the family (e.g., hereditary diseases) a flag should be added to the appropriate disease(s).
MedDRA LLT code should be used in the main descriptive column for disease/surgical procedure/etc. Imprecise dates can be used for both start and end dates. See the companion document for format specifications for the continuing column.

B.1.7.2 Text for relevant medical history and concurrent conditions (not including reaction/event)

User Guidance:

If structured information is not available in the sender's database, this field should be used. Otherwise, it is preferable to send structured data in segment B.1.7.1.

B.1.8 Relevant past drug history (repeat as necessary)

Name of drug as reported	MedID	PhPID	Start date	End date	Indication	Reactions

User Guidance:

This segment concerns drugs previously taken. It does not concern drugs taken concomitantly or drugs which might have potentially been involved in the current reaction(s)/event(s). Information concerning concomitant and other suspect drugs should be included in section B4. The information provided here can also include previous experience with similar drugs. Medical judgment should be exercised in completing this section. When completing the item concerning the name of the drug, it is important to use the words provided by the primary source. Trade name, generic name or class of drug can be used.
To standardise this information, the ICH M5 guideline should be used. Based on the medicinal product name as reported by the primary source, the most specific identifier, being either the Medicinal Product Identifier (MedID) or the Pharmaceutical Product Identifier (PhPID) should be provided. If a MedID and a PhPID for the reported medicinal product are not available, this field should be left blank.
The term "none" should be used when there is no previous exposure to the drug or vaccine.
MedDRA LLT code should be used in the Indication and Reaction columns. In the event of previous exposure to drug(s) or vaccine(s) without reaction, the MedDRA code "No adverse drug effect" should be used in the Reaction column. Imprecise dates can be used for both start and end dates.

B.1.9 In case of death

B.1.9.1 Date of death

User Guidance:

An imprecise date can be used. See the companion document for format specifications.

B.1.9.2 Reported cause(s) of death (repeat as necessary)

User Guidance:

MedDRA LLT code should be used

B.1.9.3 Was autopsy done?

Yes/No/Unknown

B.1.9.4 Autopsy-determined cause(s) of death (repeat as necessary)

User Guidance:

MedDRA LLT code should be used

B.1.10 For a parent-child/fetus report, information concerning the parent

User Guidance:

This section should be used in the case of a parent-child/fetus report where the parent had no reaction/event. See user guidance for section B.1. Guidance regarding confidentiality is provided in B.1.1, and should be considered before providing the parent identification. For the subsections B.1.10.4 through B.1.10.8, the guidances provided for B.1.3 through B.1.5 and B.1.7 through B.1.8 should be reviewed.

B.1.10.1 Parent identification

B.1.10.2 Parent age information

User Guidance:

The date of birth should be used if the precise birthday is known; otherwise the age should be used.

B.1.10.2.1 Date of birth of parent

User Guidance:

If the full date of birth is not known, an incomplete date can be used. See the companion document for format specifications.

B.1.10.2.2 Age of parent

B.1.10.3 Last menstrual period date

User Guidance:

A full precision date should be used. See the companion document for format specifications. If a precise date is not available, the gestation period at time of exposure in B.4.k.9 should be completed.

B.1.10.4 Body weight (kg) of parent

B.1.10.5 Height (cm) of parent

B.1.10.6 Sex of parent

B.1.10.7 Relevant medical history and concurrent conditions of parent (not including reaction/event)

B.1.10.7.1 Structured information (parent)(repeat as necessary)

Disease / surgical procedure/ etc.	Start date	Continuing Y/N/U	End date	Comments

User Guidance:

MedDRA LLT code should be used in the main descriptive column for disease/surgical procedure/etc.

B.1.10.7.2 Text for relevant medical history and concurrent conditions of parent (not including reaction/event)

B.1.10.8 Relevant past drug history of parent (repeat as necessary)

Name of drug as reported	MedID	PhPID	Start date	End date	Indication	Reactions (if any and known)

User Guidance:

To standardise this information, the ICH M5 guideline should be used. Based on the medicinal product name as reported by the primary source, the most specific identifier, being either the Medicinal Product Identifier (MedID) or the Pharmaceutical Product Identifier (PhPID) should be provided. If a MedID and a PhPID for the reported medicinal product are not available, this field should be left blank. MedDRA LLT code should be used in the Indication and Reaction columns.

B.2 Reaction(s)/event(s)

User Guidance:

The designation of "i" in this section indicates that each item is repeatable and that it corresponds to the same "i" in all subsections. A separate block (i) should be used for each reaction/event term. For example, if two reactions are observed, the first reaction would be described in items B.2.1.0 through B.2.1.6, and the other reaction would be described in items B.2.2.0 through B.2.2.6.

B.2.i.0 Reaction/event as reported by the primary source

User Guidance:

The original reporter's words and/or short phrases used to describe the reaction/event should be provided. These can also be included in the narrative B.5.1.

B.2.i.1 Reaction/event in MedDRA terminology

User Guidance:

Only the MedDRA Lowest Level Term (LLT) most closely corresponding to the reaction/event as reported by the primary source should be provided. In the exceptional circumstance when a MedDRA term cannot be found the sender should use good clinical judgment to complete this item with the best MedDRA approximation (see MedDRA™ TERM SELECTION:POINTS TO CONSIDER). MedDRA terms should be provided as code.

B.2.i.2 Term highlighted by the reporter and seriousness at event level

B.2.i.2.1 Term highlighted by the reporter

- yes, highlighted by the reporter

User Guidance:

A highlighted term is a reaction/event that the primary source indicated was a major concern or reason for reporting the case. If the information is not explicitly provided by the initial reporter the term should not be considered a highlighted term.

B.2.i.2.2 Seriousness criteria at event level (more than one can be chosen)

- Results in death
- Is life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity (as per reporter's opinion)
- Is a congenital anomaly/birth defect

- Other medically important condition

User Guidance:

The seriousness criteria of the reaction/event should be based on the definitions provided in the ICH E2A and E2D guidelines.

B.2.i.3 Date of start of reaction/event

User Guidance:
See the companion document for format specifications.

B.2.i.4 Date of end of reaction/event

User Guidance:

This field should include the date corresponding to the date the reaction/event is assessed as resolved/recovered or resolved/recovered with sequelae (B.2.i.6).

B.2.i.5 Duration of reaction/event

User Guidance:

This section can usually be computed from start/end of reaction/event. Both dates and duration can be useful (e.g., for a reaction/event of short duration such as anaphylaxis or arrhythmia).
Imprecise dates can be used. See the companion document for format specifications.

B.2.i.6 Outcome of reaction/event at the time of last observation

- ***recovered/resolved***
- ***recovering/resolving***
- ***not recovered/not resolved***
- ***recovered/resolved with sequelae***
- ***fatal***
- ***unknown***

User Guidance:

In case of irreversible congenital anomalies the choice ***not recovered/not resolved*** should be used.
"***Fatal***" should be used when death is possibly related to the reaction/event. Considering the difficulty of deciding between "reaction/event caused death" and "reaction/event contributed significantly to death", both were grouped in a single category. Where the death is unrelated, according to both the reporter and the sender, to the reaction/event, death should not be selected here, but should be reported only under section B.1.9.

B.3 Results of tests and procedures relevant to the investigation of the patient

User Guidance:

This section should capture the tests and procedures performed to diagnose or confirm the reaction/event, including those tests done to investigate (exclude) a non-drug cause (e.g., serologic tests for infectious hepatitis in suspected drug-induced hepatitis). Both positive and negative results should be reported. While structured information is preferable, provisions have been made to transmit the information as free text in B.3.2.

B.3.1 Structured information (repeat as necessary)

Date	Test	Result	Unit	Normal low range	Normal high range	More information available (*Y/N*)

User Guidance:

Imprecise dates can be used; units and normal ranges should be in free text unless covered by a controlled vocabulary. The column entitled "more information available" accepts only yes or no (see the companion document for the appropriate format). "Yes" means that more documentation is available upon request e.g., ECG strips, chest Xray. "No" means that no more documentation is available.
MedDRA LLT codes should be used to code test names.

If results and units cannot be split, B.3.2 should be used. More than one test can be included in B.3.2.

B.3.2 Results of tests and procedures relevant to the investigation

B.4 Drug(s) information

User Guidance:

This section covers both suspect drugs and concomitant medications (including biologics). In addition, the section can be used to identify drugs thought to have an interaction. For each drug, the characterization of the drug role (B.4.k.1) is that indicated by the primary reporter, (i.e., the original source of the information) and the sender. The designation of "k" in this section indicates that each item is repeatable and that it corresponds to the same "k" in all subsections. A separate block (k) should be used for each drug. Drugs used to treat the reaction/event should not be included here.

B.4.k.1 Characterization of drug role

Suspect / Concomitant / Interacting / Drug Not Administered / Blinded

User Guidance:

This field contains the characterization of the drug as provided by primary reporter or if this information is missing, by the sender. All spontaneous reports should have at least one suspect drug (see Section 1.5). If the reporter indicates a suspected interaction, "***interacting***" should be selected. All interacting drugs are considered to be suspect drugs.

"***Drug not administered***" can be used for example in two circumstances:

- in clinical trial: if the adverse event occurred after the informed consent was signed but prior to the administration of the study drug e.g., during the screening period or the washout procedure. In general the adverse event should be reported as due to the trial procedure. In that case, the rest of the section B.4 should be left blank and the information on the suspect cause of the event should be provided in the section B.5.
- medication error: if the patient did not receive the actual prescribed drug but another one, repeatable section B.4 should be completed with the information about the prescribed drug (including the fact that it was not administered), as well as the information on the dispensed drug as the "suspect" drug.

"***Blinded***":

The ICH E2A guideline recommends that the case safety reports with blinded therapy should not be reported. However, if it is important to exchange a case safety report during a clinical trial, this value should be used. In that case the fields of the section B.4.k.2 Drug identification should be populated with the characteristics of all the blinded study drug(s).

B.4.k.2 Drug identification

User Guidance:

Medicinal product names and active ingredient names should be provided as they were reported. To standardise this information, the ICH M5 guideline should be used. In case of investigational drugs, only a code might be known and provided. If more than one active ingredient is specified, each should be included in item B.4.k.2.2,and can be repeated as necessary.

B.4.k.2.0 Medicinal product unique identifier

User Guidance:

Based on the medicinal product name as reported by the primary source, the most specific identifier either the Medicinal Product Identifier (MedID) or the Pharmaceutical Product Identifier (PhPID) should be provided. If a MedID and a PhPID for the reported medicinal product are not available, this field should be left blank.

B.4.k.2.0.1 MedID and MedID operation date

B.4.k.2.0.2 PhPID and PhPID operation date

B.4.k.2.1 Medicinal product name as reported by the primary source

User Guidance:

The name should be that used by the reporter. It is recognized that a single product can have different proprietary names in different countries, even when produced by a single manufacturer.

B.4.k.2.2 Active ingredient identifier (repeat as necessary)
User Guidance:

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

B.4.k.2.2.1 Active ingredient name
B.4.k.2.2.2 Active ingredient TermID and TermID operation date

B.4.k.2.3 Identification of the country where the drug was obtained.
User Guidance:

See the companion document for the appropriate codes and format.

B.4.k.3 Holder and authorization/application number of drug
User Guidance:

If the ICH M5 MedID is not available for the reported medicinal product, the name of the holder should be provided with the authorization number in the country where the drug was obtained when the case report is sent to that country. These items apply to both applications and authorizations. Pharmaceutical companies should provide this information for their own suspect drug(s).

B.4.k.3.1 Authorization/Application Number
B.4.k.3.2 Country of authorization/application
User Guidance:

See the companion document for the appropriate codes and format.

B.4.k.3.3 Name of holder/applicant

B.4.k.4 Structured Dosage Information (repeat as necessary)
(e.g., 2 mg three times a day)

B.4.k.4.1 dose (number)	*2*
B.4.k.4.2 dose (unit)	*mg*
B.4.k.4.3 number of separate dosages	*3*
B.4.k.4.4 number of units in the interval	*1*
B.4.k.4.5 definition of the interval unit	*day*

User Guidance:

For B.4.k.4.2 the dose unit should be provided in accordance with the ICH M5 units and measurements controlled vocabulary if available. For each unit, the respective TermID and the TermID operation date should be specified. Please note the above side-by-side illustration of how the structured dosage should be provided. For the more complex example of 5mg (in one dose) every other day, subsections B.4.k.4.1 through B.4.k.4.5 would be 5, mg, 1, 2, day, respectively. In the same way, 50mg daily would be 50, mg, 1, 1, day.

In the case of a parent-child/fetus report, the dosage section applies to the parental dose.
If any of these pieces of information is unknown, the field should be left blank.
For a dosage regimen that involves more than one dosage form and/or changes in dosage, the information should be provided in section B.4.k.4.10 as text. Categories for "definition of the interval unit" are described in attachment 1

B.4.k.4.6 Date of start of drug

B.4.k.4.7 Date of last administration
User Guidance:

For ongoing drug administration after the onset of the reaction/event, this item should be blank and Action(s) taken with drug (B.4.k.11) should be used.

B.4.k.4.8 Duration of drug administration

User Guidance:

This item should be used if exact dates of drug administration are not available at the time of the report, but there is information concerning the duration of drug administration. The information requested is the overall duration of drug administration and covers intermittent administration. See the companion document for the appropriate format.

B.4.k.4.9 Batch/lot number

User Guidance:

This information is particularly important for vaccines and biologics. The most specific information available should be provided. For expiration date and other related information, see additional information on drug (B.4.k.13).

B.4.k.4.10 Dosage text

User Guidance:

This item should be used in cases where provision of structured dosage information is not possible.

B.4.k.5 Cumulative dose to the reaction/event

User Guidance:

The cumulative dose provided should be the total dose administered until the first sign, symptom or reaction. Where possible, cumulative dose to the reaction/event should be structured as follows: (For standardised units see the user guidance of B.4.k.4.2.)

B.4.k.5.1 cumulative dose to first reaction (number)

B.4.k.5.2 cumulative dose to first reaction (unit)

B.4.k.6 Pharmaceutical Dose form

User Guidance:

Pharmaceutical dose form should be provided as TermID using the ICH M5 pharmaceutical dose form controlled vocabulary. If the pharmaceutical dose form TermID is not available, free text in B.4.k.6.1 should be used.

B.4.k.6.1 Pharmaceutical dose form

B.4.k.6.2 Pharmaceutical dose form TermID and TermID operation date

B.4.k.7 Route of administration

User Guidance:

Route of administration should be provided as TermID using the ICH M5 Route of administration controlled vocabulary. If the route of administration TermID is not available, free text in B.4.k.7.1 should be used. For a parent-child/fetus report, this indicates the route of administration of a drug given to the child/fetus. This is usually an indirect exposure, such as transmammary, but can include more usual routes of administration for other drugs given to the child. The parent's route of administration should be provided in B.4.k.8.

B.4.k.7.1 Route of administration

B.4.k.7.2 Route of administration TermID and TermID operation date

B.4.k.8 Parent route of administration (in case of a parent child/fetus report)

User Guidance:

This section should be used in a parent-child/fetus report and linked parent reports to indicate the route of administration to the parent. The parent route of administration should be provided as TermID using the ICH M5 Route of administration controlled vocabulary. If the Route of administration TermID is not available, free text in B.4.k.8.1

should be used.

B.4.k.8.1 Parent Route of administration
B.4.k.8.2 Route of administration TermID and TermID operation date

B.4.k.9 Gestation period at time of exposure
User Guidance:

The gestational age at the time of the earliest exposure should be used. Gestation period at time of exposure should be expressed by providing both a number and designation of units of days, weeks, months or trimester. See the companion document for format specifications.

B.4.k.10 Indication for use in the case (repeat as necessary)
User Guidance:

The indication as reported by the primary source should be provided in B.4.k.10.1. The MedDRA LLT code should be used in B.4.k.10.2.

B.4.k.10.1 Indication as reported by the primary source
B.4.k.10.2 Indication in MedDRA terminology (LLT code)

B.4.k.11 Action(s) taken with drug
- Drug withdrawn
- Dose reduced
- Dose increased
- Dose not changed
- Unknown
- Not applicable

User Guidance:

These data, taken together with the outcome of the reaction (B.2.i.6), provide the information concerning dechallenge. "***Not applicable***" should be used in circumstances such as when the patient has died or the treatment had been completed prior to reaction/event.

B.4.k.12 Drug-reaction(s)/event(s) matrix (repeat B.4.k.12.1 through B.4.k.12.4 as necessary)
B.4.k.12.1 Reaction(s)/event(s) assessed
User Guidance:

Generally the reaction(s)/event(s) assessed are ordered from the most important or the most serious to the least important. MedDRA LLT code should be used.

B.4.k.12.2 Relatedness of drug to reaction(s)/event(s) (repeat B.4.k.12.2.1 through B.4.k.12.2.3 as necessary)
User Guidance:

This section provides the means to transmit the degree of suspected relatedness of each drug to the reaction(s)/event(s). The repeating items could also be used to provide the assessment of relatedness by different sources or methods of assessment. For the purpose of reporting, there is an implied suspicion of causality for spontaneous reports. It is recognized that information concerning the relatedness, especially for spontaneous reports, is often subjective and might not be available.
• The following example illustrates the extensive functionality contained in this section.
• Assume a patient being treated with two medications: Drug A and Drug B.
• Assume the patient has had three adverse events: Event 1, Event 2, and Event 3
• The reporter provided assessment of causality for events 1 and 2 for both Drug A and Drug B, but not for either drug concerning event 3. The reporter's assessment of causality is based on overall impression, which the sender codes as "global introspection".
• The sender applies two methods of causality assessment, one with an algorithm (coded algorithm) and the other a

bayesian analysis that provides a decimal probability (coded Bardi) but the sender does so only for the drug the sender manufactures (in this case Drug A).

• From the above there are 4 sets of data for the reporter (2drugsX2eventsX1method of assessment) and 6 sets for the sender (1drugX3eventsX2methods of assessment) for a total 10 sets of data.

• The appropriate item with the information is B.4.k.12 2(and its 3 subfields 1-3). In this example, k is replaced by Drug A and Drug B respectively. Please note the subfields 1-3 are repeatable. Thus:

B.4.k.12.1	B.4.k.12.2.1	B.4.k.12.2.2	B.4.k.12.2.3
k(1) = DRUG A			
event1	reporter	global introspection	related
	company	algorithm	possibly related
	company	Bardi	0.76
event2	reporter	global introspection	not related
	company	algorithm	possibly related
	company	Bardi	0.48
event3	company	algorithm	unlikely related
	company	Bardi	0.22
k(2) = DRUG B			
event1	reporter	global introspection	not related
event2	reporter	global introspection	not related

The order of the rows is not important since each one represents a complete set, however, the E2B message and M2 specifications state that all assessments for Drug A (k=1) should appear before Drug B (k=2).

For subsection B.4.k.12.1 MedDRA LLT codes should be used. Subsections B.4.k.12.2.1 through B.4.k.12.2.3 do not call for a standardised methodology.

B.4.k.12.2.1 Source of assessment (e.g., initial reporter, investigator, regulatory agency, company)

B.4.k.12.2.2 Method of assessment (e.g., global introspection, algorithm, Bayesian calculation).

B.4.k.12.2.3 Result

B.4.k.12.3 Time intervals between drug administration and start of reaction/event

User Guidance:

The major uses of intervals are to cover circumstances both in which the dates are known but the interval is very short (e.g., minutes, such as in anaphylaxis), and in which only imprecise dates are known but more information concerning the interval is known. Dates if available, should be transmitted in the appropriate items, rather than intervals. If the sender wants to provide time intervals as well then the first day of administration should be counted as "1".

The complexity of using intervals highlights the desirability of providing dates. See the companion document for format specifications.

B.4.k.12.3.1 Time interval between beginning of drug administration and start of reaction/event

B.4.k.12.3.2 Time interval between last dose of drug and start of reaction/event

B.4.k.12.4 Did reaction recur on readministration?

- yes/no/unknown

User Guidance:

Unknown indicates that a rechallenge was done but it is not known whether the reaction recurred. This field should not be completed if it is unknown whether a rechallenge was done.

B.4.k.13 Additional information on drug

User Guidance:

This should be used to specify any additional information pertinent to the case that is not covered by above sections (e.g., beyond expiration date, batch and lot tested and found to be within specifications). This item can also be used to provide additional information concerning the indication for the drug. For cases where the suspect drug was taken by the father, this should be indicated in this field as e.g., Drug taken by the father.

B.5 Narrative case summary and further information (repeat as necessary)

B.5.1 Case narrative including clinical course, therapeutic measures, outcome and additional relevant information

User Guidance:

A focused, factual and clear description of the case should be given, including the words or short phrases used by the reporter.

B.5.2 Reporter's comments

User Guidance:

This item should be used to include the reporter's comments on the diagnosis, causality assessment or other issues considered relevant.

B.5.3 Sender's diagnosis/syndrome and/or reclassification of reaction/event (repeat as necessary)

User Guidance:

This section provides the sender with an opportunity to combine signs and symptoms that were reported into a succinct diagnosis. The reasoning would be included in section B.5.4. MedDRA LLT code should be used.

B.5.4 Sender's comments

User Guidance:

This section provides information concerning the sender's assessment of the case and can be used to describe disagreement with, and/or alternatives to the diagnoses given by the initial reporter. In case of linkage of multiple ICSRs using A.1.12, the reason should be provided in these comments.

3. GLOSSARY

Parent-child/fetus report: Report in which the administration of medicines to a parent results in a suspected reaction/event in a child/fetus.

Receiver: The intended recipient of the transmission.

Reporter: Reporter is the primary source of the information, i.e., the person who initially reports the facts. This should be distinguished from the sender of the message, though the reporter could also be a sender.

Sender: The person or entity creating the message for transmission. Although the reporter and sender can be the same person, the function of the sender should not be confused with that of the reporter.

ATTACHMENT 1

Definition of Interval List

Minutes
Hours
Days
Weeks
Months
Years
Cyclical
As necessary
Total

ATTACHMENT 2

Examples of how to populate fields relevant to identifying cases and their reports

The figure provides an example of how one would populate the fields relevant to identifying cases and their reports. Patient XX suffers three separate adverse events (AE1, AE2, AE3) spaced over a time period.

Example of a simple single report from a company to a regulator

Hospital X reports AE1 to Company K who then in turn sends ICSR1 to Regulator. Population of relevant fields for this case is illustrated in the first row of the table. Company K populates A.1.0.1 with Company K's (case) safety report unique identifier "JP-K-001".

Company K populates A.1.10.2 with "JP-K-001" because company K is the initial sender of the report. Because there has not been a previous E2B/M2 electronic report, the identifiers in A.1.0.1 and A.1.10.2 are the same.

Example of company to company to company to regulator transmission

Hospital X reports AE1 to Company B who then in turn sends ICSR2 to Company C.

Population of relevant fields for this case is illustrated in the second row of the table. Company B populates A.1.0.1 with Company B's (case) safety report unique identifier "JP-B-001".

Company B populates A.1.10.2 with "JP-B-001" because company B considers itself the initial sender of the report because it is unaware that Company K also sent an ICSR for this case.

Company C sends ICSR3 to Company D. The third row of the table indicates how Company C populates the relevant fields. Company C populates A.1.0.1 with "JP-C-001".

Company C populates A.1.10.2 with "JP-B-001", leaving the field unchanged from the way Company B populated it. In addition, Company C populates A.1.11.1 (Source of the case identifier) with the name of company B, "B". A.1.11.2 is populated with Case Identifier in the Previous Transmission by Company B "JP-B-001".

Company D sends ICSR4 to Regulator. The fourth row of the table indicates how Company D populates the relevant fields. Company D populates A.1.0.1 with "JP-D-001". Company D retains in fields A.1.10.2, A.1.11.1, and A.1.11.2 the information populated by Company C, and Company D adds to the retained information in repeatable field A.1.11.1 "C" to represent that Company C is another source of the case identifier, and Company D adds in field A.1.11.2 "JPC-001" to represent Company C's case identifier from the previous transmission.

Example of a simple single report with follow-up from a company to a regulator

Hospital X reports AE1 to Company E who then in turn sends ICSR5 to Regulator. Population of relevant fields for this case is illustrated in the fifth row of the table. Company E populates A.1.0.1 with Company E's (case) safety report unique identifier "JP-E-001". Company E populates A.1.10.2 with "JP-E-001" because company E is the initial sender of the report.

Because to Company E's knowledge, there has not been a previous E2B/M2 electronic report, the identifiers in A.1.0.1 and A.1.10.2 are the same.

ICSR6 represents Hospital X's follow-up information about AE1 to Company E. Company E submits follow-up to ICSR5 to the regulator. The relevant fields, A.1.0.1 and A.1.10.2, are populated the same as for ICSR5. ICSR6, a follow-up report, is differentiated from ICSR5 by A.1.7, Date of Receipt of the Most Recent Information for this Report.

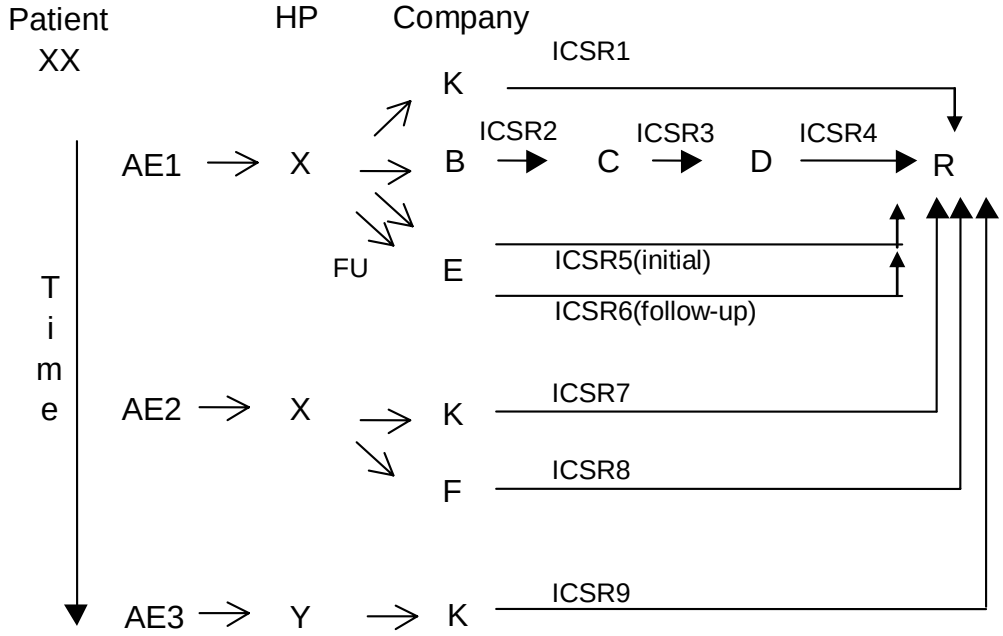
Example of Linking Two Separate Adverse Events Affecting the Same Patient

Patient XX later suffers a separate adverse event, AE2. Hospital X reports AE2 to Company K who then in turn sends ICSR7 to Regulator. Population of relevant fields for this new case is illustrated in the seventh row of the table. Company K populates A.1.0.1 with Company K's (case) safety report unique identifier "JP-K-002". Company K assigns a new (case) safety report unique identifier "JP-K-002" because "JP-K-001", as described above, represent a separate adverse event. Company K populates A.1.10.2 with "JP-K-002" because company K is the initial sender of the report. Because there has not been a previous E2B/M2 electronic report, the identifiers in A.1.0.1 and A.1.10.2 are the same. The previous report from Company K, "JP-K-001", for patient XX should be represented in A.1.12, Identification Number of the Report which is Linked to this Report.

In a contrasting example, Hospital X also reports AE2 to Company F. Company F had not previously received an AE concerning Patient XX, and therefore there is no linked report and A.1.12 is not populated. As in the first example concerning ICSR1, ICSR8 is a simple single report from a company to a regulator.

Example of Linking Three Separate Adverse Events Affecting the Same Patient

Patient XX later suffers a third, separate and distinct adverse event, AE3. Hospital Y reports AE3 to Company K who then in turn sends ICSR9 to Regulator. Population of relevant fields for this new case is illustrated in the ninth row of the table. Company K populates A.1.0.1 with Company K's (case) safety report unique identifier "JP-K-003". Company K assigns a new (case) safety report unique identifier "JP-K-003" because "JP-K-001" and "JP-K-002", as described above, represent separate, adverse events. Company K populates A.1.10.2 with "JPK-003" because company K is the initial sender of the report. The previous reports from Company K, "JP-K-001" and "JP-K-002", for patient XX should be represented in the repeatable field A.1.12, Identification Number of the Report which is Linked to this Report.



AE: Adverse Event report(case)
HP: Hospital observing the event
→ Report of AE
→ ICSR report
FU : Follow up

Tabular representation of fields contents for the above examples

	A.1.0.1.	A.1.10.2	A.1.11.1	A.1.11.2	A.1.12	
ICSR1(K)	JP-K-001	JP-K-001				
ICSR2(B)	JP-B-001	JP-B-001				
ICSR3(C)	JP-C-001	JP-B-001	B	JP-B-001		
ICSR4(D)	JP-D-001	JP-B-001	B C	JP-B-001 JP-C-001		
ICSR5(E)	JP-E-001	JP-E-001				*
ICSR6(E)	JP-E-001	JP-E-001				*
ICSR7(K)	JP-K-002	JP-K-002			JP-K-001	
ICSR8(F)	JP-F-001	JP-F-001				
ICSR9(K)	JP-K-003	JP-K-003			JP-K-001 JP-K-002	

*These cases have different dates of most recent information (A.1.7)