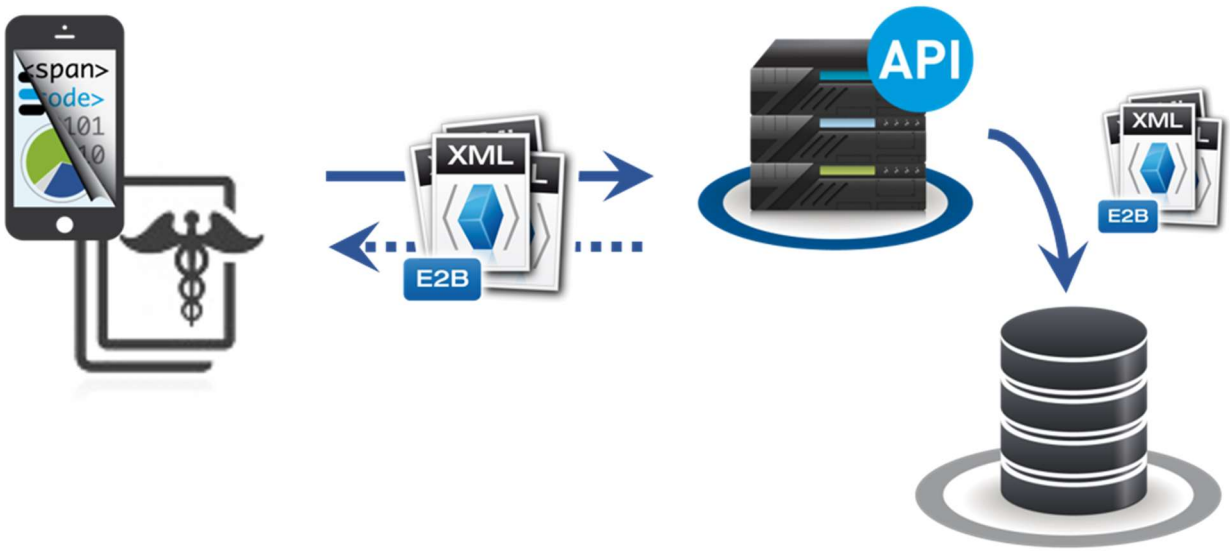
Uppsala Monitoring Centre
– Building a global safety culture

WHO Collaborating Centre for International Drug Monitoring



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Simplified E2B Guide for Primary Reporters

– For faster and more streamlined transfer of safety data. From primary reporters to National Competent Authorities, Pharmaceutical Companies and other organizations collecting such data.

ABOUT THIS DOCUMENT

TARGET AUDIENCE

This document is intended for vendors, systems developers and similar groups that need to understand the fundamentals of E2B. This is to allow systems to create safety data using the standard E2B format and to transfer safety data to recipients capable of managing E2B.

The guide only covers the essentials for a primary reporting system but should also be sufficient in a broader sense. For a complete E2B reference, the "ICH E2B Guideline" should be used (Ref No 1).

This guide only focuses on the E2B message itself (basically a file in XML-format). It does not cover the details of how to transfer the data to the recipient since this may vary from one receiver to another. One example how to define a simplified data transfer standard is described in "WEB-RADR API Implementation Guide" (Ref No 2).

Note!
This guide is only to be used for organizations that need to communicate safety data from their system (one-way).
This guide is not applicable for organizations required to also receive information in E2B format (two-way), i.e. an ICSR management system**.**

DEFINITIONS AND ABBREVIATIONS

Abbreviation	Definition
ADR	Adverse Drug Reaction
E2B	The ICH standard for electronic transfer of ICSRs. In this document E2B refers to R2.
EHR	Electronic Health Records
HCP	Health Care Professional
ICSR	Individual Case Safety Report
Mobile app	Mobile application software
NCA	National Competent Authority
UMC	Uppsala Monitoring Centre
XML	eXtensible Markup Language (Data transfer format)

VERSION

Version type	Version	Date
Document version	1.1	2016-04-15

REFERENCES

Ref No	Name	URL/Document Id
1.	ICH E2B Guideline	http://estri.ich.org/
2.	WEB-RADR API Implementation Guide	01-15-001 The Guide Can be provided upon request from UMC

BACKGROUND

One of the core activities for a National Pharmacovigilance Centre is to handle spontaneous reported Adverse Drug Reactions (ADRs). In order to support overall work flow from collection, processing to evaluation of ADRs, fit-for-purpose ADR management tools are essential. However, the foundation of global pharmacovigilance is to collect, to structure and to share drug safety data with different stakeholders.

E2B

E2B is a standard for sharing of drug safety information developed by ICH. It is primarily used for the reporting of suspected ADRs in the post marketing phase of a medicinal drug (or vaccine). However, it is also used for reporting of ADRs in clinical trials. The standard defines the transmission of individual ADR reports bundled in batches. I.e. it is not a standard for transfer of summary data.

Some crucial parts that the E2B standard defines are:

- Structure of the message to be sent
- Codes to use for the structured data
- Format of data items
- Minimum requirements
- Transfer protocol
- Acknowledgement of received data

The standard was initially defined to be used when transferring safety data between Pharmaceutical Companies and National Competent Authorities (NCAs) and for this purpose the complete complexity of the standard is required.

However, when using the standard for reporting of ADRs from Health Care Professionals (HCPs) or from patients (e.g. data originated from Electronic Health Records (EHR) or when using a mobile app for reporting) a limited set of the standard is sufficient to get the job done.

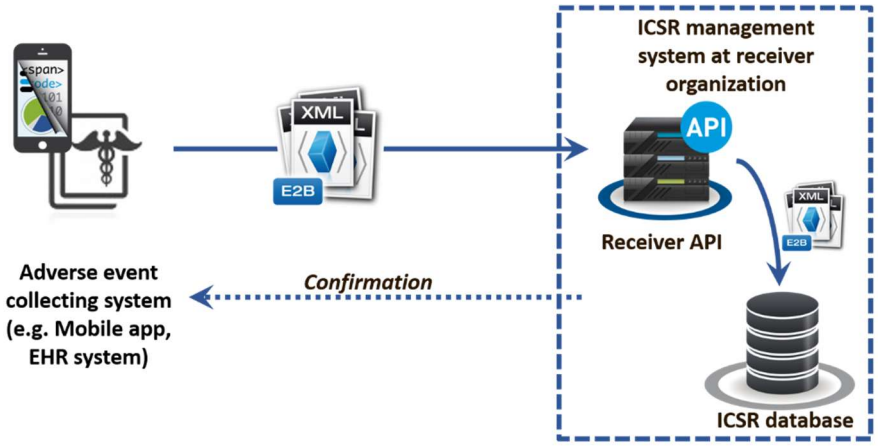


Figure 1 – The scenario suitable for the simplified approach outlined in this document. The key constraint is that the communication of adverse event data is only a one-way, not a two-way communication.

This guide aims to describe the limited set of the E2B standard.

EXAMPLE SET UP USED IN THE GUIDE

In our examples throughout the guide we use a hypothetic patient reporting system (PRS) managed by Acme with the identifier “ACME”. Acme is an organization located in Sweden (country code=SE).

The database system collects data about the patient and extracts essential data to be transferred in an E2B message. The hypothetic NCA in Sweden is named Demo Pharmacy Board with the identifier “DPB”.

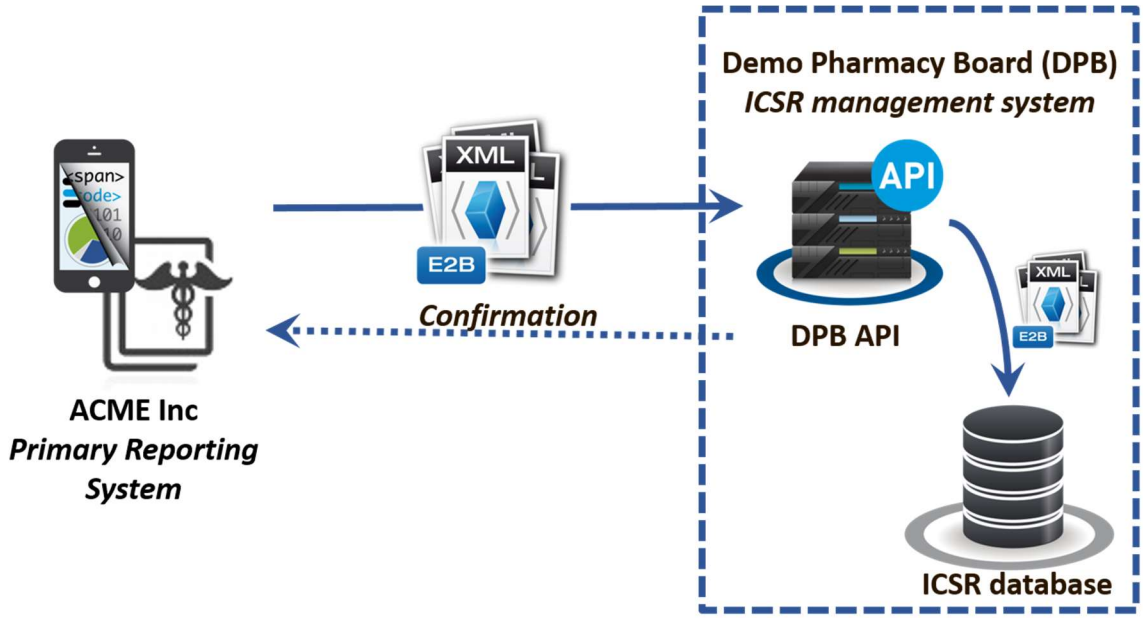


Figure 2 – Organization set up for the example used in this guide

AN EXAMPLE OF A BASIC E2B FILE

Unlike other available E2B guidelines we will start with an example of the simplest file possible. We will explain the structure and the content and thereafter extend the example to become a more realistic scenario.

Below is a complete E2B message that can be understood by any E2B aware system:

```
<?xml version="1.0" encoding="UTF-8"?>
<!DOCTYPE ichicsr SYSTEM "http://eudravigilance.ema.europa.eu/dtd/icsr21xml.dtd">
<ichicsr>
      <ichicsrmessageheader>
            <messagetype/>
            <messageformatversion>2.1</messageformatversion>
            <messageformatrelease/>
            <messagenumb>SE-ACME-12345<messagenumb>
            <messagesenderidentifier>ACME</messagesenderidentifier>
            <messagereceiveridentifier>DPB</messagereceiveridentifier>
                  <messagedateformat>204</messagedateformat>
            <messagedate>20160102093453</messagedate>
      </ichicsrmessageheader>
      <safetyreport>
            <safetyreportid>SE-ACME-012347</safetyreportid>
            <primarysourcecountry>SE</primarysourcecountry>
            <reporttype>1</reporttype>
            <receiptdateformat>102</receiptdateformat>
            <receiptdate>20160101</receiptdate>
            <authoritynumb></authoritynumb>
            <primarysource>
                  <qualification>5</qualification>
            </primarysource>
            <sender>
                  <sendertype>6</sendertype>
                  <senderorganization>Acme</senderorganization>
            </sender>
            <receiver/>
            <patient>
                  <patientbirthdateformat>102</patintbirthdateformat>
                  <patientbirthdate>19790815</patientbirthdate>
                  <reaction>
                        <primarysourcereaction>a diffuse rash on the palms of the hands and on
                                    lower back</primarysourcereaction>
                  </reaction>
                  <drug>
                        <drugcharacterization>1</drugcharacterization>
                        <medicinalproduct>Panadol</medicinalproduct>
                  </drug>
                  <summary>
                        <narrativeincludeclinical>Desc…</narrativeincludeclinical>
                  </summary>
            </patient>
      </safetyreport>
</ichicsr>
```

We will take you through the example from top to bottom. Details of each individual item are to be found in Appendix 1 – Detailed item descriptions.

XML VERSION AND DTD REFERENCE

The first row of the message defines that it is an xml document, the version of the xml standard (should always be 1.0) and the encoding used. `UTF-8` is the recommended encoding however `ISO-8859-1` is also commonly used. Hence, it is of importance that the entire content of the message uses the coding as defined.

```
<?xml version="1.0" encoding="UTF-8"?>
```

The second row specifies the Document Type Definition (DTD) that has been used.

```
<!DOCTYPE ichicsr SYSTEM "http://eudravigilance.ema.europa.eu/dtd/icsr21xml.dtd">
```

ICHICSR

The `ichicsr` node is the container (root node) of the entire E2B message.

ICHICSRMESSAGEHEADER

```
<ichicsrmessageheader>
      <messagetype/>
      <messageformatversion>2.1</messageformatversion>
      <messageformatrelease/>
      <messagenumb>SE-ACME-12345<messagenumb>
      <messagesenderidentifier>ACME</messagesenderidentifier>
      <messagereceiveridentifier>DPB</messagereceiveridentifier>
      <messagedateformat>204</messagedateformat>
      <messagedate>20160102093453</messagedate>
</ichicsrmessageheader>
```

The `ichicsrmessageheader` section contains information about the message itself, such as;

- ✓ `messagedate`: the date 20160102093453 when the message was created according to the date format (as always in E2B for date items).
- ✓ `messagedateformat`: 204 i.e. full date and time with year, month, day, hour, minutes and seconds (CCYYMMDDHHMMSS)
- ✓ `messagesenderidentifier`: the identifier of the sender ACME of the message.
- ✓ `messagereceiveridentifier`: `the` identifier of the receiver DPD of the message.

SAFETYREPORT

In general, when reporting of ADRs from primary notifier systems, there is only one ADR report included in the message. However, according to the E2B standard multiple ADR reports can be included in one message. For each ADR report the safety report section is repeated.

```
<safetyreport>
      <safetyreportid>SE-ACME-012347</safetyreportid>
      <primarysourcecountry>SE</primarysourcecountry>
      <reporttype>1</reporttype>
      <receiptdateformat>102</receiptdateformat>
      <receiptdate>20160101</receiptdate>
```

```
<authoritynumb></authoritynumb>
```

The safety report section contains information about the case, such as;

- ✓ `safetyreportid`: the id number of the case in sender's database system.
  The format of the safety report id is according to ICH E2B standard and must follow below structure: **`SE-ACME-012347`**. **`SE`** is the country code of the sender, **`ACME`** is the identifier of the sender and **`012347`** is the local report number (serial number of the report).
  The reason for this structure is that a safety report id must be unique in order to avoid duplicate reports (Note! follow-up reports should have identical safety report ids).
- ✓ `reporttype`: indicates type of the case report. Most commonly this value is set to 1 – "Spontaneous", however other values are possible to capture. For more details, see Appendix 1 – Detailed item descriptions and Appendix 3 – Study specific information.
- ✓ `receiptdate`: date when the report became available to the sender (Acme in this case)
- ✓ `authoritynumb`: this item is empty in the example. The reason is that the case report has yet not been sent to the NCA. However, at the NCA this item should be assigned with the `safetyreportid` generated by the NCA.

PRIMARYSOURCE

Primary source contains information about the primary reporter of the case, most commonly a HCP or a patient.

```
<primarysource>
      <qualification>5</qualification>
</primarysource>
```

- ✓ `qualification` of the primary reporter is captured with the value 5 -"Consumer or other non-health professional". For additional options, see Appendix 1 – Detailed item descriptions.

SENDER

The sender section describes who the sender of the case is.

```
<sender>
      <sendertype>6</sendertype>
      <senderorganization>Acme</senderorganization>
</sender>
```

- ✓ `senderorganization`: the organization **`Acme`** is the sender of the case.
- ✓ `sendertype` has the value 6 -"Other". For more options see Appendix 1 – Detailed item descriptions.

RECEIVER

The receiver section is rarely used and therefore we have left this section empty in the example.

PATIENT

The patient section is where all the information about the patient, the ADR(s) and the medicinal drug(s) are collected. The section has subsections for the repeatable information.

In the patient section itself the patient details are collected;

```
<patient>
      <patientbirthdateformat>102</patintbirthdateformat>
      <patientbirthdate>19790815</patientbirthdate>
      <reaction>
```

- ✓ `patientbirthdate`: date of birth 19790815 of the patient according to the date format (as always in ICH E2B for date items).
- ✓ `Patientbirthdateformat`: 102 i.e. full date with year, month and day (CCYYMMDD).

REACTION

The reaction section can be repeated as many times as necessary in order to gather information about all reactions the patient may suffer from.

```
<reaction>
      <primarysourcereaction>a diffuse rash on the back and
      on the palm of the hands</primarysourcereaction>
</reaction>
```

In our example the reaction section only has a single item with information about the reaction, more specifically in the free text item `primarysourcereaction`.

The item `primarysourcereaction` should always contain information about the reaction as described by the primary reporter.

Other essential information about a reaction can also be added to the example file, as will be described on page 12.

Note! For systems having MedDRA terminology implemented, the version of MedDRA and the specific MedDRA code for the reaction reported should be captured in below items;

- ✓ `reactionmeddraversionllt`: version of MedDRA terminology.
- ✓ `reactionmeddrallt`: reaction/event code from MedDRA terminology (Lowest Level Term=LLT or Preferred Term=PT).

See Appendix 1 – Detailed item descriptions.

DRUG

Similar to the reaction section, the drug section can also be repeated to give a complete picture of all medications a patient is taking. At least one medicinal drug must be recorded, preferably as a **trade name**, in the medicinalproduct item. This is a free text item that captures up to 70 characters (70AN=AlphaNumeric).

```
<drug>
      <drugcharacterization>1</drugcharacterization>
      <medicinalproduct>Panadol</medicinalproduct>
</drug>
```

In our example the patient was on Panadol (active ingredient is paracetamol). The role of the medicinal drug is also indicated, i.e. whether the medicinal drug is suspected or concomitant. The value 1 in `drugcharacterization` indicates that the medicinal drug was suspected for the actual reaction. For other options see Appendix 1.

Note! For systems having a standardized drug dictionary implemented,the trade name from the dictionary should be captured in same item as above, i.e. in item `medicinalproduct`.

SUMMARY

In our example, the last item with information is the item `narrativeincludeclinical`.

Narratives should include free text information that describes the case as written by the primary reporter, i.e. by the HCP or the patient.

EXTENDING THE EXAMPLE

Our example file (in xml format) contains basic and simple information. However, in most scenarios case reports capture more extensive information about the patient, about the medicinal drugs and the reactions.

By adding additional information to the example file the case report will be more complete. All the items in the examples, and a number of additional items, are described in Appendix 1. However, it does not contain the complete list of items available in the ICH E2B specification.

ADD SOME ADDITIONAL PATIENT INFORMATION

Assume that we would like to include **sex**, **height** and **weight** of the patient in the E2B message. Is this information part of ICH E2B standard? According to Appendix 1 the item names respectively are `patientsex`, `patientweight` and `patientheight`.

The ICH E2B standard also states that **weight** should be expressed in kilogram and that the maximum size of the item is 6 characters (6N=numeric). To indicate **sex** of the patient, coded values 1=male and 2=female are to be used.

Adding the three items to the example file, assuming that we are dealing with a male patient that is 179 cm tall and weighs 79 kilograms would give us the xml "snippet" below.

Note! The correct order of the items in the XML-file is of importance.

```
<patient>
      <patientbirthdateformat>102</patintbirthdateformat>
      <patientbirthdate>19790815</patientbirthdate>
      <patientweight>179</patientweight>
      <patientheight>79</patientheight>
      <patientsex>1</patientsex>
```

ADD MORE INFORMATION ABOUT THE REACTION

Other essential information that adds value to the described reaction is start date `reactionstartdate` and stop date `reactionenddate` of the reaction. The format of the dates according to the ICH E2B standard (see complete list in Appendix 2 – Common code lists in the E2B message) is also required;

602=CCYY
610=CCYYMM
102=CCYYMMDD
203=CCYYMMDDHHMM

Outcome of the reaction `reactionoutcome` also adds value to a case and according to the E2B standard one option (1-6) can be selected. All six options are to be found in Appendix 1 – Detailed item descriptions.

Adding the date items and the outcome of the reaction to the example file would give us the xml "snippet" below.

```
<reaction>
      <primarysourcereaction>a diffuse rash on the palms of the hands
      and on lower back </primarysourcereaction>
      <reactionstartdateformat>102</reactionstartdateformat>
      <reactionstartdate>20151213</reactionstartdate>
      <reactionenddateformat>102</reactionenddateformat>
      <reactionenddate>20151220</reactionenddate>
      <reactionoutcome>1</reactionoutcome>
</reaction>
```

ADD MORE INFORMATION ABOUT THE DRUG

More detailed information about the medicinal drug may be added to the xml-file. E.g. dosage information can be captured as free text information but preferably in a structured format. The route of administration, the start and stop dates of the medicinal drug and the action taken with the drug are other useful information.

In below example the structured dosage information for Panadol is based on the assumption "One gram three times a day". The route of administration `drugadministrationroute` is stated as "oral". For more values, see Appendix 2 – Common code lists in the E2B message.

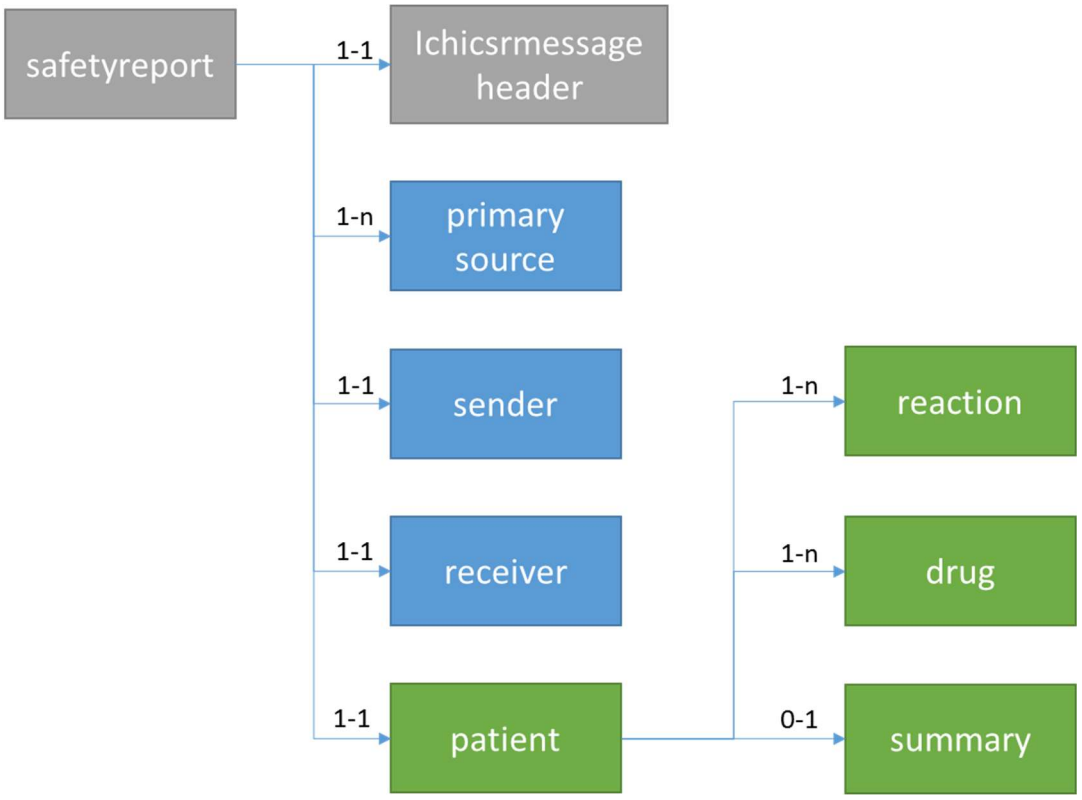
```
<drug>
      <drugcharacterization>1</drugcharacterization>
      <medicinalproduct>Panadol</medicinalproduct>
      <drugstructuredosagenumb>1</drugstructuredosagenumb>
      <drugstructuredosageunit>002</drugstructuredosageunit>
      <drugseparatedosagenumb>3</drugseparatedosagenumb>
      <druginterval dosageunitnumb>1</druginterval dosageunitnumb>
      <druginterval dosagedefinition>804</druginterval dosagedefinition>
      <drugadministrationroute>048</drugadministrationroute>
</drug>
```

E2B STRUCTURE

The example in previous section demonstrated the most important parts of the structure of an E2B message.

Below is a graphical representation of the actual E2B structure in our example.

The grey boxes contain information in order to process the ICSR (i.e. data management). The blue boxes involve information about the reporter, sender and the receiver of the case. And finally, the green boxes contain essential data about the actual case report (information about patient, reaction and medicinal drug).



APPENDIX 1 – DETAILED ITEM DESCRIPTIONS

The below table contains a list of the most important items applicable for primary reporting systems.

Not all items below have been described earlier in this document. It is not a complete description of all available E2B items. For such a description, use the "ICH E2B Guideline" (Ref No 1).

Note! It is not necessary to include all items described in the list below. However, included items must follow same order as they appear in the list.

Node name	Description	Type	Allowed values
Ichicsrmessageheader			
messagetype	Type of message	16 AN	ichicsr
messageformatversion	Version number of the message format	3 AN	2.1
messageformatrelease	Release number of the message format	3 AN	
messagenumber	Unique number of this message	100 AN	
messagesenderidentifier	Identifier of the sender	60 AN	
messagereceiveridentifier	Identifier of the receiver	60 AN	
messagedateformat	Date format	3 N	204 (Appendix 2; date format)
messagedate	Complete date and time of this message	14 N	
safetyreport			
safetyreportid	Unique id of the case in sender's database system	100 AN	Requires the structure: Country code – Organization short name – report id. (i.e. SE-MPA-12345)
primarysourcecountry	Country of the primary source	2 A	
reporttype	Type of report	1 N	1=Spontaneous 2=Report from study 3=Other 4=Not available to sender (unknown)
Serious	Is it a serious case?	1 N	1=Yes 2=No
seriousnessdeath	If Serious is "Yes" above, select appropriate options (Yes and No) for each criterion	1 N	1=Yes 2=No
seriousnesslifethreatening			
seriousnesshospitalization			
seriousnessdisabling			
seriousnesscongenitalanomali			
seriousnessother			
receivedateformat	Date format	3N	102 (Appendix 2; date format)

Node name	Description	Type	Allowed values
receivedate	Date when first information of this case was received	8N	
receiptdateformat	Date format	3N	102 (Appendix 2, date format)
receiptdate	Date when latest information of this case was received (follow-up)	8N	
authoritynumb	Report number at NCA. (In most cases, not present in primary source reporting)		
primarysource			
qualification	Qualification of the reporter	1N	1=Physician 2=Pharmacist 3=Other Health Professional 4=Lawyer 5=Consumer or other non-health professional
If reporttype in safetyreport section is set to 2 – "Report from study" additional study information is required. See Appendix 3 – Study specific information.			
studyname	*Name of study*	*100AN*	
sponsorstudynumb	*Sponsor study number*	*35AN*	
observestudytype	*Type of study*	*1N*	*1=Clinical trials* *2=Individual patient use* *3=Other studies*
sender			
sendertype	Type of sender	1N	1=Pharmaceutical Company 2=Regulatory Authority 3=Health professional 4=Regional PV Center 5=WHO Collaborating Center for International Drug Monitoring 6=Other
senderorganization	Name of the sender organization	60AN	
senderemailaddress	e-mail address of the responsible person at the sender organization	100AN	
receiver			
Note! This section is not mandatory. However, for primary reporting systems this section is required!			
patient			

Node name	Description	Type	Allowed values
patientbirthdateformat	Date Format	3N	102 (Appendix 2; date format)
patientbirthdate	Patient birth date	8N	
patientonsetage	Patient age at onset of reaction	5N	
patientonsetageunit	Patient age unit	3N	800-805 (Appendix 2; time intervals and durations)
patientagegroup	Age group, if birth date not known	1N	1=Neonate 2=Infant 3=Child 4=Adolescent 5=Adult 6=Elderly
patientweight	Patient weight in kg	6N	
parientheight	Patient height in cm	3N	
patientsex	Gender	1N	1=Male 2=Female
patientmedicalhistorytext	Free text description of any relevant medical history for the patient	10000 AN	
reaction			
primarysourcereaction	Reaction/event as reported by primary source	200AN	
reactionmeddraversionllt	MedDRA version	8AN	
reactionmeddrallt	Reaction/event in MedDRA	250AN	
reactionstartdateformat	Date Format	3N	102, 203, 610, 602 (Appendix 2; date format)
reactionstartdate	Start date of reaction	12N	
reactionenddateformat	Date Format	3N	102, 203, 610, 602 (Appendix 2; date format)
reactionenddate	End date of reaction	12N	
reactionduration	Duration of reaction (can be used instead of reactionenddate)	5N	
reactiondurationunit	Unit of duration	3N	801-807 (Appendix 2; time intervals and durations)
reactionoutcome	Outcome of reaction	1N	1=recovered/resolved 2=recovering/resolving 3=not recovered/not resolved 4=recovered/resolved with sequelae 5=fatal 6=unknown
drug			

Node name	Description	Type	Allowed values
drugcharacterization		1N	1=Suspect 2=Concomitant 3=Interacting
medicinalproduct	Name of the drug	70AN	
drugbatchnumber	Batch/lot number (important to capture for biologicals)	35AN	
drugdosagetext	Dosage in free text	100AN	
drugdosageform	Form in free text	50AN	
drugadministrationroute	Route of administration of drug	3N	Appendix 2; route of administration
drugstartdateformat		3N	102, 610, 602 Appendix 2; date format)
drugstartdate	Start of drug intake	8N	
drugenddateformat		3N	102, 610, 602 (Appendix 2; date format)
drugenddate	End of drug intake	8N	
drugtreatmentduration	Duration of drug administration (can be used instead of drugenddate)	5N	
drugtreatmentdurationunit	Unit of the duration	3N	801-806 (Appendix 2; time intervals and durations)
actiondrug	Action taken with drug	1N	1=Drug withdrawn 2=Dose reduced 3=Dose increased 4=Dose not changed 5=Unknown 6=Not applicable
drugrecurreadministration	Did reaction recur on re-administration? (Information whether the drug caused a similar reaction, as drug did before withdrawal)		1=Yes 2=No 3=Unknown
drugadditional	Free text description related to the drug	100AN	
Summary			
narrativeincludeclinical	Free text description of the case	20000AN	

APPENDIX 2 – COMMON CODE LISTS IN THE E2B MESSAGE

Coded values are extensively used in the E2B message as described throughout the guide.

In this appendix, the most commonly used code lists are explained.

DATE FORMAT

The **date format should always precede a date node** and indicates what format has been used for the date string in that specific item.

Code	Description
602	CCYY
610	CCYYMM
102	CCYYMMDD
203	CCYYMMDDHHMM
204	CCYYMMDDHHMMSS

TIME INTERVALS AND DURATIONS

Time intervals and durations use the following code list in E2B

Code	Description
807	Seconds
806	Minutes
805	Hours
804	Days
803	Weeks
802	Months
801	Years
810	Trimester
811	Cyclical
812	As Necessary
813	Total

DRUG ADMINISTRATION ROUTE

The route of administration table below is extensive and several items are probably too difficult for patients to understand.

Based on usage scenario, it might be advisable to simplify the list to only contain the most commonly used routes.

Code	Description
001	Auricular (otic)
002	Buccal
003	Cutaneous
004	Dental
005	Endocervical
006	Endosinusial
007	Endotracheal
008	Epidural
009	Extra-amniotic
010	Hemodialysis
011	Intra corpus cavernosum
012	Intra-amniotic
013	Intra-arterial
014	Intra-articular
015	Intra-uterine
016	Intracardiac
017	Intracavernous
018	Intracerebral
019	Intracervical
020	Intracisternal
021	Intracorneal
022	Intracoronary
023	Intradermal
024	Intradiscal (intraspinal)
025	Intrahepatic
026	Intralesional
027	Intralymphatic
028	Intramedullar (bone marrow)
029	Intrameningeal
030	Intramuscular
031	Intraocular
032	Intrapericardial
033	Intraperitoneal
034	Intrapleural

Code	Description
035	Intrasynovial
036	Intratumor
037	Intrathecal
038	Intrathoracic
039	Intratracheal
040	Intravenous bolus
041	Intravenous drip
042	Intravenous (not otherwise specified)
043	Intravesical
044	Iontophoresis
045	Nasal
046	Occlusive dressing technique
047	Ophthalmic
048	Oral
049	Oropharingeal
050	Other
051	Parenteral
052	Periarticular
053	Perineural
054	Rectal
055	Respiratory (inhalation)
056	Retrobulbar
057	Sunconjunctival
058	Subcutaneous
059	Subdermal
060	Sublingual
061	Topical
062	Transdermal
063	Transmammary
064	Transplacental
065	Unknown
066	Urethral
067	Vaginal

APPENDIX 3 – STUDY SPECIFIC INFORMATION

If a generated case report originates from e.g. a public health program (PHP) with an active monitoring system set up, not collected in a spontaneous way, the case report should be identified as a study report.

To indicate that a report comes from a study the `reporttype` in `safetyreport` section must be set to 2 – "Report from study".

```
<safetyreport>
      <safetyreportid>SE-ACME-012347</safetyreportid>
      <primarysourcecountry>SE</primarysourcecountry>
      <reporttype>2</reporttype>
      <receiptdateformat>102</receiptdateformat>
      <receiptdate>20160101</receiptdate>
```

In addition, details about the specific study/monitoring programme should be entered in three specific study items in the `primarysource` section

```
<primarysource>
      <qualification>5</qualification>
      <studyname>Cohort Event Monitoring programme on Artesunate</studyname >
      <sponsorstudynumb>CEMArt01</sponsorstudynumb>
      <observestudytype>3</observestudytype>
</primarysource>
```

The observestudytype is restricted to three values with the following explanations:

1 – Clinical trials

2 – Individual patient use (E.g. compassionate use programs (CUP) or named patient basis)

3 – Other studies (E.g. pharmacoepidemiology, pharmacoeconomics, intensive monitoring, post marketing surveillance (PMS) etc.).

APPENDIX 4 – AEFI SPECIFIC INFORMATION

If a generated case report originates from an immunization program, i.e. Adverse Event Following Immunization (AEFI) collected in a spontaneous way, the case report should be identified as a spontaneous report.

Set `reporttype` to 1 – "Spontaneous", to indicate an AEFI spontaneous case report in the `safetyreport` section.

```
<safetyreport>
      <safetyreportid>SE-ACME-012347</safetyreportid>
      <primarysourcecountry>SE</primarysourcecountry>
      <reporttype>1</reporttype>
      <receiptdateformat>102</receiptdateformat>
      <receiptdate>20160101</receiptdate>
```

The WHO Global Vaccine Safety Initiative (GVSI) has been appointed to enhance vaccine pharmacovigilance according to the strategic document named Global Vaccine Safety Blueprint. For optimal vaccine safety monitoring and meaningful analysis of AEFI data, systematic and standard collection of critical parameters is essential. A limited number of variables are required to properly manage AEFI information. This includes a unique identification of the report, the primary source of information, patient characteristics, details of the event(s) and vaccine(s) of interest and the possibility of collecting additional information if needed.

A core data set, i.e. 25 AEFI Core Variables, endorsed by the WHO Global Advisory Committee on Vaccine Safety (GACVS) has been developed to allow for comparisons and pooling of essential AEFI information for action.

http://www.who.int/vaccine_safety/initiative/detection/en/

The majority of the **AEFI core elements** can be mapped into ICH E2B specific items. See below specification and table for details.

AEFI Core Variables (Revised Dec 2015)

		Suggested Heading	Description of the Basic core variable
1		Date AEFI report first received at national centre	Date when the information of the AEFI case first reached the national level
2	Identity	Country where this AEFI reported	The name of the country where the data is first entered
3	Identity	*Location (address)*	Geographic location of the case (address)
4		Worldwide unique number	Unique number used for communicating the details of the case at the international level
5	Case	*Patient identifier*	The name of the patient or initials as decided by the country
6	Case	*Date of birth (or)*	Birthday
	Case	Age at time of onset (or)	Age
	Case	Age group at onset	Age Group (< 1 year, 1- 5years, > 5 years)
7	Case	Sex	Male or Female
8	Case	*Medical History*	Free text
9	Vaccine	*Primary suspect vaccine name (generic)*	The vaccine that is suspected to have caused the AEFI
10	Vaccine	Other vaccines given just prior to AEFI	Other vaccines given prior to the AEFI
11	Vaccine	*Vaccine Batch number*	Batch number of all vaccines mentioned above
12	Vaccine	*Vaccine dose number for this particular vaccinee*	The dose number for the vaccinee
13	Vaccine	*Diluent batch/ lot number*	The batch/ lot number of diluent (if applicable)
14	Event	*Date and time of vaccination*	Date and time of vaccination
15	Event	*Date and time of AEFI onset*	Date and time of AEFI onset
16	Event	*Adverse event*	The case diagnosis + signs and symptoms
17	Event	*Outcome of AEFI*	Recovered/resolved; recovering/resolving; not recovered/not resolved; recovered/resolved with sequelae; fatal; unknown
18	Event	*Serious*	If the event resulted in death, threatened the patient's life, caused disability, hospitalization or congenital anomaly
19	Reporter	Name of first reporter of AEFI	Name of first reporter of AEFI
20	Reporter	Institution/location	The place of the reporter (address)
21	Reporter	Position/department	Reporter's designation
22	Reporter	e-mail Id	Reporter's e mail id
23	Reporter	Telephone	Reporters phone number
24	Reporter	Date of report	Date when the report was compiled by the reporter
25	Other	Comments (if any)	Free text

IMPORTANT: *Italics Critical variables*

Red Font: New Variables - GACVS Dec 2015

	AEFI Core Variables	Sensitive information *(for data protection)*	ICH E2B item *for export of data*	Free text item	Item length
1	Date AEFI report first received at National level		<receivedate>		8N
2	Country where the AEFI occurred		<occurcountry>		2A
3	*Location (address)*	x	-		
4	Unique identification of the report		<duplicatenumb>	x	100AN
5	*Patient identifier*		<patientinitial>	x	10AN
6	*Date of birth (or)*		<patientbirthdate>		8N
	Age at time of onset (or)		<patientonsetage>		5N
	Age group at onset		<patientagegroup>		1N
7	Sex		<patientsex>		1N
8	*Medical history*		<patientmedicalhistorytext>	x	10000AN
9	*Primary suspect vaccine name*		<drugcharacterization>1</drugcharacterization>		1N
			<medicinalproduct>	x	70AN
10	Other vaccines given just prior to AEFI		<drugcharacterization>2</drugcharacterization>		1N
			<medicinalproduct>	x	70AN
11	*Vaccine batch/lot number*		<drugbatchnumb>		35AN
12	*Vaccine dose number for the vaccinee*		<drugdosagetext>	x	100AN
13	*Diluent batch/lot number*		<drugadditional>	x	100AN
14	*Date and Time of vaccination*		<drugstartdate>		8N
15	*Date and Time of AEFI onset*		<reactionstartdate>		12N
16	*Adverse event*		<primarysourcereaction>	x	200AN
			<reactionmeddraversionllt>		8AN
			<reactionmeddrallt>		250AN
17	*Outcome of AEFI*		<reactionoutcome>		1N
18	*Serious case*		<serious>		1N
			<seriousnessdeath> <seriousnesslifethreatening> <seriousnesshospitalization> <seriousnessdisabling> <seriousnesscongenitalanomali> <seriousnessother>		1N
19	Name of initial reporter of AEFI case	x	<reportergivename> <reporterfamilyname>		35AN 50AN
20	Institution/Location		<reporterorganization> <qualification> <reporterdepartment>		60AN 1N 60AN
21	Position/Department				
22	E-mail address	x	-		
23	Telephone	x	-		
24	Date of report		<reportercomment>	x	500AN
25	Comment (if any)		<narrativeincludeclinical>	x	20000AN

APPENDIX 5 – THE COMPLETE E2B RELATIONSHIP MODEL DEFINED BY ICH

The below model is copied from the "ICH E2B Guideline" (ref No 1).

It shows the complete E2B data model and indicates all safety data available for transfer, using the E2B standard. The complete model might be relevant for more advanced reporting systems, where safety data from e.g. laboratory tests is available.