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EudraVigilance User Manual

Individual Case Safety Report form

Version 1.1

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Version

Only applicable for updated documents

Describe changes from previous version in the form of a table.

Date	Version number	Summary of changes
23 June 2017	1.0	Original version
22 January 2018	1.1	Section 3.9 (Time-to-Onset and Rechallenge matrix table) updated to explain how the rechallenge information is populated in the ICSR form for the cases submitted under ICH-E2B(R2) format.

Overview

The main objective of this user manual is to provide information to users regarding the new Individual Case Safety Report form (ICSR form). Section 1 provides an introduction and the general principles applied for the creation of the form. Section 2 elaborates how the form can be accessed by the users, and Section 3 provides details on the format and content of the form, including the specificities on the relevant sections and fields.

Section 3 describes all sections of the form with the aim to help users to understand how the individual fields have been populated and which data elements are used to populate the fields.

The term 'data element' is used sometimes in this manual when referring to ICH-E2B(R3) data elements.

The term 'field' is used in this manual when referring to an actual cell within a row or a column in the ICSR form.

The ICSR form is also referred as 'the form' in this user manual.

The figures included in this manual are examples of an ICSR Level 3 form. They have been populated with the aim to illustrate the format and content of the different sections. The data included is fictitious and has no meaning from a safety perspective.

Appendix I to IV provides users with the codes for all the ICH-E2B(R3) data elements used to populate the form per levels of access.

This user manual should be used in conjunction with the supporting documents listed in section 9.

1. Introduction

Following the implementation of the ICH-E2B(R3), the Individual Case Safety Report Form (ICSR form) has been created to provide a readable format for the ICH-E2B(R3) data elements needed to assess the individual case reports of suspected adverse drug reactions (ADR). This form replaces the CIOMS¹ form when this was used to review individual case reports submitted to the EudraVigilance database.

The ICSR form is not a reporting template and it is not intended for the initial reporting of ADRs by patients, consumers or healthcare professionals to regulatory authorities. In the same way, it cannot be used for the reporting of suspected ADRs by Marketing Authorisation Holders (MAHs) to regulatory authorities.

The ICSR form is generated automatically from the EudraVigilance database according to specific rules explained within this user manual. It is implemented according to the level of access established by the EudraVigilance access policyⁱ. Resultantly, there are 3 different ICSR forms: Level 1, Level 2a and Level 3. These 3 forms follow the same principles and structure but contain different ICH-E2B(R3) data elements in order to comply with the EudraVigilance access policy.

1.1. General principles

The ICSR form is populated using the electronic ICH-E2B(R3) data elements submitted to EudraVigilance during the electronic submission of ICSRs. In general these data elements are

¹ International reporting of adverse reactions. Final report of a CIOMS working group. Geneva: CIOMS, 1990

populated in the same way (text, numbers, figures) as they have been submitted by the sender, or sometimes using abbreviations. Furthermore, some fields populated in the form are the result of a calculation from combining two data elements. This user manual explains how the form is populated, the rationale behind certain fields and which specific rules have been followed for the calculations of specific fields.

Information and definitions of the data elements are provided in the ICH E2B Expert Working Group implementation guide for electronic transmission of ICSRsⁱⁱ and the EU ICSR implementation guideⁱⁱⁱ.

Access to EudraVigilance data per stakeholders group is established in the EudraVigilance access policy. Details of the data elements accessible for each Stakeholder group are provided in Annex B of the EudraVigilance access policy.

As the main objective of the form is to present the safety data for analysis of the individual cases during the signal detection, validation and evaluation processes, the form does not contain all the possible ICH-E2B(R3) data elements but rather a selection of those considered necessary to assess the data. Users have other electronic means to retrieve data elements not included in this form that may be needed for other purposes.

It is acknowledged that when the ICSR form is used as a tool for the full revision of the safety data, for instance during the assessment of a signal, this would be performed using forms Level 3 and 2a. The ICSR form Level 1 provides an overview of some core data elements while guaranteeing personal data protection and therefore caution should be exercised when making conclusions based only on the ICSR form Level 1.

This form should be considered as an output from EudraVigilance used to review the safety data and should be used in conjunction with other outputs such as the electronic Reaction Monitoring Report (eRMR), line listings, summary tabulations, Reporting Odds Ratio (ROR) evaluations and other information retrieved from the EudraVigilance database.

The ICSR forms are provided in PDF format.

2. Access to the ICSR form

Access to the ICSR form is provided to the stakeholders by means of the Adrreports.eu portal, the EudraVigilance Data Analysis System (EVDAS) and EudraVigilance WEB trader (EVWEB). Table 1 provides an overview of the ICSR form level of access per stakeholder group and system component.

Table 1. ICSR form level of access per stakeholder group and system component

Stakeholder Group	ICSR form Level	Adrreports.eu portal	EVDAS/ EVWEB
Stakeholder Group I Medicines regulatory authorities, the European commission and the EMA	Level 1	✓	N/A
	Level 2a	N/A	N/A
	Level 3	N/A	✓
Stakeholders Group II Healthcare professionals and the public	Level 1	✓	No access
	Level 2a	N/A	No access
	Level 3	N/A	No access

Stakeholder Group	ICSR form Level	Adrreports.eu portal	EVDAS/ EVWEB
Stakeholders Group III Marketing Authorisation holders	Level 1	✓	✓
	Level 2a	N/A	✓
	Level 3	N/A	Sender based
Stakeholders Group IV Academia	Level 1	✓	No access
	Level 2a	N/A	Via ad-hoc preparation of data set by the Agency following specific request
	Level 3	N/A	No access
Stakeholders Group V WHO – Uppsala Monitoring Centre	Level 1	✓	No access
	Level 2a	N/A	No access
	Level 3	N/A	No access
Stakeholders Group VI Medicines Regulatory Authorities in third countries	Level 1	✓	No access
	Level 2a	N/A	Via ad-hoc preparation of data set by the Agency following specific request
	Level 3	N/A	No access

2.1. Access via Adrreports.eu portal²

The ICSR form Level 1 can be accessed via the European Database of Suspected Adverse Drug Reactions (Adrreports.eu portal). In order to access the ICSR forms the user should first view a line listing of the relevant individual cases. The links to the ICSR forms are provided at the end of the line listing. Instructions about how to retrieve a line listing are provided in the training module:

EV-G3 - ADR website user guide.

2.2. Access via EVDAS

Users of EVDAS can retrieve the ICSR forms by generating first an individual case line listing. Line listings can be accessed directly from the links provided in the eRMR or by using any relevant report from the EVDAS catalogue for which they have access.

Once the line listing has been retrieved, users have the following two options to get the ICSR forms:

1. By using the 'download selected ICSR forms functionality' from the EVDAS output. Users can select all or specific ICSRs. Please be aware that this functionality will not be available from the exported line listing (e.g. Excel, PDF).

² <http://www.adrreports.eu/>

Figure 1. ICSR forms download functionality - EVDAS output example for Stakeholder Group I

Select / Unselect All **Download Selected ICSR forms** Download Selected E2B forms Download Selected Narrative text

MedDRA reported indication All Indications MedDRA Article 57 authorised indication All Product Indications MedDRA/

All Indications All Indications All Product Indications All Product Indications All Patient Medical History All Patient Medica

Select ICSR	EV Safety Report Identifier	Case Report Number	Sender	Report Type	EV Document Type	Country	Receive Date
<input checked="" type="checkbox"/>	EU-EC- [REDACTED]	[REDACTED]	[REDACTED]	Spontaneous	EVPM ICSR(s)	[REDACTED]	[REDACTED]

- By clicking on the individual links provided for each case at the end of the line listing. These links will be active from the line listing output in EVDAS or when exported (e.g. Excel, PDF).

Figure 2. Link to the ICSR form in the EVDAS line listing example for Stakeholder Group I

Structured Medical History (Continuing - Text)	Narrative Present	Narrative, reporter's comments and sender's comments (first 3000 characters)	ICSR	E2B	Complete Narrative, reporter's comments and sender's comments
	Yes (1161 CHARS)		ICSR	E2B	Narrative, reporter comments and sender comments

Instructions for the EVDAS reports are provided in the following training modules:

- EV-G1a - MAH's level 1 access via EVDAS
- EV-G2 - EVDAS Report Manual
- EV-M5a - EVDAS Training for NCAs
- EV-M5b - EVDAS training for MAHs

Depending on the EVDAS registration for the individual users, the system will automatically grant access to the ICSR forms Level 1, 2a and 3 according to the user's profile. Instructions on the registration process can be found via the [EudraVigilance webpage](#).

Marketing Authorisation Holders will get access to the ICSR forms according to the following criteria:

- For ICSRs submitted previously by the specific MAH, access to the ICSR form level 3 is provided ('sender based access').
- For ICSR submitted via the Medical Literature Monitoring Service (MLM), access to the ICSR form level 3 is provided.

- For ICSRs containing a suspect/interacting active substance for which the MAH holds a marketing authorisation of a medicinal product (containing the specific substance) in the EEA, access to the ICSR form level 2a is be provided.
- For ICSRs containing a suspect/interacting combination of active substances for which the MAH holds a marketing authorisation of a medicinal product (containing the specific combination or one of the single active substances) in the EEA, access to the ICSR form level 2a is provided.
- For the remaining ICSRs, the ICSR form level 1 is provided.

2.3. Access via EVWEB

Instructions on the use of EVWEB are provided in the EV-G7- EVWEB User Guide.

Once the ICSR are retrieved from the ICSR tab in EVWEB, the ICSR forms can be retrieved by clicking on the ICSR form tab.

ICSRs section in EVWEB

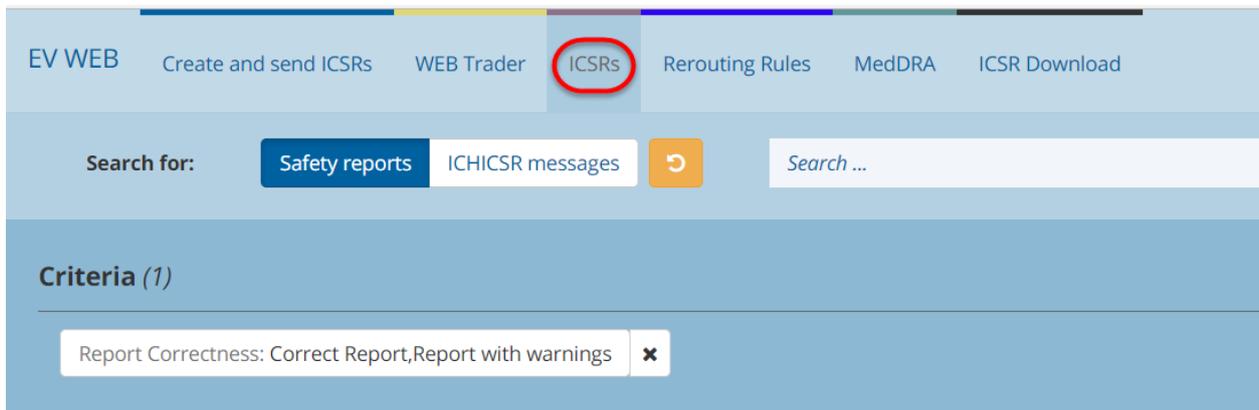


Figure 3. ICSR form link in EVWEB

Open	Follow-up	Add to follow-ups	Add to workspace	Export: ICSR Form	XML	RTF	HTML
Local Report Number	Transmission Date	Safety Report ID					
EU-EC-10000212829	2017/06/13 14:53:29	US-PHV-misspelling-01					
Case Number	Sender Identifier						
US-PHV-misspelling-01	MAHTEST07WT						

3. Format and content of the ICSR form

3.1. General rules

The ICSR form has been created using the data elements described in the EU ICSR implementation guide and the ICH E2B(R3) guideline. As it is not practical and feasible to include all the ICH-E2B(R3) data elements in a readable form, a selection of the data elements was performed focusing on the main objective of the form, which is to facilitate the revision of the safety data submitted to the EudraVigilance.

The sections and fields provided in the form have been structured and displayed in a way that facilitates the analysis of the data and provides the user with the key elements to assess the temporal and causal association between the drugs and the reactions. The different fields are grouped in the form into logical sections (e.g. drug, reaction, medical history), so that the user can easily visualise all the available information for a specific topic.

The ICSR form is stratified in sections, and sections contain fields that are populated using the ICH-E2B(R3) code/verbatim. The population of some fields requires a calculation based on the information reported, these rules are further elaborated in this guideline. Annexes I to IV in this user manual provide the data elements that are used to populate the different fields in the ICSR forms level 1, 2a and 3.

Dates are always populated with the following format through the whole form: DD/MM/YYYY. If the date or month are not reported, then only MM/YYYY or YYYY will be populated in the form.

If a data element has not been reported, or it has been reported with a nullflavor flag, other than MSK (see section 3.2), the field in the form will remain blank.

Some of the rules detailed in this document are only applicable to a specific form level and this is based on the different levels of access. The figures to illustrate the different sections in the form are examples based on form level 3 which is the form that contains the most data fields.

3.2. Nullflavors flags

The ICH-E2B(R3) guideline details the concept of nullflavor. This is based on the HL7/ISO ICSR schema that requires that mandatory data elements must always be part of the ICSR message and should not be empty.

The nullflavor values will be populated in the form only when the value is 'Masked' (MSK). The field in the form will show the code ('MSK') and not the name/verbatim ('Masked')³. Fields reported with nullflavor values other than MSK, will appear as blank in the ICSR forms.

The EU ICSR implementation guide provides guidance for the use of nullflavor flags in the EU.

3.3. Dynamism of the ICSR form

Considering the amount of ICH-E2B(R3) data elements, the multiplicity introduced by the ICH-E2B(R3), the diversity of information provided in the ICSRs and the fact that there are 3 ICSR forms with different level of access, the ICSR form has been implemented in a 'dynamic way' that permits enhancement of visualisation of the data. This dynamism is implemented at section level or at data field level.

Dynamism at section level means that for some specific sections in the form, if no data has been submitted for the entire section, or the only data submitted is a nullflavor flag (other than 'MSK'), the section will not be populated in the form. This is to avoid having completely empty sections in the forms. An example of a dynamic section would be patient's death section. If the case is not fatal and therefore no information is provided in the data elements related to the death (e.g. date of death,

³ The definition of Mask as per the ICH E2B(3) implementation guide is as follows:

There is information on this item available but it has not been provided by the sender due to security, privacy or other reasons. There could be an alternate mechanism for gaining access to this information. Note: using this nullflavor can provide information considered to be a breach of confidentiality, even though no detail data is provided. Its primary purpose is for those circumstances where it is necessary to inform the receiver that the information does exist without providing any detail.

reported cause of death), the section 'death' will not be populated in the form. On the contrary, if there is at least one data element reported, the whole section will be populated.

There are some 'core' sections in the form that will not follow this dynamism (Static Sections) in order for the form to be recognisable by the users and have consistency in the format through the different level of access. It is anticipated that these core sections will contain some data in the vast majority of cases for valid ICSRs. [Table 2](#) provides an overview of the sections that are implemented in a dynamic or static way.

Table 2. Dynamic and static sections of the ICSR forms

ICSR form Section	Dynamic Section	Static Section
General information		✓
Patient		✓
Reaction/Event		✓
Drug Information		✓
Drug Information (cont.)		✓
Time to onset and Rechallenge matrix table	✓	
Relevant medical history and concurrent conditions	✓	
Past drug history	✓	
Death	✓	
Case narrative		✓
Literature reference	✓	
Reporter's comments	✓	
Sender's diagnosis	✓	
Sender's comments	✓	
Laboratory test	✓	
Information concerning the Parent for a Parent-Child/Foetus Report	✓	
Related reports	✓	

Dynamism at data field level means that some specific fields in the form will only appear when data is submitted for that data element. For example, for a spontaneous ICSR, the study registration number and study name within the 'General Information' section will not appear in the form (provided that no data has been submitted in those data fields), as they would appear blank.

The dynamism at the data field level is limited to the following data fields:

- Study registration number
- Study name
- Study type
- Parent route of administration
- Cumulative Dose to First Reaction
- Additional information on drug (free text)
- Text for Relevant Medical History and Concurrent Conditions (not including reaction / event)

- Text for Relevant Medical History and Concurrent Conditions of the parent (not including reaction / event)

For the rest of the fields, that are not subject to this dynamism at data field level, if no data is reported, or it has been reported with a nullflavor (other than 'MSK') the field will remain blank.

3.4. Header

The ICSR form contains a header with the following 3 elements:

1. The EudraVigilance module (i.e. EVPM, EVCTM) is displayed in the left hand corner for the level 2a and 3 forms.
2. The title 'Individual Case Safety Report Form' is displayed in the centre of the header.
3. The word 'EudraVigilance' to reflect the source of this report is included in the right hand corner of the header.

Figure 4. Example of the ICSR header



In line with the level of access, Level 1 and 2a forms will be populated for cases within the EVPM (EudraVigilance post-authorisation module).

3.5. General information

The first table of the form contains administrative and general information on the case. This includes information about the sender, dates, country, studies, reporter's qualification, and also provides information on whether the case is considered serious and if it has been medically confirmed. [Figure 6](#) provides a fictitious example of this section for a Level 3 form.

Figure 5. Example of General Information section for an ICSR form level 3

General Information	
Worldwide Unique Case Identification Number	IT-Beta-lactam-3462832
Sender type	Pharmaceutical Company
Sender's Organisation	Beta-lactam antibiotics S.L.
Date Report Was First Received from Source	10/11/2002
Date of Most Recent Information	10/11/2002
Type of Report	Report from study
Primary source country	IT
Study registration number	983200163
Study Name	Open-label trial and randomized, double-blind, placebo-controlled, crossover trial
Study Type	Clinical trials
Reporter's qualification	Physician, Consumer
Case serious?	Yes
Medically confirmed?	Yes

Some specific rules for the population of the fields in this section are provided in the subsections below.

3.5.1. Worldwide Unique Case Identification Number

In the ICSR form Level 1 published via Adrreports.eu portal, the EudraVigilance local report number is provided.

3.5.2. Sender's organisation

In the ICSR form Level 1 published via Adrreports.eu portal, the sender organisation is displayed as 'EEA Regulator' when C.3.1 (sender type) = 2 (Regulatory Authority) or = 4 (regional pharmacovigilance centre).

3.5.3. Type of report

The type of report within the general information table is populated following these specific rules:

If C.1.3 (type of report) = 1 (Spontaneous report):

- Then C.5.1.r.1 (study registration number), C.5.2 (Study name) and C.5.4 (Study type) fields should not appear in the form unless there is data submitted in any of those fields. If any of the fields are populated, then the 3 cells should appear in the form.

If C.1.3 (type of report) = 2 (Report from study)

- Then C.5.1.r.1 (Study registration number), C.5.2 (Study name) and C.5.4 (Study type) fields should always appear even if there is no data submitted.

If C.1.3 (type of report) = 3 (Other) or 4 (not available to sender)

- Then C.5.1.r.1 (Study registration number), C.5.2 (Study name) and C.5.4 (Study type) fields should appear in the form only if data is submitted in any of those fields. If any of the fields are populated, then the 3 fields should appear in the form.

As the Stakeholders II group only has access to spontaneous reports, C.1.3 (type of report) will always be 'Spontaneous'.

3.5.4. Primary Source Country

This field is populated using C.2.r.3 (Reporter's Country Code) and C.2.r.5 (Primary Source for Regulatory Purposes). C.2.r.3 provides the different countries of the reporters when there is more than one reporter and C.2.r.5 provides the information on which country should be used for regulatory purposes.

In the ICSR form Level 1, this field will be replaced by EEA/Non-EEA.

For legacy data (i.e. data submitted under ICH-E2B(R2) terminology), the population of this field will use the following algorithm:

- use 'occurrence country',
- if missing use 'primary source country',
- if missing, use country code for 'worldwide unique case identification number'.

3.5.5. Reporter's qualification

C.2.r.4 (qualification), which is a repeatable field, can be reported using 5 different values or as nullflavor: 'UNK'. To populate this data element in the ICSR form, each distinct value is concatenated and appears only once regardless of how many times is reported. (e.g. a report containing 5 physicians, 2 pharmacists and 3 consumers should appear as 'physician, pharmacist, consumer').

For Level 1 access provided via Adrreports.eu portal, the information should be grouped as Healthcare professional (HCP)/Non-Healthcare Professional . If there is more than one HCP or non-HCP, these should not be repeated.

If C.2.r.4 = 5 (Consumer or other non-health professional), this should be always abbreviated to 'consumer'.

3.5.6. Case serious?

Seriousness criteria under ICH-E2B(R3) terminology is reported for each individual suspected reaction. The field 'case serious?' within the general information table is populated at case level. This means that if any of the seriousness criteria has been reported for any of the suspected ADRs, the case will be considered serious and the 'case serious?' field will be populated as 'Yes'. If no seriousness criteria has been reported for any of the individual ADRs, the case will be considered non-serious and the field 'case serious?' will be populated as 'No' in the ICSR form.

3.5.7. Medically confirmed?

The field 'Medically confirmed?' is populated using the data element E.i.8 (Medical Confirmation by Healthcare Professional). This field is used for events reported by non-HCPs to indicate whether the occurrence of the event was subsequently confirmed by a HCP. This will be populated at case level, that means that if for any of the suspected ADRs, E.i.8 has been reported as 'true', the field in the form will be populated as 'Yes'. When the E.i.8 has been reported as 'false', or appear as blank the field in the form will be left blank. This to avoid the population of forms non-medically confirmed at case level when at least one reporter is a HCP.

3.6. Patient

This table contains information about the patient concerned in the case report.

Figure 6. Example of Patient section for an ICSR form level 3

Patient						
Initials	Date of Birth	Age	Age Group	Sex	Weight	Height
KD	15/11/1972	43	Adult	Female	53.25 kg	120 cm

3.6.1. Age

In the ICSR form Level 1 published via Adrreports.eu portal, the patient age will be displayed as age group according to an age grouping scheme applied in EV.

In the ICSR form level 2a and 3, the age of the patient is populated using the following algorithm:

- use D.2.2.a and D.2.2.b [reported patient age (number and unit)],

- if missing, use age calculated based on difference between D.2.1 [date of birth] and first E.i.4 [reaction start date], if available in a valid date format DD/MM/YYYY.

In case of multiple reactions that occurred beyond a 12 months onset period, age is not calculated.

3.6.2. Age group

The age group field is populated using D.2.3 [patient age group (as per reporter)]. When this data element is populated with option 1=Neonate (Preterm and Term newborns), this is abbreviated as 'neonate' in the form.

3.7. Reaction / Event

This table contains information about the suspected ADRs/events included in the case. See annexes for the specific fields included in this table.

The number of columns of this table will be fixed but the number of rows will correspond to the number of suspected ADRs submitted, the table therefore will expand accordingly.

Figure 7. Example of Reaction /event section for an ICSR form level 3

Reaction / Event					
MedDRA LLT	Start Date	Stop Date	Duration	Outcome	Seriousness*
Drug reaction with eosinophilia and systemic symptoms	01/08/1992	31/08/2002	30d	Recovering/resolving	hospital.
Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes	05/06/1993			not recovered/not resolved/ongoing	death, life threat., congen.
End stage liver disease	20/08/1992			fatal	death, disability, other
B-cell small lymphocytic lymphoma				recovered/resolved	life threat., other

3.7.1. MedDRA LLT

The name of the suspected ADRs populated in this section will be the verbatim for the corresponding MedDRA Lowest Level Term (LLT) with latest MedDRA version available.

3.7.2. Duration

This field includes the duration of the reaction and is populated using E.i.6a [Duration of Reaction / Event (number)] and E.i.6b [Duration of Reaction / Event (unit)]. If those fields are not reported and full dates are reported for E.i.4. (date of start of the reaction/event) and E.i.5 (date of end of reaction/event), the duration of the reaction is then calculated.

3.7.3. Seriousness

This field provides the seriousness criteria provided per each of the suspected adverse drug reactions (ADRs). If more than one seriousness criteria have been submitted per reaction, the values are concatenated in the same field. The seriousness criteria reported in this field are used to determine whether the case is considered serious or non-serious and populate the field 'case serious?' in the general information table accordingly (see section 3.5.6).

When this field appears blank, it means that the suspected ADR has not been considered serious.

Due to space limitations in the ICSR forms, the seriousness criteria are populated using the following abbreviations:

- death = results in death;
- life threat. = life threatening;
- hospital. = requires hospitalization/prolongation of hospitalization;
- disability = results in disability/incapacity;
- congen. = congenital anomaly/birth defect;
- other = other medically important information.

These abbreviations are also referenced in the footer of the ICSR form (See section 3.21).

Special attention should be given for the cases reported under ICH-E2B(R2) terminology. For those cases the seriousness criteria was reported at case level and it is unknown at the level of the reaction. As the ICH-E2B(R3) terminology provides the seriousness criteria at the level of the reaction, when the ICH-E2B(R2) data is migrated to ICH-E2B(R3) format, all the reactions in the cases will appear with all the serious criteria reported at the level of the case. Figures 9 and 10 show an example of this.

In figure 9, populated under ICH-E2B(R2) format, using only the electronic data elements and without reading the case narrative, it is unknown which reaction involved hospitalisation and which reaction was life threatening; therefore under ICH-E2B(R3) format (figure 10) all the reactions in the case have been allocated with the seriousness criteria 'life threatening' and 'hospitalisation'.

Figure 8. Seriousness criteria reported under ICH-E2B(R2)

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE 48 Year	3. SEX Female	4. WEIGHT	5. HEIGHT	6. EVENT ONSET 10/08/2005	8 - 12. CHECK ALL APPROPRIATE TO ADVERSE REACTION
7+13. DESCRIBE REACTION(S) (including relevant tests/lab data) Verbatim Term: PULMONARY EMBOLISM Reaction / Event (MedDRA ll1t): Pulmonary embolism Outcome of Reaction: Verbatim Term: ACUTE RESPIRATORY FAILURE Reaction / Event (MedDRA ll1t): Acute respiratory failure Outcome of Reaction: Verbatim Term: HYPOTENSION Reaction / Event (MedDRA ll1t): Hypotension Outcome of Reaction: Verbatim Term: ATRIAL FIBRILLATION Reaction / Event (MedDRA ll1t): Atrial fibrillation Outcome of Reaction: recovered/resolved								<input type="checkbox"/> RESULTS IN DEATH <input checked="" type="checkbox"/> INVOLVED OR PROLONGED INPATIENT HOSPITALISATION <input type="checkbox"/> DISABILITY/ INCAPACITY <input checked="" type="checkbox"/> LIFE THREATENING <input type="checkbox"/> CONGENITAL ANOMALY/ BIRTH DEFECT <input type="checkbox"/> OTHER MEDICALLY IMPORTANT CONDITION

Figure 9. Seriousness criteria populated under ICH-E2B(R3) format

Reaction / Event					
MedDRA LLT	Start Date	Stop Date	Duration	Outcome	Seriousness ¹
Pulmonary embolism	09/08/2005				life threat., hospital.
Acute respiratory failure	09/08/2005				life threat., hospital.
Hypotension	09/08/2005				life threat., hospital.
Atrial fibrillation	13/08/2005			recovered/resolved	life threat., hospital.

More information on the impact of the data migration between ICH-E2B(R2) and ICH-E2B(R3) are provided in the following training modules:

- PhV-M2a - Implementing ISO ICSR/ICH E2B(R3): Impact on adverse reaction reporting;

- EV-M5a - EVDAS training for National Competent Authorities.

3.8. Drug information

The drug information provided in the ICSR form is divided in 2 consecutive tables named 'drug information' and 'drug information (cont.)'.

The width of the reaction '*start date*' column vs therapy '*start date*' column as well as reaction '*stop date*' column vs therapy '*stop date*' column are always equal. This is with the aim to enhance visualisation of these 4 fields, so reviewers can easily see the temporal association between the initiation of a treatment and the development of a suspected ADR.

Figure 10. Example of fields to assess temporal association

Reaction / Event					
MedDRA LLT	Start Date	Stop Date	Duration	Outcome	Seriousness*
Drug reaction with eosinophilia and systemic symptoms	01/08/1992	31/08/2002	30d	Recovering/resolving	hospital.
Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes	05/06/1993			not recovered/not resolved/ongoing	death, life threat., congen.
End stage liver disease	20/08/1992			fatal	death, disability, other
B-cell small lymphocytic lymphoma				recovered/resolved	life threat., other

Drug Information							
Role†	Drug	Start Date	Stop Date	Duration	Dose	Units in Interval	Action taken
S	valproic acid/Brand name 200 mg	15/01/1992	01/02/1992	60d	10 mg/kg	1 per 2w	Drug withdrawn
C	Paracetamol/Brand name 500mg	1990			500mg	As necessary	Dose reduced

Figure 11. Example of Drug sections for an ICSR form level 3

Drug Information							
Role†	Drug	Start Date	Stop Date	Duration	Dose	Units in Interval	Action taken
S	valproic acid/Brand name 200 mg	15/01/1992	01/02/1992	60d	10 mg/kg	1 per 2w	Drug withdrawn
C	Paracetamol/Brand name 500mg	1990			500mg	As necessary	Dose reduced

Drug Information (cont.)							
Info‡	Drug	Indication	Cumul. dose to 1st Reaction	Pharm. Form	Route of Admin.	Parent Route of Admin.	Batch / Lot #
7	valproic acid/Brand name 200 mg	Epilepsy grand mal	1200 mg	Prolonged Release Tablets	transplacental	intravenous	AO852369
9	Paracetamol/Brand name 500mg	Headache fullness	15 g	Oral Solution	Oral		123654PP

Additional Information on Drug
The patient received an overdose of valproate as a consequence of a medication error

3.8.1. Drug

The name of the product and substance is populated using the following rules:

Once the ISO IDMP data elements are available, the population of the product and substance information should follow the EU ICSR Implementation guide [I.C.3.6.1.5](#) decision flow diagram for entering Medicinal Product Information.

Before the ISO IDMP data elements are available, the population of the product and substance should use the information as reported by the primary source and should be in line with the population of product and substance in the other EV outputs (EVDAS Line listings, ADR website, etc).

The substance will be populated using the recoded name. For the cases where the substance is not recoded the reported name will be used for the population of the field.

The name of the medicinal product will be implemented according to the following rules:

- ICSR form Level 1 - Centrally authorised medicinal products (CAPs): the recoded name will be used
- ICSR form Level 1 – Nationally authorised medicinal products (NAPs): the name of the product is not provided.
- ICSR form levels 2a and 3 – CAPs and NAPs: The medicinal product name will be populated using the recoded name. For the cases where the product is not recoded the reported name will be used for the population of the field.

If a drug contains more than one value in the subsequent columns (e.g. therapy start date, therapy stop date, therapy duration, indication, pharmaceutical dose, route of administration) the information of those data element is included in the same field which is subdivided without repeating the drug row. The cells and the tables expand according to the fields reported.

3.8.2. Role

This field contains information on the drug role characterisation and it is populated using the data element **G.k.1** (Characterisation of Drug Role).

If one of the drugs reported has been characterised more than once (e.g. paracetamol is reported as suspect and concomitant) the drug-row is repeated to reflect the different drug-role characterisations.

In the section, the drugs are populated in the order they have been reported and according to the following sequence:

1. Suspect drugs
2. Interacting drugs
3. Concomitant drugs
4. Drugs not administered.

Due to space limitations in the ICSR forms, the drug role characterisation is populated using the following abbreviations:

- S=suspect
- C=concomitant
- I=interacting
- N=not administered

These abbreviations are also referenced in the footer of the ICSR form (See section **3.21**).

3.8.3. Duration

This field provides information on the duration of the drug administration. It populated using data elements G.k.4.r.6a [Duration of Drug Administration (number)] and G.k.4.r.6b [Duration of Drug Administration (unit)]. If those fields are not available and full dates are provided for the data elements G.k.4.r.4 (therapy start date) and G.k.4.r.5 (therapy stop date), the duration of the drug administration is calculated.

3.8.4. Units in Interval

This field provides the value (drug amount in units) for the time interval between each administered dose (G.k.4.r.1a-b), reported in data element G.k.4.r.2 [Number of units in the interval] plus the definition of the time interval reported in G.k.4.r.3.

When a specific time interval for drug administration is not known, 'cyclical', 'as necessary' or 'total' may have been used.

The dose and units in interval follows a different structure in ICH-E2B(R2) and ICH-E2B(R3) format. The data field B.4.k.5.3 (number of separate dosages) does not exist in ICH-E2B(R3) terminology. In order to convert the information provided in the cases reported under ICH-E2B(R2) into ICH-E2B(R3) structure, the method of conversion agreed in the backwards and forwards conversion should be followed:

Conversion ICH-E2B(R2) to ICH-E2B(R3): If set, use as multiplication factor of dose number: $\text{dose(R3)} = \text{dose(R2)} * \text{number of separate dosages}$

<http://estri.ich.org/e2br3/index.htm>, (Step 4 ICH IG Package)

As an example, when the dose has been reported in ICH-E2B(R2) as *50mg X 2 every day*. It will be converted in ICH-E2B(R3) as *100mg per 1 day*.

3.8.5. Info

This field provides additional information reported for the drugs and it is populated using the data element G.k.10.r [Additional Information on Drug (coded)].

Due to space limitations in the ICSR form this data element is populated using the codes and not the verbatim. The meaning of the codes are provided to the users in the footer of the ICSR form (See section 3.21) and also outlined here:

- 1=Counterfeit
- 2= Overdose
- 3=Drug taken by the father
- 4=Drug taken beyond expiry date
- 5=Batch and lot tested and found within specifications
- 6=Batch and lot tested and found not within specifications
- 7=Medication error
- 8=Misuse
- 9=Abuse

- 10=Occupational exposure
- 11=Off label use

3.8.6. Additional information on Drug

This field is populated in the Drug information (cont.) table in a dynamic way. It is only populated if information is reported for the data element G.k.11 [Additional information on drug (free text)] otherwise this 'box' for the free text should not appear in the form.

3.8.7. Indication

This field provides information on the indication for use of the drug. It is populated using the data field G.k.7.r.2b [Indication (MedDRA code)] and displays the corresponding MedDRA LLT with latest MedDRA version available. For the cases where the indication is not reported, this field remains blank.

3.8.8. Cumulative dose to first reaction

This field is populated in the Drug information (cont.) table in a dynamic way. Only if information for the data elements G.k.5.a [Cumulative Dose to First Reaction (number)] and G.k.5.b [Cumulative Dose to First Reaction (unit)] is reported for any of the drugs, then the column is populated with the information provided. When this data element is not reported for any of the drugs, to avoid having an empty column, the column should not be populated.

3.8.9. Pharm. Form

This field provides information on the pharmaceutical form and it is populated using the data element G.k.4.r.9.2b (Pharmaceutical Dose Form TermID). If no information is reported in that data element, but information is reported in the free text G.k.4.r.9.1 [Pharmaceutical Dose Form (free text)], the field is populated using the free text element.

3.8.10. Route of Admin.

This field provides information on the drug route of administration for the patient concerned in the case. It is populated using the data element G.k.4.r.10.2b (Route of Administration TermID). If no information is reported in that data element but information is reported in the free text G.k.4.r.10.1 [Route of Administration (free text)], the field is populated using the free text element.

3.8.11. Parent route of administration

This field is populated in the Drug information (cont.) table in a dynamic way and therefore the column will only appear in the table in case of parent-child report cases.

This field is populated using the data element G.k.4.r.11.2b (Parent Route of Administration TermID) and if not provided, the free text G.k.4.r.11.1 [Parent Route of Administration (free text)] is used for the population of this field for levels 2a and 3.

3.9. Time-to-Onset and Rechallenge matrix table

To further assist with the analysis on temporal association, the ICSR form provides a table that reflects the time to onset (TTO) and information whether the reaction recurred after the drug was reintroduced to the patient's treatment (rechallenge).

This table is implemented in a dynamic way so only the drug event combinations with information about TTO and/or rechallenge should be displayed. If no information is reported at all, or reported just with nullflavors, then the table should not appear in the form.

Figure 12. Example of Time to onset and rechallenge matrix table for an ICSR form level 3

Time-to-Onset and Rechallenge matrix table			
Reaction/Event (MedDRA LLT)	Drug	TTO (days)	Rechallenge?/Reaction recurred?
Drug reaction with eosinophilia and systemic symptoms	valproic acid/Brand name 200 mg	187	No/NA
	Paracetamol/Brand name 500mg	186	Yes/Yes
Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes	valproic acid/Brand name 200 mg	125	Yes/No
	Paracetamol/Brand name 500mg	140	No/NA
End stage liver disease	valproic acid/Brand name 200 mg	20	Yes/No
	Paracetamol/Brand name 500mg	123	No/NA
B-cell small lymphocytic lymphoma	valproic acid/Brand name 200 mg	20	Yes/No
	Paracetamol/Brand name 500mg	123	No/NA

The TTO is provided per drug-event combination for the suspect/interacting drugs, and it is populated using the following algorithm:

- Difference between E.i.4 (reaction start date) and earliest G.k.4.r.4 (therapy start date) (only if dates are reported in a valid date format DD/MM/YYYY).
- For the cases where the same drug is administered in different periods, when different start dates provided, if any of the start dates are empty or not completed in valid format, the TTO will not be calculated as it may not be accurate.
- If TTO cannot be calculated as above, the minimum value for G.k.9.i.3.1a/b (Time Interval between Beginning of Drug Administration and Start of Reaction / Event and the units) is used to populate this field.
- When the TTO is more than 24 hours, the TTO will be displayed as 'days'. The following conversion rules apply when needed:
 - Decade=3650 days
 - Year=365 days
 - Trimester=90 days
 - Month=30 days
 - Week=7 days
 - Day=1 days

As TTO information is not provided for level 1 access and therefore this section in the Level 1 form does not contain the TTO column.

Rechallenge information is populated using the data from G.k.9.i.4 (Did Reaction Recur on Re-administration?). The possible options for the column Rechallenge?/Reaction recurred? Are as follows:

- Yes/Yes: rechallenge was done, reaction recurred
- Yes/No: rechallenge was done, reaction did not recur
- Yes/Unk: rechallenge was done, outcome unknown
- No/N/A: no rechallenge was done, recurrence is not applicable

Special attention should be given for the legacy data (i.e. data submitted under ICH-E2B(R2) terminology) due to the differences in reporting rechallenge information between ICH-E2B(R2) and ICH-E2B(R3).

The ICH-E2B(R2) field *(B.4.k.17.1) Did reaction recur on readministration?* is provided at the level of the drug and therefore when these cases are migrated to ICH-E2B(R3) format, the information provided in the R2 field *B.4.k.17.1* for an specific drug, is included in the ICSR form (levels 2a and 3) for all the reactions reported in the case for the concerned drug; this is regardless of the reaction/s that recurred. Users should use the rest of the data in the ICSR (e.g. case narrative) to determine which ones were the reactions concerned in the rechallenge information.

The following logic has been followed when migrating rechallenge information for the ICH-E2B(R2) cases to ICH-E2B(R3) format:

- ICH-E2B(R2) value 1=yes (rechallenge was done, reaction recurred) is mapped to ICH-E2B(R3) value 1= yes/yes (rechallenge was done, reaction recurred)
- ICH-E2B(R2) value 2=No (rechallenge was done, reaction did not recurred) is mapped to ICH-E2B(R3) value 2=yes/no (rechallenge was done, reaction did not recur)
- ICH-E2B(R2) value 3= Unknown (rechallenge was done, outcome unknown or no rechallenge was done, recurrence is not applicable) is not mapped to any ICH-E2B(R3) value

Rechallenge information in the ICSR form level 1 is only provided for cases submitted under ICH-E2B(R3) format.

3.10. Relevant Medical history and Concurrent Conditions

This table reflects the medical history, concurrent conditions and surgical procedures that are submitted in a structured way. It is acknowledged that there could be other relevant information provided in the case narrative that is not coded or submitted in a structured way and therefore will not appear in this section.

This section provides information on the terms reported as medical history, concurrent conditions, surgical procedures together with the dates for those conditions and information regarding whether the reported condition is known to be present at the time of the report.

This table also provides information relating to whether the term has been reported to also be present in another family member (e.g. hereditary diseases) and additional relevant information about the medical condition that cannot be captured in the structured data element.

Figure 13. Example of medical history and concurrent conditions section for an ICSR form level 3

Relevant Medical History and Concurrent Conditions					
MedDRA LLT	Start Date	End Date	Continuing	Family History	Comments
Atrial fibrillation	10/10/1985		Yes	Yes	The patient was diagnosed with atrial fibrillation in another hospital and no records are in our files
Pneumothorax	04/01/1987		No		The pneumothorax was a spontaneous pneumothorax and the patient had to be intubated for more than a week.
Varicella		05/10/1999	No		It was unknown if the patient had been immunised against the virus
Text for Relevant Medical History and Concurrent Conditions (not including reaction / event) Unclear if the patient had surgeries in the past					

3.10.1. MedDRA LLT

This field provides information related to the term reported in the data field **D.7.1.r.1b** [Medical history (disease / surgical procedure / etc.) (MedDRA code)], and displays the corresponding MedDRA LLT with latest MedDRA version available.

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

The data element **D.7.2** [Text for Relevant Medical History and Concurrent Conditions (not including reaction / event)] is implemented in a dynamic way and will not appear in the Relevant Medical history and Concurrent Conditions section if no information is reported or the element is populated with a nullflavor.

This data element captures information about any other medical history that could not be coded in data elements **D.7.1**, and can be populated using free text. This data element should not be confused with **D.7.1.r.5** (comments) provided in the table; that provides additional relevant information about a specific medical condition that cannot be captured otherwise in the structured data element.

Please note that the term 'None' should be used when there is no relevant medical history and no concurrent conditions reported. If relevant medical history is not documented in the report, this data element is set to unknown (i.e. nullFlavor=UNK) and this should not be confused with 'None'.

3.11. Past drug history

This section provides drugs previously administered and which have been stopped before the onset of the suspected ADRs. This section should not have been used for drugs taken concomitantly or drugs which might have potentially been involved in the current ADRs.

This section contains the drugs, populated as per section **3.8.1**, the start and end dates and the indications and reactions displayed with the corresponding MedDRA LLT with latest MedDRA version available.

Figure 14. Example of past drug history section for an ICSR form level 3

Past drug history				
Drug	Start Date	End Date	Indication	Reaction
Cotrimoxazole	01/08/1994	31/09/1994	Acute pulmonary histoplasmosis	Eye disorder
Acetylsalicylic acid	05/05/1993		Headache	Gastrointestinal disorder

3.12. Death

This section provides information on the death of the concerned patient in the case report. It gives information on the date of death, cause of death together with data about autopsy.

Figure 15. Example of Death section for an ICSR form level 3

Death			
Date of Death	Reported Cause	Autopsy done?	Autopsy-determined Cause of Death
31/08/2002	Pancreatic cancer		Pancreatic cancer resectable

Data elements **D.9.2.r.1b** [reported cause of death (MedDRA code)] and **D.9.2.r.2** [reported cause of death (free text)] are combined in one cell ('reported cause of death') and **D.9.2.r.2** should be in brackets. The same rule applies for **D.9.4.r.1b** [autopsy determined cause of death (MedDRA code)] and **D.9.4.r.2** [autopsy determined cause of death (free text)].

Reported cause of death (**D.9.2.r.1b**) and autopsy determined cause of death (**D.9.4.r.1b**) are displayed with the corresponding MedDRA LLT with latest MedDRA version available.

3.13. Case narrative

The textbox for case narrative section is implemented in a static way so it is displayed even if no data has been reported. When no data is provided, the following verbatim is displayed in the section: "Case narrative has not been submitted to EudraVigilance".

Figure 16. Example of case narrative section for an ICSR form level 3

Case Narrative

Multis post annis respiciebat nee accendi regendos, Colonel Aureliano Buendía erat Meminerit ut perspiciantur distant pater eius diei cum glacie flumen equitatur. Tunc Macondo et aedificavit civitatem luto Canabrava uiginti domibus limpidae aquae fluminis ripa tutaquod lectum decurrerent polito lapide candido et enormi sicut ovaprehistoric. Multa nomina tam recenti re mundi, etseñalarías interuenit mentio ille digitus. Familiae quotannis mense Martioet adpropinquaverunt castello castrametati essent gypsies pannosi et tibiis ingenti tumultukettledrums deret eo nova. Primum adduxerunt magnes. Gravitas cum gypsyindomitae barbam et passer manus quae inferebant nomine Melquiades fecit, Ipse palam ostendit quid mirum audax sapientum octavusAlcumistae certi est. Abiit domum ad domum et omnes trahentes conflatile duos ingotsabhorrent mundi videt lebetes et mortaria ruere forcipes atque prominentibus trullis ferreis vestri site, et reddat trabes indè ab clavis et desperatio irrumet trying efficta est, maior etiam obiecta diu ubi acerrima ex humiliati suntappetenda et secum trahens turbulentis post confusionem Melquiades 'magicalis vincirent. Nihil habent pregonaba the gypsy vita circa omnes acerbam accentut experrecta animas eorum. José Arcadio Buendía, cuius.

This section is populated using the following algorithm:

- Use data element **H.1** (Case Narrative Including Clinical Course, Therapeutic Measures, Outcome and Additional Relevant Information).

- If H.1 is not populated but H.5.r.1.a/b (Case Summary and Reporter's Comments Text/ Case Summary and Reporter's Comments Language) is submitted, then this section is populated using H.5.r.1.a/b.
- If both H.1 and H.5.r.1.a/b are populated, only H.1. will be displayed.

Please note that data element H.5.r.1.a (Case Summary and Reporter's Comments Text) is intended to provide information on the clinical course of the case, therapeutic measures, outcome and other relevant information, as well as the reporter's comments on the case in a language different from that used in Sections H.1, H.2 (Reporter's comments), and H.4. (Sender's comments).

3.14. Literature reference

This section provides information on the literature article(s) that describe the individual case.

Figure 17. Example of literature reference section for an ICSR form level 3

Literature Reference

Mudalel ML, Dave KP, Humme JP, Solga SF. N-acetylcysteine treats intravenous amiodarone induced liver injury. World Journal of Gastroenterology 21: 2816-2819, No. 9, Mar 2015

Trikudanathan G, Arain M, Mallery S, Freeman M, Attam R. Endoscopic necrosectomy in children. Journal of Pediatric Gastroenterology and Nutrition 59: 270-273, No. 2, Aug 2014

Additional documents are included

When the sender has sent a copy of the literature article using data element C.4.r.2 (included documents), then it is displayed in this section via the following verbatim: *"Additional documents are included"*.

Please note that to obtain the actual literature article; users will have to use other means such as the EudraVigilance Data Analysis System (EVDAS).

3.15. Reporter's comments

This section is populated using data element H.2 (reporter's comments) and captures the reporter's comments on the diagnosis, causality assessment or other issues considered relevant. Free text is displayed.

Figure 18. Example of Reporter's comments section for an ICSR form level 3

Reporter's Comments

Gloria statuitque simul uenarum finem castellum ad ostium tabernaculi. Byquinis reales, videre possent gypsy at digitis uenarum inspicere. Removeatur Science has distantias super Melquiades. Mox homoVides quid usquam gentium domi relicto. A meridie Demonstratio magnificantes vitrum cum giganteas incendio miram fecit: multum illiin medio plateae et paleas videlicet radios succenderuntsolar. qui ad consolacionem inriti magnetesIpse armatus Inuentionem multumque fatigatus noua belli usu. Melquiades rursus temptaret

3.16. Sender's Diagnosis / Syndrome and / or Reclassification of Reaction / Event (MedDRA LLT)

This section is populated using data element H.3.r.1.b [Sender's Diagnosis / Syndrome and / or Reclassification of Reaction / Event (MedDRA code)] and it is intended to provide combination of signs and symptoms that were reported into succinct diagnosis. It is displayed with the corresponding MedDRA LLT alongside the latest MedDRA version that is available.

Figure 19. Example of Sender Diagnosis section for an ICSR form level 3

Sender's Diagnosis / Syndrome / or Reclassification of Reaction / Event (MedDRA LLT)

hepatic failure

3.17. Sender's comments

This field is populated using data element H.4 (Sender's comments) and it is intended to capture the sender's assessment of the case. The field can be used to describe disagreement with, and/or alternatives to the diagnoses given by the reporter(s). Free text is displayed.

Figure 20. Example of Sender Diagnosis section for an ICSR form level 3

Sender's Comments

The diagnosis of the hepatic failure has not be documented with biopsy

3.18. Laboratory test

This section provides information on the tests and procedures performed to diagnose or confirm the reaction/event, including those test done to investigate (exclude) a non-drug cause.

Figure 21. Example of laboratory test for an ICSR form level 3

Laboratory Test					
Test Name	Test Date	Results	Normal High Value	Normal Low Value	Comments
blood pressure	01/01/2009	90/170 mm[Hg]	70 mm[Hg]	140 mm[Hg]	She has normally the blood pressure well controlled
Drug-induced lymphocyte stimulation test	15/08/2002	positive for valproic acid			The test was done in another lab
Bilirubin conjugated	25/08/2002		17 umol/L	5 umol/L	

The section provides first F.r.2.2b (test name MedDRA code) displayed at MedDRA LLT with latest MedDRA version available and then F.r.1 [the test(s) dates].

The test results are populated using data elements F.r.3.2 [Test Result (value / qualifier)] combined with element F.r.3.2. [Result Unstructured Data (free text)] which is provided in brackets.

3.19. Parent child report

A parent child report is considered if information in any of the data elements containing D.10 is submitted. In that case, the section 'information concerning the parent for a parent-child/foetus report' is populated at the end of the form. This section contains 3 tables: (1) Parent, (2) Relevant Medical History and concurrent conditions of the parent and (3) Past Drug history of the parent. If for any of the 3 tables, there is no data submitted, that specific table will not appear.

In addition to this parent section, a column is inserted in the drug table to populate the values for the parent route of administration. Even if no values have been reported for G.k.4.r.11.2b (Parent Route of Administration TermID) or G.k.4.r.11.1 [Parent Route of Administration (free text)], this column should be inserted when any value containing D.10 is submitted.

Figure 22. Example of information concerning the Parent in an ICSR form level 3

Information Concerning the Parent for a Parent-Child/Foetus Report

Parent						
Initials	Date of Birth	Age	Weight	Height	Sex	Last Menstrual Period Date
JD	22/06/1937	30	65 kg	169 cm	Female	08/08/2001

Relevant Medical History and Concurrent Conditions of the Parent				
MedDRA LLT	Start Date	End Date	Continuing	Comments
Malignant hypertension	01/06/1956		Yes	The mother had uncontrolled hypertension for several years
White coat hypertension	05/06/1980	18/09/1980	No	

Text for Relevant Medical History and Concurrent Conditions of the parent (not including reaction / event)
Unclear if the parent had surgeries

Past Drug History of the Parent				
Drug	Start Date	End Date	Indication (MedDRA Term)	Reaction (MedDRA LLT)
Alimta Recoded	01/01/2009	01/01/2009	Asbestosis	Breast external beam radiation therapy
Amiodarone tablets RECODED	15/12/1986	15/12/1989	Borderline hypertension	Pericoronitis
Avloclor 250 MG RECODED				

3.19.1. Parent

In the ICSR form Level 1 published via Adrreports.eu portal, the parent's age will be displayed as age group according to an age grouping scheme applied in EudraVigilance.

3.19.2. Relevant medical history and concurrent conditions of the parent

The section first provides **D.10.7.1.r.1b** [(Medical history (disease/surgical procedure/etc.) (MedDRA code))]. This data element is displayed at MedDRA LLT with the latest MedDRA version available.

The data field **D.10.7.2** [Text for Relevant Medical History and Concurrent Conditions of the parent (not including reaction / event)] captures information about any other medical history for the parent that could not be coded in the data elements **D.10.7.1.r.** This field is implemented in a dynamic manner.

Please note that the data element **D.10.7.1.r.5** (comments) provides additional information about the specific medical condition that could not be captured otherwise in the structured data element.

3.19.3. Past drug history of the parent

The population of the drugs within the past drug history of the parent follows the same rule as per the drug section using the corresponding data elements with code **D.10.8**.

3.20. Related Reports

The section on related reports provides information on duplicates and linked reports. The section provides the cases identifiers using **C.1.9.1.r.2** for the duplicates reports and **C.1.10.r** (Identification number of report which is linked to this report) for the linked cases.

Figure 23. Example of information concerning related reports in an ICSR form level 3

Related Reports	
Relation	Case Identifier
Duplicate	IT-Beta-lactam-1452365
Duplicate	IT-GHJORT-9874563
Linked	IT-Beta-lactam-1458963
Linked	IT-GHJKLO-3462832

3.21. Footer

The ICSR form contains a footer to clarify the abbreviations used within the form. These abbreviations appear only in the first page and are related to the seriousness criteria (Section 3.7.3), drug role (Section 3.8.2) and additional information on drug.

The footer also contains information about when the report was retrieved from EudraVigilance.

Figure 24. Example of the footer in an ICSR form level 3

* death=results in death; life threat.=life threatening; hospital.=requires hospitalization/prolongation of hospitalization; disability=results in disability/incapacity;
congen.=congenital anomaly/birth defect; other=other medically important information; (blank)=non-serious
† S=suspect; C=concomitant; I=interacting; N=not administered
‡ 1=Counterfeit; 2= Overdose; 3=Drug taken by the father; 4=Drug taken beyond expiry date; 5=Batch and lot tested and found within specifications;
6=Batch and lot tested and found not within specifications; 7=Medication error; 8=Misuse; 9=Abuse; 10=Occupational exposure; 11=Off label use;
(blank)=no additional information

Report run: 04/11/2015 14:10:55

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4. Annex I – ICSR Form Level 3 – ICH-E2B(R3) data elements

General Information	
Worldwide Unique Case Identification Number	C.1.8.1
Sender type	C.3.1
Sender's Organisation	C.3.2
Date Report Was First Received from Source	C.1.4
Date of Most Recent Information	C.1.5
Type of Report	C.1.3
Primary source country	C.2.r.3 & C.2.r.5
Study registration number	C.5.1.r.1
Study Name	C.5.2
Study Type	C.5.4
Reporter's qualification	C.2.r.4
Case serious?	
Medically confirmed?	E.i.8

Patient						
Initials	Date of Birth	Age	Age Group	Sex	Weight	Height
D.1	D.2.1	D.2.2a/b	D.2.3	D.5	D.3	D.4

Reaction / Event						
MedDRA LLT	Start Date	Stop Date	Duration	Outcome	Seriousness*	
E.i.2.1b	E.i.4	E.i.5	E.i.6a/b	E.i.7	E.i.3.2a-f	

Drug Information							
Role†	Drug	Start Date	Stop Date	Duration	Dose	Units in Interval	Action taken
G.k.1	G.k.2.1.1b or G.k.2.1.2b or G.k.2.3.r1-3 G.k.2.2	G.k.4.r.4	G.k.4.r.5	G.k.4.r.6a/ b	G.k.4.r.1a/b	G.k.4.r.2 & G.k.4.r.3	G.k.8

Drug Information (cont.)							
Info‡	Drug	Indication	Cumul. dose to 1st Reaction	Pharm. Form	Route of Admin.	Parent Route of Admin.	Batch / Lot #
G.k.10.r	G.k.2.1.1b or G.k.2.1.2b or G.k.2.3.r1-3 G.k.2.2	G.k.7.r.2b	G.k.5a/b	G.k.4.r.9.2b or G.k.4.r.9.1	G.k.4.r.10.2b or G.k.4.r.10.1	G.k.4.r.11.2b or G.k.4.r.11.1	G.k.4.r.7
Additional Information on Drug G.k.11							

Time-to-Onset and Rechallenge matrix table			
Reaction/Event (MedDRA LLT)	Drug	TTO (days)	Rechallenge?/Reaction recurred?
E.i.2.1b	G.k.2.1.1b or G.k.2.1.2b or G.k.2.3.r1-3 or G.k.2.2	E.i.4 (-) G.k.4.r.4 or G.k.9.i.3.1a/b	G.k.9.i.4

Relevant Medical History and Concurrent Conditions					
MedDRA LLT	Start Date	End Date	Continuing	Family History	Comments
D.7.1.r.1b	D.7.1.r.2	D.7.1.r.4	D.7.1.r.3	D.7.1.r.6	D.7.1.r.5
Text for Relevant Medical History and Concurrent Conditions (not including reaction / event) D.7.2					

Past drug history				
Drug	Start Date	End Date	Indication	Reaction
D.8.r.2b or D.8.r.3b D.8.r.EU.r.2b or D.8.r.EU.r.1	D.8.r.4	D.8.r.5	D.8.r.6b	D.8.r.7b

Death			
Date of Death	Reported Cause	Autopsy done?	Autopsy-determined Cause of Death
D.9.1	D.9.2.r.1b & D.9.2.r.2	D.9.3	D.9.4.r.1b & D.9.4.r.2

Case Narrative

H.1 or H.5.r.1.a/b

Literature Reference

C.4.r.1
C.4.r.2

Reporter's Comments

H.2

Sender's Diagnosis / Syndrome / or Reclassification of Reaction / Event (MedDRA LLT)

H.3.r.1b

Sender's Comments

H.4

Laboratory Test					
Test Name	Test Date	Results	Normal High Value	Normal Low Value	Comments
F.r.2.2b	F.r.1	F.r.3.2 & F.r.3.3 & F.r.3.4	F.r.5	F.r.4	F.r.6

Information Concerning the Parent for a Parent-Child/Foetus Report

Parent						
Initials	Date of Birth	Age	Weight	Height	Sex	Last Menstrual Period Date
D.10.1	D.10.2.1	D.10.2.2a/b	D.10.4	D.10.5	D.10.6	D.10.3

Relevant Medical History and Concurrent Conditions of the Parent					
MedDRA LLT	Start Date	End Date	Continuing	Comments	
D.10.7.1.r.1b	D.10.7.1.r.2	D.10.7.1.r.4	D.10.7.1.r.3	D.10.7.1.r.5	
Text for Relevant Medical History and Concurrent Conditions of the parent (not including reaction / event)					
D.10.7.2					

Past Drug History of the Parent				
Drug	Start Date	End Date	Indication (MedDRA Term)	Reaction (MedDRA LLT)
D.10.8.r.3b or D.10.8.r.2b or D.10.8.r.1	D.10.8.r.4	D.10.8.r.5	D.10.8.r.6b	D.10.8.r.7b

Related Reports	
Relation	Case Identifier
Duplicate	C.1.9.1.r.2
Linked	C.1.10.r

5. Annex II – ICSR Form Level 2a – ICH-E2B(R3) data elements

General Information	
Worldwide Unique Case Identification Number	C.1.8.1
Sender type	C.3.1
Sender's Organisation	C.3.2
Date Report Was First Received from Source	C.1.4
Date of Most Recent Information	C.1.5
Type of Report	C.1.3
Primary source country	C.2.r.3 & C.2.r.5
Study registration number	C.5.1.r.1
Study Name	C.5.2
Study Type	C.5.4
Reporter's qualification	C.2.r.4
Case serious?	
Medically confirmed?	E.i.8

Patient				
Age	Age Group	Sex	Weight	Height
D.2.2a/b	D.2.3	D.5	D.3	D.4

Reaction / Event					
MedDRA LLT	Start Date	Stop Date	Duration	Outcome	Seriousness*
E.i.2.1b	E.i.4	E.i.5	E.i.6a/b	E.i.7	E.i.3.2a-f

Drug Information							
Role†	Drug	Start Date	Stop Date	Duration	Dose	Units in Interval	Action taken
G.k.1	G.k.2.1.1b or G.k.2.1.2b or G.k.2.3.r1-3 G.k.2.2	G.k.4.r.4	G.k.4.r.5	G.k.4.r.6a/ b	G.k.4.r.1a/b	G.k.4.r.2 & G.k.4.r.3	G.k.8

Drug Information (cont.)							
Info‡	Drug	Indication	Cumul. dose to 1st Reaction	Pharm. Form	Route of Admin.	Parent Route of Admin.	Batch / Lot #
G.k.10.r	G.k.2.1.1b or G.k.2.1.2b or G.k.2.3.r1-3 G.k.2.2	G.k.7.r.2b	G.k.5a/b	G.k.4.r.9.2b or G.k.4.r.9.1	G.k.4.r.10.2b or G.k.4.r.10.1	G.k.4.r.11.2b or G.k.4.r.11.1	G.k.4.r.7
Additional Information on Drug G.k.11							

Time-to-Onset and Rechallenge matrix table			
Reaction/Event (MedDRA LLT)	Drug	TTO (days)	Rechallenge?/Reaction recurred?
E.i.2.1b	G.k.2.1.1b or G.k.2.1.2b or G.k.2.3.r1-3 or G.k.2.2	E.i.4 (-) G.k.4.r.4 or G.k.9.i.3.1a/b	G.k.9.i.4

Relevant Medical History and Concurrent Conditions					
MedDRA LLT	Start Date	End Date	Continuing	Family History	Comments
D.7.1.r.1b	D.7.1.r.2	D.7.1.r.4	D.7.1.r.3	D.7.1.r.6	D.7.1.r.5
Text for Relevant Medical History and Concurrent Conditions (not including reaction / event) D.7.2					

Past drug history				
Drug	Start Date	End Date	Indication	Reaction
D.8.r.2b or D.8.r.3b D.8.r.EU.r.2b or D.8.r.EU.r.1	D.8.r.4	D.8.r.5	D.8.r.6b	D.8.r.7b

Death			
Date of Death	Reported Cause	Autopsy done?	Autopsy-determined Cause of Death
D.9.1	D.9.2.r.1b & D.9.2.r.2	D.9.3	D.9.4.r.1b & D.9.4.r.2

Literature Reference

C.4.r.1

Reporter's Comments

H.2

Sender's Diagnosis / Syndrome / or Reclassification of Reaction / Event (MedDRA LLT)

H.3.r.1b

Sender's Comments

H.4

Laboratory Test					
Test Name	Test Date	Results	Normal High Value	Normal Low Value	Comments
F.r.2.2b	F.r.1	F.r.3.2 & F.r.3.3 & F.r.3.4	F.r.5	F.r.4	F.r.6

Information Concerning the Parent for a Parent-Child/Foetus Report

Parent				
Age	Weight	Height	Sex	Last Menstrual Period Date
D.10.2.2a/b	D.10.4	D.10.5	D.10.6	D.10.3

Relevant Medical History and Concurrent Conditions of the Parent					
MedDRA LLT	Start Date	End Date	Continuing	Comments	
D.10.7.1.r.1b	D.10.7.1.r.2	D.10.7.1.r.4	D.10.7.1.r.3	D.10.7.1.r.5	

Past Drug History of the Parent				
Drug	Start Date	End Date	Indication (MedDRA Term)	Reaction (MedDRA LLT)
D.10.8.r.3b or D.10.8.r.2b or D.10.8.r.1	D.10.8.r.4	D.10.8.r.5	D.10.8.r.6b	D.10.8.r.7b

Related Reports	
Relation	Case Identifier
Duplicate	C.1.9.1.r.2
Linked	C.1.10.r

6. Annex III – ICSR Form Level 1 MAHs – ICH-E2B(R3) data elements

General Information	
Worldwide Unique Case Identification Number	C.1.8.1
Sender type	C.3.1
Sender's Organisation	C.3.2
Type of Report	C.1.3
Primary source country	C.2.r.3 & C.2.r.5
Study registration number	C.5.1.r.1
Study Name	C.5.2
Study Type	C.5.4
Reporter's qualification	C.2.r.4
Case serious?	

Patient		
Age	Age Group	Sex
	D.2.3	D.5

Reaction / Event			
MedDRA LLT	Duration	Outcome	Seriousness*
E.i.2.1b	E.i.6a/b	E.i.7	E.i.3.2a-f

Drug Information					
Role†	Drug	Duration	Dose	Units in Interval	Action taken
G.k.1	G.k.2.1.1b or G.k.2.1.2b or G.k.2.3.r1-3 G.k.2.2	G.k.4.r.6a/ b	G.k.4.r.1a/b	G.k.4.r.2 & G.k.4.r.3	G.k.8

Drug Information (cont.)					
Info‡	Drug	Indication	Pharm. Form	Route of Admin.	Parent Route of Admin.
G.k.10.r	G.k.2.1.1b or G.k.2.1.2b or G.k.2.3.r1-3 G.k.2.2	G.k.7.r.2b	G.k.4.r.9.2b	G.k.4.r.10.2b	G.k.4.r.11.2b
Additional Information on Drug G.k.11					

Rechallenge matrix table		
Reaction/Event (MedDRA LLT)	Drug	Rechallenge?/Reaction recurred?
E.i.2.1b	G.k.2.1.1b or G.k.2.1.2b or G.k.2.3.r1-3 or G.k.2.2	G.k.9.i.4

Literature Reference

C.4.r.1

Information Concerning the Parent for a Parent-Child/Foetus Report

Parent	
Age	Sex
D.10.2.2a/b	D.10.6

7. Annex IV – ICSR Form Level 1 – Adrreports.eu – ICH-E2B(R3) data elements

General Information	
EudraVigilance Local Report Number	
Sender type	C.3.1
Sender's Organisation	C.3.2
Type of Report	C.1.3
Primary source country	C.2.r.3 & C.2.r.5
Reporter's qualification	C.2.r.4
Case serious?	

Patient		
Age	Age Group	Sex
D.2.2a/b	D.2.3	D.5

Reaction / Event			
MedDRA LLT	Duration	Outcome	Seriousness*
E.i.2.1b	E.i.6a/b	E.i.7	E.i.3.2a-f

Drug Information					
Role†	Drug	Duration	Dose	Units in Interval	Action taken
G.k.1	G.k.2.1.1b or G.k.2.1.2b or G.k.2.3.r1-3 G.k.2.2	G.k.4.r.6a/ b	G.k.4.r.1a/b	G.k.4.r.2 & G.k.4.r.3	G.k.8

Drug Information (cont.)					
Info‡	Drug	Indication	Pharm. Form	Route of Admin.	Parent Route of Admin.
G.k.10.r	G.k.2.1.1b or G.k.2.1.2b or G.k.2.3.r1-3 G.k.2.2	G.k.7.r.2b	G.k.4.r.9.2b	G.k.4.r.10.2b	G.k.4.r.11.2b
Additional Information on Drug G.k.11					

Rechallenge matrix table		
Reaction/Event (MedDRA LLT)	Drug	Rechallenge?/Reaction recurred?
E.i.2.1b	G.k.2.1.1b or G.k.2.1.2b or G.k.2.3.r1-3 or G.k.2.2	G.k.9.i.4

Literature Reference

C.4.r.1

Information Concerning the Parent for a Parent-Child/Foetus Report

Parent	
Age	Sex
D.10.2.2a/b	D.10.6

8. List of acronyms used in the document

Acronym	Meaning
ADR	Adverse Drug Reaction
CIOMS	Council for International Organizations of Medical Sciences
eRMR	Electronic Reaction Monitoring Report
EU	European Union
EVCTM	EudraVigilance Clinical Trial Module
EVDAS	EudraVigilance Data Analysis System
EVPM	EudraVigilance Post-Authorisation Module
EVWEB	EudraVigilance Web application
HCP	Healthcare professional
ICH	The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICSR	Individual case Safety Report
LLT	Lowest Level Term
MAH	Marketing Authorisation Holder
MedDRA	Medical Dictionary for regulatory activities
MLM	Medical Literature Monitoring
NCA	National Competent Authority of an EEA Member State
ROR	Reporting Odds Ratio

9. Supporting documents

ⁱ European Medicines Agency policy on access to EudraVigilance data for medicinal products for human use - Revision 3

http://www.ema.europa.eu/ema/index.jsp?curl=pages/includes/document/document_detail.jsp?webContentId=WC500218300&mid=WC0b01ac058009a3dc

ⁱⁱ ICH E2B Expert Working Group - Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs) E2B(R3) Data Elements and Message Specification - Version 5.01, 12 April 2013

<http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html>

http://www.ema.europa.eu/ema/index.jsp?curl=pages/includes/document/document_detail.jsp?webContentId=WC500002767&mid=WC0b01ac058009a3dc

ⁱⁱⁱ European Union individual case safety report (ICSR) implementation guide

http://www.ema.europa.eu/ema/index.jsp?curl=pages/includes/document/document_detail.jsp?webContentId=WC500165979&mid=WC0b01ac058009a3dc