

**E2B(R) CLINICAL SAFETY DATA MANAGEMENT:**

**DATA ELEMENTS FOR TRANSMISSION OF  
INDIVIDUAL CASE SAFETY REPORTS**

Revision 2

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

ICH HARMONISED TRIPARTITE GUIDELINE

**REVISION OF THE ICH GUIDELINE ON  
CLINICAL SAFETY DATA MANAGEMENT:**

**DATA ELEMENTS FOR TRANSMISSION OF  
INDIVIDUAL CASE SAFETY REPORTS**

**E2B(R)**

**Version 2.0  
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at Step 2 of the ICH Process  
on 12 May 2005  
by the ICH Steering Committee

*This Guideline has been developed by the appropriate ICH Expert Working Group E2B(R) and is subject to consultation by the regulatory parties, in accordance with the ICH Process*

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**DATA ELEMENTS FOR TRANSMISSION OF**  
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**PREAMBLE**

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

**1. INTRODUCTION**

**1.1 Scope of this guideline**

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

**1.2 Background**

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

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

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

**1.3 Notes on format of this document**

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

94 standard type of a slightly smaller font.

95  
96 If a data element has a limited set of choices, the options are presented in ***bold italic type***.  
97 The standard allows for this information to be transmitted in encoded format.

#### 98 99 **1.4 Definition of data elements**

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

120  
121 In certain instances, there are provisions for the transmission of some free text items, including a full text  
122 case summary narrative. The transmission of other unstructured data, such as full clinical records or  
123 images is outside the scope of this guideline. However technical recommendations are made in the  
124 companion document.

#### 125 126 **1.5 Minimum information**

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

136  
137 In addition, to properly process the report, the following administrative information should be provided:  
138 the sender's (case) safety report unique identifier (A.1.0.1), the date of the most recent information  
139 (A.1.7), the worldwide unique case identification number (A.1.10), the sender identifier (A.3.1.2), whether  
140 this case fulfills the local criteria for an expedited report (A.1.9), the type of report (A.1.4) and in the case  
141 of a "Report from study" the study type in which the reaction(s)/event(s) were observed (A.2.3.3).

#### 142 143 **1.6 General Principles**

## *E2B(R) Electronic Transmission of Individual Case Safety Reports*

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

151

### 152 **2. GUIDELINE: CONTENT OF THE DATA ELEMENTS**

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

155

156 The data elements are divided into sections pertaining to:

#### 157 **A: Administrative and Identification Information**

158 A.1 - Identification of the case safety report

159 A.2 - Primary source(s) of information

160 A.3 - Information on sender and receiver of case safety report

#### 161 **B: Information on the Case:**

162 B.1 - Patient characteristics

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

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

165 B.4 - Drug(s) information

166 B.5 - Narrative case summary and further information

167

168

### 169 **A. ADMINISTRATIVE AND IDENTIFICATION INFORMATION**

170

#### 171 **A.1 Identification of the case safety report**

172

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

174

175

User Guidance:

176

177

178

179

180

181

182

183

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

184

185

186

187

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

188

189

190

##### 188 **A.1.0.2 MedDRA version used in this case safety report**

User Guidance:

191

192

193

194

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

195

196

197

198

199

#### 195 **A.1.1 Identification of the country of the primary source**

User Guidance:

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

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

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

User Guidance:

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

#### A.1.3 Date of this transmission

User Guidance:

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

#### A.1.4 Type of report

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

User Guidance:

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

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

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

#### A.1.5 Seriousness

User Guidance:

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

##### A.1.5.1 Serious

- *Yes/no*

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

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

User Guidance:

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

#### A.1.6 Date report was first received from source

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258 User Guidance:

259  
260 For senders dealing with initial information, this should be the date the information was received from the primary source. When  
261 retransmitting information received from another regulatory agency or another company or any other secondary source, A.1.6  
262 should be the date the retransmitter first received the information.

263  
264 A full precision date should be used (i.e., day, month, year).  
265

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

266 User Guidance:

267  
268 This date should be changed each time follow up information is received by the sender. However if the case is amended for any  
269 other reason (e.g., internal review by the sender or expert opinion) this date should not be changed but the field A.1.13 should be  
270 populated with the value "amendment" indicating that the case was amended by the sender. (See the User Guidance for the field  
271 A.1.13)  
272

273  
274 Because reports are sent at different times to multiple receivers, the initial/follow up status is dependent upon the receiver. For  
275 this reason an item to capture follow-up status is not included. However, the date of receipt of the most recent information taken  
276 together with the "sender identifier" (A.3.2) and "sender's (case) report unique identifier" (A.1.0.1) provide a mechanism for each  
277 receiver to identify whether the report being transmitted is an initial or follow-up report. For this reason these items are considered  
278 critical for each transmission.

279 A full precision date should be used (i.e., day, month, year).  
280

### **A.1.8 Additional available documents held by sender**

#### **A.1.8.1 Are additional documents available?**

282  
283 -yes/no  
284  
285

#### **A.1.8.2 List of documents held by sender**

286 User Guidance:

287  
288 The documents received from the primary source (e.g., clinical records, hospital records, autopsy reports) should be  
289 listed. It is recognized that these documents might not be obtainable in many instances.  
290

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

291  
292 - yes/no  
293

294 User Guidance:

295  
296 The definition of expedited is dependent upon the local regulatory requirements. This item should be used by the sender to  
297 indicate whether the case fulfills the local expedited requirements. When the countries of origin and destination of the  
298 transmission differ, the receiver should be aware that the information might not be applicable to the receiver's country's  
299 regulatory requirements.  
300

### **A.1.10 Worldwide unique case identification number.**

301 User Guidance:

302  
303 Only A.1.10.1 or A.1.10.2 should be used. No case should have more than one of these items completed. The contents of  
304 whichever item is used should remain unchanged for any transmissions subsequent to the original transmission.  
305

306 When a regulator is the initial sender, A.1.10.1 should be used.  
307

308 When an entity other than a regulator is the initial sender, A.1.10.2 should be used. When a sender has not previously received a  
309 valid E2B/M2 report electronically, the identifiers (content and format) in A.1.0.1 and A.1.10.1 or A.1.10.2 should be identical.  
310 Retransmitters should use their own sender's (case) safety report unique identifier (A.1.0.1), but not change A.1.10.1 or A.1.10.2.  
311 See examples in attachment 2.  
312

#### **A.1.10.1 Regulatory authority's case report number**

#### **A.1.10.2 Other sender's case report number**

313  
314  
315  
316

317 **A.1.11 Other case identifiers in previous transmissions**

318 **-yes**

319 User Guidance:

320

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

322

323 **A.1.11.1 Source(s) of the case identifier (e.g., name of the company, name of regulatory**

324 **agency) (repeat as necessary)**

325

326

User Guidance:

327

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

328

329

330

331

332

**A.1.11.2 Case identifier(s)**

333

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

335

User Guidance:

336

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

337

338

339

340

341

342 **A.1.13 Report nullification / amendment**

343 **- nullification**

344 **- amendment**

345

User Guidance:

346

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

347

348

349

350

351

352

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

353

354

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

355 **- yes/no**

356

User Guidance:

357

358

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

359

360

361

**A.2 Primary source(s) of information**

362

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

363

364

365

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

366

367

368

369

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

370

371

**A.2.1.1 Reporter identifier (name or initials)**

372

User Guidance:

373

- 374  
375 The identification of the reporter could be prohibited by certain national confidentiality laws or directives. The  
376 information should be provided when it is in conformance with the regional confidentiality requirements. In any case, at  
377 least one subsection should be completed to ensure there is an identifiable reporter. If only the name of the reporter is  
378 known and providing this name is prohibited because of confidentiality requirements, initials can be used.  
379
- 380 **A.2.1.2 Reporter's address**  
381 User Guidance:  
382  
383 See the companion document for format specifications.  
384
- 385 **A.2.1.3 Country**  
386 User Guidance:  
387  
388 See the companion document for format specifications.  
389
- 390 **A.2.1.4 Qualification**  
391 – *Physician*  
392 – *Pharmacist*  
393 – *Other health professional*  
394 – *Lawyer*  
395 – *Consumer or other non health professional*  
396 User Guidance:  
397  
398 In some regions, consumer and lawyer reports should be transmitted only when there is medical confirmation.  
399
- 400 **A.2.2 Literature reference(s)**  
401 User Guidance:  
402  
403 References should be provided in the Vancouver Convention (known as "Vancouver style") as developed by the International  
404 Committee of Medical Journal Editors. The standard format, as well as formats for special situations can be found in the  
405 following reference which is in the Vancouver style. International Committee of Medical Journal Editors. Uniform requirements  
406 for manuscripts submitted to biomedical journals. N Engl J Med 1997; 336:309-15.  
407
- 408 **A.2.3 Study identification**  
409
- 410 **A.2.3.0 Study registration number**  
411 User Guidance  
412  
413 This field should be populated with the study registration number if applicable.  
414
- 415 **A.2.3.1 Study name**  
416 User Guidance:  
417  
418 This field should be populated by the study name as approved by the regulator in each region.  
419
- 420 **A.2.3.2 Sponsor study number**  
421 User Guidance:  
422  
423 This section should be completed only if the sender is the study sponsor or has been informed of the study number by  
424 the sponsor.  
425
- 426 **A.2.3.3 Study type in which the reaction(s)/event(s) were observed**  
427 – *Clinical trials*  
428 – *Individual patient use (e.g., "compassionate use" or named patient basis)*  
429 – *Other studies (e.g., pharmacoepidemiology, pharmacoeconomics, intensive monitoring)*  
430 User Guidance:  
431

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432 This information should be provided if the field A.1.4 Type of report has been populated with "Report from study".  
433

### 434 **A.3 Information on sender of case safety report** 435

#### 436 **A.3.1 Type**

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

443 User Guidance:

444  
445 In this context, a pharmaceutical company includes biotechnology companies and other manufacturers required to  
446 submit individual case safety reports.  
447

#### 448 **A.3.2 Sender identifier**

449 User Guidance:

450 Identifies the sender, (e.g., company name or regulatory authority name). It is important that this item should be completed.  
451  
452

#### 453 **A.3.3 Person responsible for sending the report**

454 User Guidance:

455  
456 The name of person in the company or agency who is responsible for the authorization of report dissemination. This would  
457 usually be the same person who signs the covering memo for paper submissions. The inclusion of the name of this person in the  
458 transmission could be subject to national or international regulations.  
459

#### 460 **A.3.4 Sender's address, fax, telephone and E-mail address** 461

## 462 **B. INFORMATION ON THE CASE** 463

### 464 **B.1 Patient characteristics**

465 User Guidance:

466  
467 This section applies to the subject who experienced one or several adverse reactions/events.  
468 In cases where a fetus or nursing infant is exposed to one or several drugs through the parent and experience one or several  
469 adverse reactions/events, information on both the parent and the child/fetus should be provided. Reports of these cases are  
470 referred to as parent-child/fetus reports. The following general principles should be used for filing these reports.  
471

472 If there has been no reaction/event affecting the child/fetus, the parent-child/fetus report does not apply; i.e., the B.1 fields below  
473 apply only to the parent (mother or father) who experienced the adverse reaction/event.

474 For those cases describing miscarriage or fetal demise or early spontaneous abortion, only a parent report is applicable, i.e., the  
475 B.1. fields below apply to the mother. However, if suspect drug(s) were taken by the father this information should be indicated in  
476 the field B.4.k.13.

477 If both the parent and the child/fetus sustain adverse events, two separate reports, i.e., one for the parent (mother or father) and  
478 one for the child/fetus, should be provided but they should be linked by using sections A.1.12 in each report.  
479

480 If only the child/fetus has an adverse reaction/event (other than early spontaneous abortion/fetal demise) the information provided  
481 in this section applies only to the child/fetus, and characteristics concerning the parent (mother or father) who was the source of  
482 exposure to the suspect drug should be provided in section B.1.10.  
483

484 If both parents are the source of the suspect drug(s) then the case should reflect the mother's information in section B.1.10 and the  
485 case narrative (section B.5.1) should describe the entire case, including the father's information.  
486

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

488 User Guidance:

489  
490 It is important that this field is populated. The identification of the patient may be prohibited by certain national confidentiality

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491 laws or directives. The information should be provided when it is in conformance with the confidentiality requirements. This also  
492 applies to medical record number(s) (B.1.1.1).

493 If the initials of the patient are unknown to the sender, this field should be populated with "UNKNOWN".

494 If the initials are known to the sender but cannot be transmitted due to data privacy requirements, this field should be populated  
495 with "PRIVACY".

496

### 497 **B.1.1.1 Patient medical record number(s) and the source(s) of the record number (if** 498 **allowable)**

499 User Guidance:

500

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

504

### 505 **B.1.2 Age information**

506 User Guidance:

507

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

509

#### 510 **B.1.2.1 Date of birth**

511 User Guidance:

512

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

515

#### 516 **B.1.2.2 Age at time of onset of reaction/event**

517 User Guidance:

518

519 If several reactions/events are in the report, the age at the time of the first reaction/event should be used. For fetal  
520 reaction(s)/event(s) the next item B.1.2.2.1 "Gestation period when reaction/event was observed in the fetus" should be  
521 used.

522

523 When providing the age in decades, please note that, for example, the 7th decade refers to a person in his/her 60's.

524

525 See the companion document for format specifications.

526

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

528 User Guidance:

529

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

532

#### 533 **B.1.2.3 Patient age group (as per reporter)**

534 – *Neonate*

535 – *Infant*

536 – *Child*

537 – *Adolescent*

538 – *Adult*

539 – *Elderly*

540

541 User Guidance:

542

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

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### 546 **B.1.3 Body weight (kg)**

547 User Guidance:

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549 Body weight at the time of the event/reaction.

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### 549 **B.1.4 Height (cm)**

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**B.1.5 Sex**

User guidance:

See the companion document for format specifications.

**B.1.6 Last menstrual period date**

User guidance:

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

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

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

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

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User Guidance:

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

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

User Guidance:

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

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

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

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User Guidance:

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

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**B.1.9 In case of death**

**B.1.9.1 Date of death**

User Guidance:

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

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

User Guidance:

MedDRA LLT code should be used

**B.1.9.3 Was autopsy done?**

*Yes/No/Unknown*

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

User Guidance:

MedDRA LLT code should be used

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

User Guidance:

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

**B.1.10.1 Parent identification**

**B.1.10.2 Parent age information**

User Guidance:

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

*B.1.10.2.1 Date of birth of parent*

User Guidance:

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

*B.1.10.2.2 Age of parent*

**B.1.10.3 Last menstrual period date**

User Guidance:

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

**B.1.10.4 Body weight (kg) of parent**

**B.1.10.5 Height (cm) of parent**

**B.1.10.6 Sex of parent**

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

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

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

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User Guidance:

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

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

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

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

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User Guidance:

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

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

User Guidance:

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

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

User Guidance:

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

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

User Guidance:

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

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

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

**- yes, highlighted by the reporter**

User Guidance:

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

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

**- Results in death**

**- Is life-threatening**

**- Requires inpatient hospitalization or prolongation of existing hospitalization**

**- Results in persistent or significant disability/incapacity (as per reporter's opinion)**

**- Is a congenital anomaly/birth defect**

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**- Other medically important condition**

User Guidance:

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

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

User Guidance:

See the companion document for format specifications.

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

User Guidance:

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

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

User Guidance:

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

Imprecise dates can be used. See the companion document for format specifications.

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

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

User Guidance:

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

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

User Guidance:

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

**B.3.1 Structured information (repeat as necessary)**

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

User Guidance:

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

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767 If results and units cannot be split, B.3.2 should be used. More than one test can be included in B.3.2.  
768

### 769 **B.3.2 Results of tests and procedures relevant to the investigation** 770

### 771 **B.4 Drug(s) information** 772

773 User Guidance:  
774

775 This section covers both suspect drugs and concomitant medications (including biologics). In addition, the section can be used to  
776 identify drugs thought to have an interaction. For each drug, the characterization of the drug role (B.4.k.1) is that indicated by the  
777 primary reporter, (i.e., the original source of the information) and the sender. The designation of "k" in this section indicates that  
778 each item is repeatable and that it corresponds to the same "k" in all subsections. A separate block (k) should be used for each  
779 drug. Drugs used to treat the reaction/event should not be included here.  
780

#### 781 **B.4.k.1 Characterization of drug role** 782 ***Suspect / Concomitant / Interacting / Drug Not Administered / Blinded*** 783

784 User Guidance:

785 This field contains the characterization of the drug as provided by primary reporter or if this information is missing, by  
786 the sender. All spontaneous reports should have at least one suspect drug (see Section 1.5). If the reporter indicates a  
787 suspected interaction, "**interacting**" should be selected. All interacting drugs are considered to be suspect drugs.  
788

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

- 790 - in clinical trial: if the adverse event occurred after the informed consent was signed but prior to the administration  
791 of the study drug e.g., during the screening period or the washout procedure. In general the adverse event should be  
792 reported as due to the trial procedure. In that case, the rest of the section B.4 should be left blank and the  
793 information on the suspect cause of the event should be provided in the section B.5.
- 794 - medication error: if the patient did not receive the actual prescribed drug but another one, repeatable section B.4  
795 should be completed with the information about the prescribed drug (including the fact that it was not  
796 administered), as well as the information on the dispensed drug as the "suspect" drug.  
797

798 "**Blinded**":

799 The ICH E2A guideline recommends that the case safety reports with blinded therapy should not be reported. However,  
800 if it is important to exchange a case safety report during a clinical trial, this value should be used. In that case the fields  
801 of the section B.4.k.2 Drug identification should be populated with the characteristics of all the blinded study drug(s).  
802

#### 803 **B.4.k.2 Drug identification** 804

805 User Guidance:

806 Medicinal product names and active ingredient names should be provided as they were reported. To standardise this  
807 information, the ICH M5 guideline should be used. In case of investigational drugs, only a code might be known and  
808 provided. If more than one active ingredient is specified, each should be included in item B.4.k.2.2, and can be repeated  
809 as necessary.  
810

##### 811 ***B.4.k.2.0 Medicinal product unique identifier*** 812

813 User Guidance:

814 Based on the medicinal product name as reported by the primary source, the most specific identifier either the Medicinal  
815 Product Identifier (MedID) or the Pharmaceutical Product Identifier (PhPID) should be provided. If a MedID and a  
816 PhPID for the reported medicinal product are not available, this field should be left blank.  
817

##### 818 ***B.4.k.2.0.1 MedID and MedID operation date***

##### 819 ***B.4.k.2.0.2 PhPID and PhPID operation date*** 820

##### 821 ***B.4.k.2.1 Medicinal product name as reported by the primary source*** 822

823 User Guidance:

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

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*B.4.k.2.2 Active ingredient identifier (repeat as necessary)*

User Guidance:

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

*B.4.k.2.2.1 Active ingredient name*

*B.4.k.2.2.2 Active ingredient TermID and TermID operation date*

*B.4.k.2.3 Identification of the country where the drug was obtained.*

User Guidance:

See the companion document for the appropriate codes and format.

**B.4.k.3 Holder and authorization/application number of drug**

User Guidance:

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

*B.4.k.3.1 Authorization/Application Number*

*B.4.k.3.2 Country of authorization/application*

User Guidance:

See the companion document for the appropriate codes and format.

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

**B.4.k.4 Structured Dosage Information (repeat as necessary)**

(e.g., 2 mg three times a day)

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

User Guidance:

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

In the case of a parent-child/fetus report, the dosage section applies to the parental dose.

If any of these pieces of information is unknown, the field should be left blank.

For a dosage regimen that involves more than one dosage form and/or changes in dosage, the information should be provided in section B.4.k.4.10 as text. Categories for "definition of the interval unit" are described in attachment 1

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

*B.4.k.4.7 Date of last administration*

User Guidance:

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

*B.4.k.4.8 Duration of drug administration*

User Guidance:

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

*B.4.k.4.9 Batch/lot number*

User Guidance:

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

*B.4.k.4.10 Dosage text*

User Guidance:

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

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

User Guidance:

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

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

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

**B.4.k.6 Pharmaceutical Dose form**

User Guidance:

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

*B.4.k.6.1 Pharmaceutical dose form*

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

**B.4.k.7 Route of administration**

User Guidance:

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

*B.4.k.7.1 Route of administration*

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

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

User Guidance:

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

943 should be used.

944  
945 *B.4.k.8.1 Parent Route of administration*

946 *B.4.k.8.2 Route of administration TermID and TermID operation date*

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948 **B.4.k.9 Gestation period at time of exposure**

949 User Guidance:

950  
951 The gestational age at the time of the earliest exposure should be used. Gestation period at time of exposure should be  
952 expressed by providing both a number and designation of units of days, weeks, months or trimester. See the companion  
953 document for format specifications.

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955 **B.4.k.10 Indication for use in the case (repeat as necessary)**

956 User Guidance:

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

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961 *B.4.k.10.1 Indication as reported by the primary source*

962 *B.4.k.10.2 Indication in MedDRA terminology (LLT code)*

963  
964 **B.4.k.11 Action(s) taken with drug**

965 - *Drug withdrawn*

966 - *Dose reduced*

967 - *Dose increased*

968 - *Dose not changed*

969 - *Unknown*

970 - *Not applicable*

971  
972 User Guidance:

973  
974 These data, taken together with the outcome of the reaction (B.2.i.6), provide the information concerning dechallenge.  
975 “*Not applicable*” should be used in circumstances such as when the patient has died or the treatment had been  
976 completed prior to reaction/event.

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979 **B.4.k.12 Drug-reaction(s)/event(s) matrix (repeat B.4.k.12.1 through B.4.k.12.4 as necessary)**

980 *B.4.k.12.1 Reaction(s)/event(s) assessed*

981 User Guidance:

982  
983 Generally the reaction(s)/event(s) assessed are ordered from the most important or the most serious to the least  
984 important. MedDRA LLT code should be used.

985  
986 *B.4.k.12.2 Relatedness of drug to reaction(s)/event(s) (repeat B.4.k.12.2.1 through B.4.k.12.2.3 as  
987 necessary)*

988 User Guidance:

989  
990 This section provides the means to transmit the degree of suspected relatedness of each drug to the reaction(s)/event(s).  
991 The repeating items could also be used to provide the assessment of relatedness by different sources or methods of  
992 assessment. For the purpose of reporting, there is an implied suspicion of causality for spontaneous reports. It is  
993 recognized that information concerning the relatedness, especially for spontaneous reports, is often subjective and might  
994 not be available.

995 • The following example illustrates the extensive functionality contained in this section.

996 • Assume a patient being treated with two medications: Drug A and Drug B.

997 • Assume the patient has had three adverse events: Event 1, Event 2, and Event 3

998 • The reporter provided assessment of causality for events 1 and 2 for both Drug A and Drug B, but not for either drug  
999 concerning event 3. The reporter’s assessment of causality is based on overall impression, which the sender codes as  
1000 “global introspection”.

1001 • The sender applies two methods of causality assessment, one with an algorithm (coded algorithm) and the other a

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

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

• The appropriate item with the information is B.4.k.12.2 (and its 3 subfields 1-3). In this example, k is replaced by Drug A and Drug B respectively. Please note the subfields 1-3 are repeatable. Thus:

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

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

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

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

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

*B.4.k.12.2.3 Result*

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

User Guidance:

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

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

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

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

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

*- yes/no/unknown*

User Guidance:

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

**B.4.k.13 Additional information on drug**

User Guidance:

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

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

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

User Guidance:

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

**B.5.2 Reporter's comments**

User Guidance:

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

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

User Guidance:

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

**B.5.4 Sender's comments**

User Guidance:

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

**3. GLOSSARY**

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

**Receiver:** The intended recipient of the transmission.

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

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

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1089 **ATTACHMENT 1**

1090

1091 **Definition of Interval List**

1092 Minutes

1093 Hours

1094 Days

1095 Weeks

1096 Months

1097 Years

1098 Cyclical

1099 As necessary

1100 Total

1101 **ATTACHMENT 2**

1102

1103 **Examples of how to populate fields relevant to identifying cases and their reports**

1104 The figure provides an example of how one would populate the fields relevant to identifying cases and their reports.

1105 Patient XX suffers three separate adverse events (AE1, AE2, AE3) spaced over a time period.

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1107 **Example of a simple single report from a company to a regulator**

1108 Hospital X reports AE1 to Company K who then in turn sends ICSR1 to Regulator. Population of relevant fields for  
1109 this case is illustrated in the first row of the table. Company K populates A.1.0.1 with Company K's (case) safety  
1110 report unique identifier "JP-K-001".

1111 Company K populates A.1.10.2 with "JP-K-001" because company K is the initial sender of the report. Because  
1112 there has not been a previous E2B/M2 electronic report, the identifiers in A.1.0.1 and A.1.10.2 are the same.

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1114 **Example of company to company to company to regulator transmission**

1115 Hospital X reports AE1 to Company B who then in turn sends ICSR2 to Company C.

1116 Population of relevant fields for this case is illustrated in the second row of the table. Company B populates A.1.0.1  
1117 with Company B's (case) safety report unique identifier "JP-B-001".

1118 Company B populates A.1.10.2 with "JP-B-001" because company B considers itself the initial sender of the report  
1119 because it is unaware that Company K also sent an ICSR for this case.

1120 Company C sends ICSR3 to Company D. The third row of the table indicates how Company C populates the relevant  
1121 fields. Company C populates A.1.0.1 with "JP-C-001".

1122 Company C populates A.1.10.2 with "JP-B-001", leaving the field unchanged from the way Company B  
1123 populated it. In addition, Company C populates A.1.11.1 (Source of the case identifier) with the name of company B,  
1124 "B". A.1.11.2 is populated with Case Identifier in the Previous Transmission by Company B "JP-B-001".

1125 Company D sends ICSR4 to Regulator. The fourth row of the table indicates how Company D populates the relevant  
1126 fields. Company D populates A.1.0.1 with "JP-D-001". Company D retains in fields A.1.10.2, A.1.11.1, and  
1127 A.1.11.2 the information populated by Company C, and Company D adds to the retained information in repeatable  
1128 field A.1.11.1 "C" to represent that Company C is another source of the case identifier, and Company D adds in field  
1129 A.1.11.2 "JPC-001" to represent Company C's case identifier from the previous transmission.

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1131 **Example of a simple single report with follow-up from a company to a regulator**

1132 Hospital X reports AE1 to Company E who then in turn sends ICSR5 to Regulator. Population of relevant fields for  
1133 this case is illustrated in the fifth row of the table. Company E populates A.1.0.1 with Company E's (case) safety  
1134 report unique identifier "JP-E-001". Company E populates A.1.10.2 with "JP-E-001" because company E is the  
1135 initial sender of the report.

1136 Because to Company E's knowledge, there has not been a previous E2B/M2 electronic report, the identifiers in  
1137 A.1.0.1 and A.1.10.2 are the same.

1138 ICSR6 represents Hospital X's follow-up information about AE1 to Company E. Company E submits follow-up to  
1139 ICSR5 to the regulator. The relevant fields, A.1.0.1 and A.1.10.2, are populated the same as for ICSR5. ICSR6, a  
1140 follow-up report, is differentiated from ICSR5 by A.1.7, Date of Receipt of the Most Recent Information for this  
1141 Report.

1142

1143 **Example of Linking Two Separate Adverse Events Affecting the Same Patient**

1144 Patient XX later suffers a separate adverse event, AE2. Hospital X reports AE2 to Company K who then in turn  
1145 sends ICSR7 to Regulator. Population of relevant fields for this new case is illustrated in the seventh row of the  
1146 table. Company K populates A.1.0.1 with Company K's (case) safety report unique identifier "JP-K-002". Company  
1147 K assigns a new (case) safety report unique identifier "JP-K-002" because "JP-K-001", as described above, represent  
1148 a separate adverse event. Company K populates A.1.10.2 with "JP-K-002" because company K is the initial sender  
1149 of the report. Because there has not been a previous E2B/M2 electronic report, the identifiers in A.1.0.1 and A.1.10.2  
1150 are the same. The previous report from Company K, "JP-K-001", for patient XX should be represented in A.1.12,  
1151 Identification Number of the Report which is Linked to this Report.

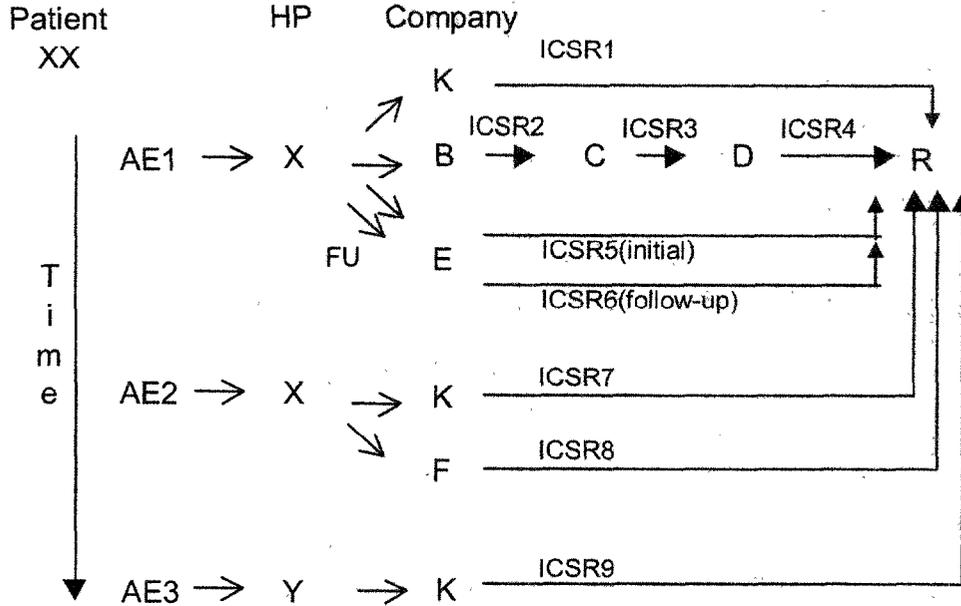
1152 In a contrasting example, Hospital X also reports AE2 to Company F. Company F had not previously received an AE  
1153 concerning Patient XX, and therefore there is no linked report and A.1.12 is not populated. As in the first example  
1154 concerning ICSR1, ICSR8 is a simple single report from a company to a regulator.

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1156 **Example of Linking Three Separate Adverse Events Affecting the Same Patient**

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1157 Patient XX later suffers a third, separate and distinct adverse event, AE3. Hospital Y reports AE3 to Company K  
 1158 who then in turn sends ICSR9 to Regulator. Population of relevant fields for this new case is illustrated in the ninth  
 1159 row of the table. Company K populates A.1.0.1 with Company K's (case) safety report unique identifier "JP-K-003".  
 1160 Company K assigns a new (case) safety report unique identifier "JP-K-003" because "JP-K-001" and "JP-K-002", as  
 1161 described above, represent separate, adverse events. Company K populates A.1.10.2 with "JPK-003" because  
 1162 company K is the initial sender of the report. The previous reports from Company K, "JP-K-001" and "JP-K-002",  
 1163 for patient XX should be represented in the repeatable field A.1.12, Identification Number of the Report which is  
 1164 Linked to this Report.



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

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