

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

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

Revision 2

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

For questions regarding this draft document contact (CDER) Roger Goetsch 301-770-9299, or (CBER) Lise Stevens-Hawkins 301-827-6085.

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  
12 May 2005**

Recommended for Adoption  
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*

1  
2 **E2B (R)**  
3 **REVISION OF THE ICH GUIDELINE ON**  
4 **CLINICAL SAFETY DATA MANAGEMENT:**  
5  
6 **DATA ELEMENTS FOR TRANSMISSION OF**  
7 **INDIVIDUAL CASE SAFETY REPORTS**

8  
9  
10 **TABLE OF CONTENTS**

11  
12  
13 **PREAMBLE**.....

14  
15 **1. INTRODUCTION**.....

16 1.1 Scope of this guideline .....

17 1.2 Background .....

18 1.3 Notes on format of this document .....

19 1.4 Definition of data elements .....

20 1.5 Minimum information .....

21 1.6 General principles.....

22  
23 **2. GUIDELINE: CONTENT OF THE DATA ELEMENTS** .....

24  
25 **A. Administrative and Identification Information**.....

26 A.1 Identification of the case safety report .....

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

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

29  
30 **B. Information on the Case** .....

31 B.1 Patient characteristics.....

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

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

34 B.4 Drug(s) information .....

35 B.5 Narrative case summary and further information .....

36  
37 **3. GLOSSARY**.....

38  
39 **ATTACHMENTS:**

40  
41 **1. Definition of Interval List.** .....

42 **2. Examples** .....

43 E2B(R)  
44 **REVISION OF THE ICH GUIDELINE ON**  
45 **CLINICAL SAFETY DATA MANAGEMENT :**  
46  
47 **DATA ELEMENTS FOR TRANSMISSION OF**  
48 **INDIVIDUAL CASE SAFETY REPORTS**  
49

50 **PREAMBLE**

51 This guideline provides additional information and clarification as well as some modifications to the ICH  
52 E2B guideline signed off on July 17, 1997 and modified as E2B(M) guideline in November 2000. It  
53 incorporates adjustments based on the experience gained after the implementation of the guideline in the  
54 three regions. It is recommended that the reader reviews this document as well as the companion  
55 document M2 ICSR Message Specification.  
56

57 **1. INTRODUCTION**  
58

59 **1.1 Scope of this guideline**

60 The objectives of the working group are to standardize the data elements for transmission of individual  
61 case safety reports by identifying and where necessary or advisable within a particular region, by defining  
62 the data elements for the transmission of all types of individual case safety reports, regardless of source  
63 and destination. This guideline includes data elements of case safety reports for both pre and post approval  
64 periods and covers both adverse drug reaction and adverse event reports. It is not intended that this format  
65 should be used for cases in the integrated safety summary of a marketing license application dossier. For  
66 adverse reactions encountered in clinical trials, this format should be used only for those subject to  
67 expedited reporting. The scope of this topic does not encompass the definition of database structures, the  
68 design of a paper report form, quality control/quality assurance aspects, or technical security issues.  
69

70 **1.2 Background**

71 Because of national and international agreements, rules, and regulations, individual case safety reports of  
72 adverse drug reactions and adverse events should be transmitted  
73 – from identified reporting sources to regulatory authorities and pharmaceutical companies;  
74 – between regulatory authorities;  
75 – between pharmaceutical companies and regulatory authorities;  
76 – within authorities or pharmaceutical companies;  
77 – from clinical investigators, via the sponsor, to ethics committees;  
78 – from authorities to the World Health Organization (WHO) Collaborating Center for International Drug  
79 Monitoring.  
80

81 The transmission of such individual case safety reports relies on paper-based formats (e.g., yellow cards,  
82 CIOMS I forms, MedWatch) or electronic media usually by on-line access, tape or file transfer.  
83 Considering the large number of potential participants in a world-wide exchange of information, there  
84 should be an electronic format capable of accommodating direct database to database transmission using  
85 message transfers. Successful electronic transmission of information relies on the definition of common  
86 data elements, provided in this document, and standard transmission procedures to be determined by the  
87 ICH Electronic Standards for the Transfer of Regulatory Information (ESTRI) Expert Working Group  
88 (M2).  
89

90 **1.3 Notes on format of this document**

91 Section 2 and its subsections designated A and B contain notes that are directed toward clarifying the  
92 nature of the data that should be provided. In addition, there are notes to assist in defining the format that  
93 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**

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 User Guidance:

175  
176 This identifier should remain constant in subsequent transmissions of the case by the same sender. Retransmitters  
177 should replace this value with their own unique identifier. The value should be a concatenation of "country code-  
178 company or regulator name-report number". Country code is the country of the primary source of the report (A.1.1).  
179 The company or regulator name is an internationally unique abbreviation or code for the sender's organisation. The  
180 report number is the organisation's international case number. Each component is separated from the other by a hyphen.  
181 For example, a report transmitted by a company to a regulatory authority concerning a case from France would populate  
182 A.1.0.1 with "FR-companyname-12345" where 12345 is a company's unique case report number.

183  
184 In the case of an organisational change, (e.g., a merger between companies or a name change), follow up reports should  
185 be identified in A.1.0.1 by the identifier of the newly named organisation. However, the worldwide unique case  
186 identifier number (A.1.10) used in previous transmissions of the case should remain the same (see below).  
187

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

189 User Guidance:

190  
191 See the companion document for appropriate format of the version. Only one version of MedDRA should be used to  
192 code all the relevant data elements. The version that should be used is always the last one released by the maintenance  
193 organisation.  
194

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

196 User Guidance:

197  
198 Generally, this item would be the only country provided. This country should be that of the reporter (see Glossary). Provisions  
199 have been made to include other countries for unusual cases concerning foreign travel and sources of manufactured material

200 (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  
201 was suspected to be an adverse drug reaction and was reported by a healthcare professional in country C. This field should be  
202 populated with the code of country C. See the companion document for appropriate country codes.

203

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

205 User Guidance:

206

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

210

### 211 **A.1.3 Date of this transmission**

212 User Guidance:

213

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

215

### 216 **A.1.4 Type of report**

217 - *Spontaneous report*

218 - *Report from study*

219 - *Other*

220 - *Not available to sender* (unknown)

221 User Guidance:

222

223 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  
224 intended to capture the type of report. If the case in the literature arises from spontaneous observations, "type of report" should be  
225 *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  
226 populated with the appropriate value (see the User Guidance for that field). If it is unclear from the literature report whether or not  
227 the case(s) cited are spontaneous observations or whether they arise from a study, then this item should be *Other*.

228

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

230

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

234

### 235 **A.1.5 Seriousness**

236 User Guidance:

237

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

239

#### 240 **A.1.5.1 Serious**

241 - *Yes/no*

242

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

244 - *Results in death*

245 - *Is life-threatening*

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

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

248 - *Is a congenital anomaly/birth defect*

249 - *Other medically important condition*

250 User Guidance:

251

252 The terms *life-threatening* and *other medically important condition* are defined in the ICH E2A and E2D guidelines.  
253 All the criteria apply to the case as a whole and should not be confused with the outcome(s) of individual  
254 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  
255 seriousness criteria of each reaction/event in accordance with the user guidance for that section.

256

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

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).

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

267 User Guidance:

268  
269 This date should be changed each time follow up information is received by the sender. However if the case is amended for any  
270 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  
271 populated with the value “amendment” indicating that the case was amended by the sender. (See the User Guidance for the field  
272 A.1.13)

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

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

282

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

284 *-yes/no*

285

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

287 User Guidance:

288

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

291

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

293 *- yes/no*

294

295 User Guidance:

296

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

301

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

303 User Guidance:

304

305 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  
306 whichever item is used should remain unchanged for any transmissions subsequent to the original transmission.

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

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

#### 313 **A.1.10.1 Regulatory authority’s case report number**

314

#### 315 **A.1.10.2 Other sender’s case report number**

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 User Guidance:

326  
327 This repeatable item should be used in conjunction with A.1.11.2 to provide all other case identifiers electronically  
328 transmitted, perhaps by multiple other senders. If the case has been received from another sender all other case  
329 identifiers included in A.1.11.1 and A.1.11.2 should be present. In addition the identifier of the previous sender  
330 (A.1.0.1) should be included here by the retransmitter. See examples in attachment 2  
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  
337 This section should be used to identify reports or cases that warrant being evaluated together. This includes, but is not limited to, a  
338 mother-child pair where both had reactions/events, siblings with common exposure, several reports involving the same patient  
339 (e.g., a report sent via paper without a valid E2B/M2 electronic report identifier), several similar reports from same reporter  
340 (cluster). The reason for the linkage between ICSRs should be provided in B.5.4. See examples in attachment 2.  
341

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

343 **- nullification**

344 **- amendment**

345 User Guidance:

346  
347 This item should be used to indicate that a previously transmitted report is either considered completely void (nullified), (for  
348 example when the whole case was found to be erroneous), or amended, (for example when after an internal review or according to  
349 an expert opinion some items have been modified such as adverse event terms, seriousness, seriousness criteria or causality  
350 assessment). It is important to use the same case report number previously submitted. The date originally reported in A.1.7  
351 should not be changed in an amended report.  
352

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

354  
355 **A.1.14 Was the case medically confirmed, if not initially from a health professional?**

356 **- yes/no**

357 User Guidance:

358  
359 This section should be completed if the primary source of information was a lawyer, consumer, or other non-health professional.  
360 It is important because of regional differences in regulations concerning lay reports.  
361

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

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

366 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  
367 published individual case, the reporter would be the investigator or first author, and details on publication  
368 and trial type should also be provided.  
369

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

371  
372 **A.2.1.1 Reporter identifier (name or initials)**

373 User Guidance:

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 **A.2.3.0 Study registration number**

410 User Guidance

411  
412 This field should be populated with the study registration number if applicable.  
413  
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, pharmacoconomics, intensive monitoring)*

430 User Guidance:  
431

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

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 Only one of the elements describing age should be used. The choice should be based upon the most precise information available.  
508  
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 When providing the age in decades, please note that, for example, the 7th decade refers to a person in his/her 60’s.  
523 See the companion document for format specifications.  
524

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

526 User Guidance:

527  
528 The gestation period at the time of exposure is captured in section B.4.k.9. See the companion document for format  
529 specifications.  
530

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

- 532 – *Neonate*
- 533 – *Infant*
- 534 – *Child*
- 535 – *Adolescent*
- 536 – *Adult*
- 537 – *Elderly*

538  
539 User Guidance:

540  
541 These terms are not defined in this document and are intended to be used as they were reported by the primary source.  
542 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.  
543

544 **B.1.3 Body weight (kg)**

545 User Guidance:

546  
547 Body weight at the time of the event/reaction.  
548

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

550  
551  
552  
553  
554  
555  
556  
557  
558  
559  
560  
561  
562  
563  
564  
  
565  
566  
567  
568  
569  
570  
571  
572  
573  
574  
575  
576  
577  
578  
579  
580  
581  
582  
583  
584  
585  
  
586  
587  
588  
589  
590  
591  
592  
593  
594  
595  
596  
597  
598  
599  
600  
601

**B.1.5 Sex**

User guidance:

See the companion document for format specifications.

**B.1.6 Last menstrual period date**

User guidance:

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

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

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

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

User Guidance:

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

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

User Guidance:

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

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

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

User Guidance:

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

602 **B.1.9 In case of death**

603 **B.1.9.1 Date of death**

604 User Guidance:

605  
606 An imprecise date can be used. See the companion document for format specifications.  
607

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

609 User Guidance:

610  
611 MedDRA LLT code should be used  
612

613 **B.1.9.3 Was autopsy done?**

614 *Yes/No/Unknown*

615  
616 **B.1.9.4 Autopsy-determined cause(s) of death (repeat as necessary)**

617 User Guidance:

618  
619 MedDRA LLT code should be used  
620

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

622 User Guidance:

623  
624 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  
625 section B.1. Guidance regarding confidentiality is provided in B.1.1, and should be considered before providing the parent  
626 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  
627 B.1.8 should be reviewed.  
628

629 **B.1.10.1 Parent identification**

630  
631 **B.1.10.2 Parent age information**

632 User Guidance:

633  
634 The date of birth should be used if the precise birthday is known; otherwise the age should be used.  
635

636 *B.1.10.2.1 Date of birth of parent*

637 User Guidance:

638  
639 If the full date of birth is not known, an incomplete date can be used. See the companion document for format  
640 specifications.

641 *B.1.10.2.2 Age of parent*

642  
643 **B.1.10.3 Last menstrual period date**

644 User Guidance:

645  
646 A full precision date should be used. See the companion document for format specifications. If a precise date is not  
647 available, the gestation period at time of exposure in B.4.k.9 should be completed.

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

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

650 **B.1.10.6 Sex of parent**

651  
652 **B.1.10.7 Relevant medical history and concurrent conditions of parent (not including**  
653 **reaction/event)**

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

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

655

656 User Guidance:

657  
658 MedDRA LLT code should be used in the main descriptive column for disease/surgical procedure/etc.  
659

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

662 **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)

663  
664 User Guidance:

665  
666 To standardise this information, the ICH M5 guideline should be used. Based on the medicinal product name as reported by the  
667 primary source, the most specific identifier, being either the Medicinal Product Identifier (MedID) or the Pharmaceutical Product  
668 Identifier (PhPID) should be provided. If a MedID and a PhPID for the reported medicinal product are not available, this field  
669 should be left blank. MedDRA LLT code should be used in the Indication and Reaction columns.  
670  
671

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

673 User Guidance:

674  
675 The designation of “i” in this section indicates that each item is repeatable and that it corresponds to the same “i” in all  
676 subsections. A separate block (i) should be used for each reaction/event term. For example, if two reactions are observed, the first  
677 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  
678 B.2.2.6.  
679

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

681 User Guidance:

682  
683 The original reporter's words and/or short phrases used to describe the reaction/event should be provided. These can  
684 also be included in the narrative B.5.1.  
685

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

687 User Guidance:

688  
689 Only the MedDRA Lowest Level Term (LLT) most closely corresponding to the reaction/event as reported by the  
690 primary source should be provided. In the exceptional circumstance when a MedDRA term cannot be found the sender  
691 should use good clinical judgment to complete this item with the best MedDRA approximation (see MedDRA™ TERM  
692 SELECTION:POINTS TO CONSIDER). MedDRA terms should be provided as code.  
693

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

695  
696 *B.2.i.2.1 Term highlighted by the reporter*

697  
698 **- yes, highlighted by the reporter**

699 User Guidance:

700  
701 A highlighted term is a reaction/event that the primary source indicated was a major concern or reason for reporting the  
702 case. If the information is not explicitly provided by the initial reporter the term should not be considered a highlighted  
703 term.  
704

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

706 **- Results in death**

707 **- Is life-threatening**

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

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

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

711 **- Other medically important condition**

712 User Guidance:

713  
714 The seriousness criteria of the reaction/event should be based on the definitions provided in the ICH E2A and E2D  
715 guidelines.  
716

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

718 User Guidance:

719 See the companion document for format specifications.  
720

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

722 User Guidance:

723  
724 This field should include the date corresponding to the date the reaction/event is assessed as resolved/recovered or  
725 resolved/recovered with sequelae (B.2.i.6).  
726

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

728 User Guidance:

729  
730 This section can usually be computed from start/end of reaction/event. Both dates and duration can be useful (e.g., for a  
731 reaction/event of short duration such as anaphylaxis or arrhythmia).  
732 Imprecise dates can be used. See the companion document for format specifications.  
733

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

- 735 – *recovered/resolved*
- 736 – *recovering/resolving*
- 737 – *not recovered/not resolved*
- 738 – *recovered/resolved with sequelae*
- 739 – *fatal*
- 740 – *unknown*

741  
742 User Guidance:

743  
744 In case of irreversible congenital anomalies the choice *not recovered/not resolved* should be used.  
745 “*Fatal*” should be used when death is possibly related to the reaction/event. Considering the difficulty of deciding  
746 between "reaction/event caused death" and "reaction/event contributed significantly to death", both were grouped in a  
747 single category. Where the death is unrelated, according to both the reporter and the sender, to the reaction/event, death  
748 should not be selected here, but should be reported only under section B.1.9.  
749

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

751 User Guidance:

752  
753 This section should capture the tests and procedures performed to diagnose or confirm the reaction/event, including those tests  
754 done to investigate (exclude) a non-drug cause (e.g., serologic tests for infectious hepatitis in suspected drug-induced hepatitis).  
755 Both positive and negative results should be reported. While structured information is preferable, provisions have been made to  
756 transmit the information as free text in B.3.2.  
757

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

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

759  
760 User Guidance:

761  
762 Imprecise dates can be used; units and normal ranges should be in free text unless covered by a controlled vocabulary. The  
763 column entitled "more information available" accepts only yes or no (see the companion document for the appropriate format).  
764 “Yes” means that more documentation is available upon request e.g., ECG strips, chest Xray. “No” means that no more  
765 documentation is available.  
766 MedDRA LLT codes should be used to code test names.



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

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

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

User Guidance:

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

### **B.4.k.1 Characterization of drug role**

#### ***Suspect / Concomitant / Interacting / Drug Not Administered / Blinded***

User Guidance:

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

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

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

"*Blinded*":

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

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

User Guidance:

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

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

User Guidance:

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

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

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

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

User Guidance:

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

826  
827  
828  
829  
830  
831  
832  
833  
834  
835  
836  
837  
838  
839  
840  
841  
842  
843  
844  
845  
846  
847  
848  
849  
850  
851  
852  
853  
854  
855  
856  
857  
858  
859  
860  
861  
862  
863  
864  
865  
866  
867  
868  
869  
870  
871  
872  
873  
874  
875  
876  
877  
878  
879  
880  
881  
882  
883

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

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:

884  
885 For ongoing drug administration after the onset of the reaction/event, this item should be blank and Action(s) taken with  
886 drug (B.4.k.11) should be used.  
887

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

889 User Guidance:

890  
891 This item should be used if exact dates of drug administration are not available at the time of the report, but there is  
892 information concerning the duration of drug administration. The information requested is the overall duration of drug  
893 administration and covers intermittent administration. See the companion document for the appropriate format.  
894

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

896 User Guidance:

897  
898 This information is particularly important for vaccines and biologics. The most specific information available should be  
899 provided. For expiration date and other related information, see additional information on drug (B.4.k.13).  
900

#### 901 *B.4.k.4.10 Dosage text*

902 User Guidance:

903  
904 This item should be used in cases where provision of structured dosage information is not possible.  
905

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

907 User Guidance:

908  
909 The cumulative dose provided should be the total dose administered until the first sign, symptom or reaction. Where  
910 possible, cumulative dose to the reaction/event should be structured as follows: (For standardised units see the user  
911 guidance of B.4.k.4.2.)  
912

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

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

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

917 User Guidance:

918  
919 Pharmaceutical dose form should be provided as TermID using the ICH M5 pharmaceutical dose form controlled  
920 vocabulary. If the pharmaceutical dose form TermID is not available, free text in B.4.k.6.1 should be used.  
921

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

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

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

926 User Guidance:

927  
928 Route of administration should be provided as TermID using the ICH M5 Route of administration controlled  
929 vocabulary. If the route of administration TermID is not available, free text in B.4.k.7.1 should be used. For a parent-  
930 child/fetus report, this indicates the route of administration of a drug given to the child/fetus. This is usually an indirect  
931 exposure, such as transmammary, but can include more usual routes of administration for other drugs given to the child.  
932 The parent's route of administration should be provided in B.4.k.8.  
933

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

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

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

938 User Guidance:

939  
940 This section should be used in a parent-child/fetus report and linked parent reports to indicate the route of  
941 administration to the parent. The parent route of administration should be provided as TermID using the ICH M5 Route  
942 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 *B.4.k.8.1 Parent Route of administration*

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

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.

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

956 User Guidance:

957  
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.

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)*

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 User Guidance:

972  
973 These data, taken together with the outcome of the reaction (B.2.i.6), provide the information concerning dechallenge.  
974 “*Not applicable*” should be used in circumstances such as when the patient has died or the treatment had been  
975 completed prior to reaction/event.  
976

978  
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

1002 bayesian analysis that provides a decimal probability (coded Bardi) but the sender does so only for the drug the sender  
 1003 manufactures (in this case Drug A).  
 1004 • From the above there are 4 sets of data for the reporter (2drugsX2eventsX1method of assessment) and 6 sets for the  
 1005 sender (1drugX3eventsX2methods of assessment) for a total 10 sets of data.  
 1006 • 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  
 1007 A and Drug B respectively. Please note the subfields 1-3 are repeatable. Thus:  
 1008

B.4.k.12.1	B.4.k.12.2.1	B.4.k.12.2.2	B.4.k.12.2.3
<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

1009 The order of the rows is not important since each one represents a complete set, however, the E2B message and M2  
 1010 specifications state that all assessments for Drug A (k=1) should appear before Drug B (k=2).  
 1011 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  
 1012 call for a standardised methodology.  
 1013  
 1014

1015 *B.4.k.12.2.1 Source of assessment* (e.g., initial reporter, investigator, regulatory agency, company)

1016 *B.4.k.12.2.2 Method of assessment* (e.g., global introspection, algorithm, Bayesian calculation).

1017 *B.4.k.12.2.3 Result*

1018  
 1019 *B.4.k.12.3 Time intervals between drug administration and start of reaction/event*

1020 User Guidance:

1021  
 1022 The major uses of intervals are to cover circumstances both in which the dates are known but the interval is very short  
 1023 (e.g., minutes, such as in anaphylaxis), and in which only imprecise dates are known but more information concerning  
 1024 the interval is known. Dates if available, should be transmitted in the appropriate items, rather than intervals. If the  
 1025 sender wants to provide time intervals as well then the first day of administration should be counted as “1”.

1026 The complexity of using intervals highlights the desirability of providing dates. See the companion document for format  
 1027 specifications.  
 1028

1029 *B.4.k.12.3.1 Time interval between beginning of drug administration and start of reaction/event*

1030  
 1031 *B.4.k.12.3.2 Time interval between last dose of drug and start of reaction/event*

1032  
 1033 *B.4.k.12.4 Did reaction recur on readministration?*

1034 **- yes/no/unknown**

1035 User Guidance:

1036  
 1037 Unknown indicates that a rechallenge was done but it is not known whether the reaction recurred. This field should not  
 1038 be completed if it is unknown whether a rechallenge was done.  
 1039

1040 **B.4.k.13 Additional information on drug**

1041 User Guidance:

1042  
 1043 This should be used to specify any additional information pertinent to the case that is not covered by above sections  
 1044 (e.g., beyond expiration date, batch and lot tested and found to be within specifications). This item can also be used to  
 1045 provide additional information concerning the indication for the drug. For cases where the suspect drug was taken by  
 1046 the father, this should be indicated in this field as e.g., Drug taken by the father.

- 1047  
1048 **B.5 Narrative case summary and further information** (repeat as necessary)  
1049  
1050 **B.5.1 Case narrative including clinical course, therapeutic measures, outcome and additional**  
1051 **relevant information**  
1052 User Guidance:  
1053  
1054 A focused, factual and clear description of the case should be given, including the words or short phrases used by the reporter.  
1055  
1056 **B.5.2 Reporter's comments**  
1057 User Guidance:  
1058  
1059 This item should be used to include the reporter's comments on the diagnosis, causality assessment or other issues considered  
1060 relevant.  
1061  
1062 **B.5.3 Sender's diagnosis/syndrome and/or reclassification of reaction/event** (repeat as necessary)  
1063 User Guidance:  
1064  
1065 This section provides the sender with an opportunity to combine signs and symptoms that were reported into a succinct diagnosis.  
1066 The reasoning would be included in section B.5.4. MedDRA LLT code should be used.  
1067  
1068 **B.5.4 Sender's comments**  
1069 User Guidance:  
1070  
1071 This section provides information concerning the sender's assessment of the case and can be used to describe disagreement with,  
1072 and/or alternatives to the diagnoses given by the initial reporter. In case of linkage of multiple ICSRs using A.1.12, the reason  
1073 should be provided in these comments.  
1074  
1075  
1076  
1077 **3. GLOSSARY**  
1078 **Parent-child/fetus report:** Report in which the administration of medicines to a parent results in a  
1079 suspected reaction/event in a child/fetus.  
1080  
1081 **Receiver:** The intended recipient of the transmission.  
1082  
1083 **Reporter:** Reporter is the primary source of the information, i.e., the person who initially reports the facts.  
1084 This should be distinguished from the sender of the message, though the reporter could also be a sender.  
1085  
1086 **Sender:** The person or entity creating the message for transmission. Although the reporter and sender can  
1087 be the same person, the function of the sender should not be confused with that of the reporter.

1088	
1089	<b>ATTACHMENT 1</b>
1090	
1091	<b>Definition of Interval List</b>
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.

1106  
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.

1113  
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.

1130  
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**

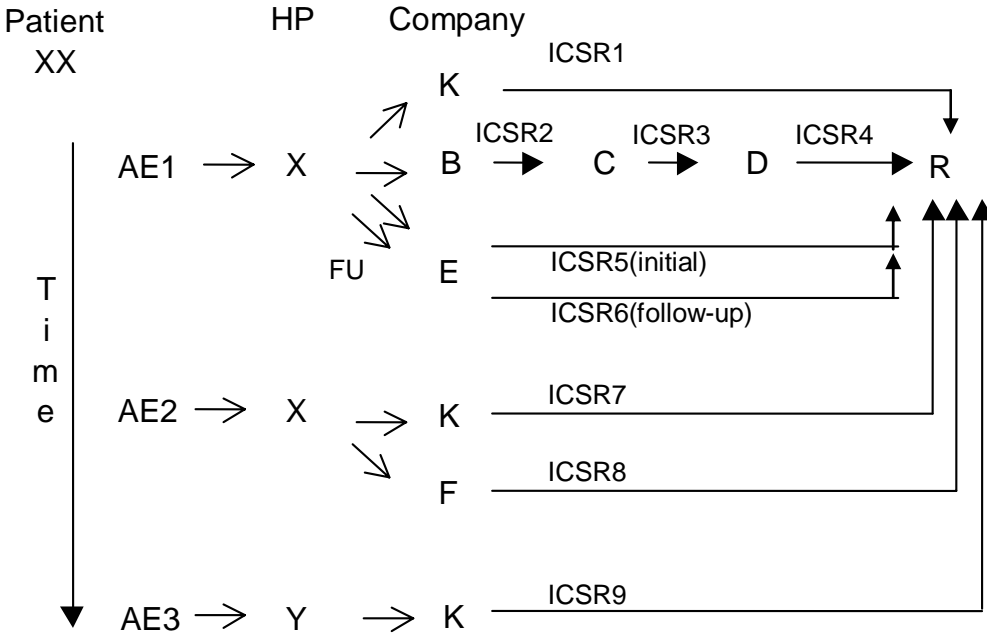
1144 Patient XX later suffers a separate adverse event, AE2. Hospital X reports AE2 to Company K who then in turn  
1145 sends ICSR7 to Regulator. Population of relevant fields for this new case is illustrated in the seventh row of the  
1146 table. Company K populates A.1.0.1 with Company K's (case) 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.

1155  
1156 **Example of Linking Three Separate Adverse Events Affecting the Same Patient**



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

1165

**Tabular representation of fields contents for the above examples**

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

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

1166  
1167  
1168